MIRROR THERAPY COMBINED WITH BILATERAL TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IMPROVES UPPER EXTREMITY MOTOR RECOVERY IN PEOPLE WITH STROKE: RANDOMIZED CONTROLLED TRIALS

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Mirror therapy combined with bilateral transcutaneous electrical nerve stimulation improves upper extremity motor recovery in people with stroke: randomized controlled trials

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CERTIFICATE OF ORIGINALITY

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it reproduces no material previously published or written, nor material that has been accepted for the award of any other degree or diploma, except where due acknowledgment has been made in the text.

(Signed)

PAN Hong (Student Name)

DEDICATION

I would like to dedicate this PhD thesis to my beloved grandma, Late Ms. Su-Qing Xiao.

ABSTRACT

Previous evidence showed that mirror therapy (MT) alone or bilateral transcutaneous electrical nerve stimulation (Bi-TENS) alone is an effective treatment for improving the paretic side recovery of upper extremity motor function in people with stroke. Given the advantage of MT can recruit additional neural pathway to elicit cortical activation, it is reasonable to hypothesize that MT combined with Bi-TENS can exert synergistic effects to improve the recovery of upper extremity motor function in people with stroke.

This thesis begins with study 1 of systematic review and meta-analysis. The positive findings suggest that MT combined with electrical stimulation may be effective in improving upper extremity motor function in people with stroke, especially for sub-acute stroke (SMD 0.56, 95% CI 0.1-1.01, $P = 0.02$, $I^2 = 63\%$).

In study 2, we investigated the abilities of paretic grip strength, Fugl-Meyer Assessment-Upper Extremity (FMA-UE), Wolf Motor Function Test (WMFT), and Upper Extremity Functional Index (UEFI) to predict the Stroke Impact Scale (SIS) in people with chronic stroke. We identified the UEFI as the most potent predictor for SIS in people with stroke ($\beta = 0.487$).

In study 3, we conducted one cross-sectional study to identify reliable and valid outcome measures for the main study. We then examined the psychometric properties of two potentials assessment tools. Both UEFI (intraclass correlation coefficient $[ICC]_{3,1} = 0.87$) and SATIS-Stroke ($ICC_{3,1} = 0.91$) were proved to be reliable and valid for the assessments of upper

extremity motor function in daily life living and the satisfaction with social participation, respectively, in people with stroke.

In study 4 and 5, our main study, we examined whether the combination of MT + Bi-TENS would be more effective than the combination of Sham-MT + Bi-TENS for improving upper extremity impairment, motor function, and health-related outcome measures in people with sub-acute and chronic stroke, respectively.

Our findings reveal that MT + Bi-TENS + conventional therapy group showed significantly greater improvement in FMA-UE scores at A_1 (Mean Difference (MD) = 5.7, $P < 0.001$) and A_2 (MD = 11.8, $P < 0.001$), maximum paretic grip strength at A_1 (MD = 2.9, $P < 0.001$) and A_2 (MD = 4.6, $P < 0.001$), and C-CIM scores at A_2 (MD = 3.9, $P = 0.002$) in 30 people with sub-acute stroke compared with Sham-MT + Bi-TENS + conventional therapy in people with sub-acute stroke.

MT + Bi-TENS group showed significantly improvement in FMA-UE (Mean Difference (MD) = 5.2, $P < 0.001$) and WMFT (MD = 3.7, $P = 0.001$) scores at A_2 compared with Sham-MT + Bi-TENS in 60 people with chronic stroke.

RESEARCH OUTPUT ARISING FROM THIS THESIS

PUBLICATIONS

Pan H, Ng SSM, Liu TW, Tsoh J, Wong TWL. (2023). Psychometric properties of the Chinese (Cantonese) version of the Upper Extremity Functional Index in people with chronic stroke. *Front Neurol*, 14: 989403.

Pan H, Liu TW, Ng SSM, Tsoh J, Wong TWL, Lam SSL, Li CSK, Chan CCC, Lai CYY. (2024). Testing the psychometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke. *Disabil Rehabil*, 46 (1): 159-169.

Pan H, Liu TW, Ng SSM, Chen PM, Chung RCK, Lam SSL, Li CSK, Chan CCC, Lai CWK, Ng WWL, Tang MWS, Hui E, Woo J. (2024). Effects of mirror therapy with electrical stimulation for upper limb recovery in people with stroke: a systematic review and meta-analysis. *Disabil Rehabil*, 46 (24):5660-5675.

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6 MWT	Six-minute Walk Test
ABC	Activity-specific balance confidence
ADLs	Activity daily livings
BBS	Berg Balance Scale
Bi-TENS	Bilateral transcutaneous electrical stimulation
CG	Control group
CI	Confidence interval
CIM	Community Integration Measure
C-CIM	Chinese version of community integration measure
C-SATIS-Stroke	Chinese version of SATIS-Stroke
C-UEFI	Chinese version of Upper Extremity Functional Index
CT	Conventional therapy
D	Day
ECR	Extensor carpi radialis
ECRB	Extensor carpi radialis brevis
ECRL	Extensor carpi radialis longus
ED	Extensor digitorum
EDC	Extensor digitorum communis
EG	Experimental group
iEMG	Integrated electromyography
EMG-BF-FES	Electromyographic biofeedback functional electrical stimulation
EMG-BF-NMES	Electromyographic biofeedback neuromuscular electrical stimulation

EPB	Extensor polliics brevis
ES	Electrical stimulation
ET	Electrode type
FDS	Flexor digitorum superficialis
FES	Functional electrical stimulation
FTSTS	Five Times Sit-to Stand
FMA	Fugl-Meyer Assessment
FMA-LE	Fugl-Meyer Assessment-Lower Extremity
FMA-UE	Fugl-Meyer Assessment-Upper Extremity
HRQOL	Health-related quality of life
IADL	Instrumental activities of daily living
ICC	Intraclass correlation coefficient
EMG-BFES	EMG-triggered biofeedback functional electrical stimulation
IPL	Inferior parietal lobule
IR	Interquartile range
MAL	Motor Activity Log
MC	Muscle contraction
MD	Mean difference
MEPs	Motor-evoked potentials
Min	Minute
MT	Mirror therapy
Mo	Month
MGAS	Mesh glove afferent stimulation
MS	Muscle stimulation
N	Number

NA	Not available
NMES	Neuromuscular electrical stimulation
PW	Pulse width
SAFFE	Survey of activities and fear of falling in the elderly
SD	Standard deviation
SICI	Short-interval intra-cortical inhibition
SIS	Stroke Impact Scale
SMD	Standard mean difference
ST	Sensory threshold
tDCS	Transcranial direct current stimulation
TENS	Transcutaneous electrical nerve stimulation
TMS	Transcranial magnetic stimulation
TUGT	Timed Up and Go Test
UEFI	Upper Extremity Functional Index
Uni-TENS	Unilateral transcutaneous electrical nerve stimulation
W	Week
WMFT	Wolf Motor Function Test
Yrs	Years

CHAPTER ONE

General Introduction

1.1 A summary of stroke

1.1.1 Definition of stroke and its prognosis

Stroke is defined as an acute episode of focal neurological deficits of the brain, retina, or the spinal cord with the lasting time more than one day (Hankey, 2017). It can also be diagnosed by imaging techniques if there is focal intracerebral, subarachnoid haemorrhage, or infarction with relevant clinical symptoms (Sacco et al., 2013).

According to the American Heart Association, strokes includes two major types: ischemic stroke, and haemorrhagic stroke (Fukaguchi et al., 2021). The ischaemic stroke, attributed to the embolism or thrombosis, comprise the major type of stroke, accounting for 80% to 85% of stroke types (Seiffge et al., 2019). The haemorrhagic stroke is due to bleeding into the brain with multifactorial factors, e.g., hypertensive disease and vascular malformation, accounting for almost 15% of stroke types (Albuquerque, 2013).

For the prognosis of all stroke, the case mortality rates are about 15% at 1 month to almost 50% at 5 years (Hankey, 2017). For the haemorrhagic stroke, the case mortality rates are about 55% to 70% from 1 year to 5 years (Hankey, 2017). For the long-term prognosis, the survival rates had been demonstrated no significant difference in haemorrhagic stroke and ischemic stroke (Poon et al., 2014).

1.1.2 The incidence of stroke

Stroke is the top leading cause of death and disability globally and almost 13 million stroke incidents, 7 million stroke-related deaths, and 143 million stroke-related disability-adjusted life

years were estimated globally in 2019 (Prust et al., 2024). Moreover, almost 25% of global population will undergo a stroke in their lifetime in the future (Feigin et al., 2018), and the risk rate has increased by almost 10% over past three decades (Prust et al., 2024).

In USA, to the year of 2030, an additional almost 3.5 million people will suffer the new stroke with the projected about 21% increase in the epidemiology (Virani et al., 2021). In China, the pooled data of cross-sectional study showed that the prevalence rate of haemorrhagic stroke was about average 250/100,000 person-years (Wang et al., 2017). In Hong Kong, according to the stroke research and prevention group research, about 55,000 old adults had stroke incidence in 2006, increased to more than 60,000 in 2010, and stroke cases is projected to increase to almost 164,000 by the 2036 (Department of Health HKSAR, 2022).

1.1.3 The costs of stroke

Stroke is associated with high economic burden because of the costs related to treatment and care (Giebel, 2020). In USA, stroke related direct (e.g., hospitalization, rehabilitation, or drugs), and indirect (e.g., wages of missed work days) costs reached to almost total US $ 60 billion on the end of the year of 2019 and it is projected to get to almost US $ 140 billion by the year of 2030, which represents an almost 200 and 70 percentage increase in the direct and indirect costs, respectively (Beese et al., 2024).

In China, the data demonstrated that the total costs were almost 58000 CNY, with 27000 CNY direct medical costs, and 31000 CNY indirect costs for each people with stroke for each year (Lv et al., 2023; Meng et al., 2022). In Hong Kong, the total direct costs of stroke were spent almost HK$ 1400 million in 2006 and it is projected to increase to approximately HK$ 4000

million per year with the direct costs for the people aged 65 and above by the year of 2036 (Department of Health HKSAR, 2022). For the cost of rehabilitation training services, it was predicted with about HK$150 million and it is projected to increase to around HK$270 million for people with stroke aged 65 and above in Hong Kong (Department of Health HKSAR, 2022).

1.2 The upper extremity impairments in stroke survivors

Upper extremity motor impairment following stroke is often disabling and persistent (Pollock et al., 2014). Nearly 85% people with stroke survivors suffer from the upper extremity motor impairment (Klamroth-Marganska et al., 2014; Woodbury et al., 2013) and even four years after a stroke, approximately 50% of survivors still have problems with upper extremity motor function (Pollock et al., 2014). Four major type of motor impairment after stroke are summarized as follow: muscle weakness, sensory deficits, dexterity, spasticity.

1.2.1 Muscle weakness

The definition of muscle weakness is the reduced ability to produce normal levels of muscle tension or strength even with maximal conscious voluntary effort on the paretic hand (Arene& Hidler, 2009), which is regarded as a very common physical impairment after stroke (Kwong et al., 2017). Hunnicutt & Gregory (2017) showed that the strength of paretic knee extensor strength, knee flexor strength, and plantarflexor strength were an average of 64%, 65%, and 65% of the nonparetic side strength in 375 people with stroke, respectively. Andrews & Bohannon (2000) demonstrated that after stroke, the muscle strength of the paretic side, ranged from approximately 60% to 90% of the strength of the non-paretic side. Andrews & Bohannon

(2000) also demonstrated that muscle weekness in elbow flexion was more severe than in elbow extension on both paretic and non-paretic sides in 48 people with stroke.

After stroke, the possible reason for muscle weakness is the loss of motor units (Chokroverty et al., 1976). The loss of motor units would induce the neurophysiological properties alteration, which would affect the muscle recruitment, the order of recruitment, discharge rate, and discharge pattern (Shin et al., 2018) after stroke. Hu et al. (2012) demonstrated that after stroke, a total of 181 motor units were extracted from the paretic side during 10 contraction trials in two people with stroke, compared to 209 motor units from the non-paretic side, which indicated a lower motor unit recruitment rate on the paretic side. Suresh et al. (2011) showed that both two people with stroke exhibited significantly lower motor unit recruitment rate on the paretic side compared to the non-paretic side (1.2 vs. 2.1, $P < 0.001$; 1.5 vs. 6.6, $P < 0.001$, respectively). These findings suggest that organizational changes in motor units, specifically reduced recruitment rate, may contribute to muscle weakness in people with stroke.

1.2.2 Sensory deficits

Sensory deficits are defined as abnormalities in the perception of pain, touch, temperature, or proprioception (Carey & Matyas, 2011). After stroke, the prevalence of sensory impairment can reach nearly 85%, encompassing various sensory deficits such as light touch (up to 90%) (Doyle et al., 2010), temperature sensation (almost 85%) (Hunter & Crome, 2002), pain perception (about 65%) (Hunter, 2002), proprioception (up to 25%) (Tyson et al., 2008), and vibration sense (about 45%) (Acerra et al., 2005). These impairments can significantly hinder the ability to explore the surrounding environment and perform daily living tasks in people with stroke (Carey & Matyas, 2011).

After stroke, sensory deficits may be caused by specific lesions of the brain following stroke that affect sensory processing. Baier et al. (2014) demonstrated that posterior insular cortex may play an important role for endocing temperture perception in the brain. The results indicated that sensory stimulation induced significantly higher activation in the contralesional posterior insular cortex (-3.47 ± 0.35 vs. -1.46 ± 0.26, $P < 0.01$) compared to the ipsilesional posterior insular cortex in 24 stroke survivors. Other study showed that people with stroke with impairments in sense of touch showed significant involvement in spscific brain regions, e.g., anterior, posterior insular cortex, and white matter extending to the prefrontal cortex, compared to healthy people without impairments in sense of touch (Preusser et al., 2015).

1.2.3 Spasticity

The definition of spasticity is a motor disorder with the feature of velocity-dependent increase in muscle tone (Rivelis et al., 2024). After stroke, the impaired upper motor neurons can disrupt corticospinal communication, leading to the disinhibition of spinal reflexes (Kuo & Hu, 2018). After stroke, during passive muscle stretching, sensory input from the muscle spindles can be transmitted to the spinal cord (Kuo & Hu, 2018). Loss of supra-spinal inhibitory control can result in excessive muscle activation, leading to increased spasticity in people with stroke (Nardone & Schieppati, 2005).

Opheim et al. (2014) demonstrated that upper extremity spasticity, including elbow flexors, elbow extensors, writs flexors, and wrist extensors, was observed in nearly 25% of people with stroke by day 3 and this increased to around 46% one year following the stroke.Takahashi et al. (2022) demonstrated that people with stroke who exhibited triceps surae muscle spasticity

(Modified Ashworth Scale > 1) had significantly higher H-reflexes (mean score: 1.1 vs. 0.9, P = 0.03) compared to those with stroke who did not have spasticity. Spasticity showed significant correlations with motor function after stroke. Takahashi et al. (2022) demonstrated a significant positive correlation between D1 inhibition (resulting from presynaptic Ia inhibition of the afferent fibers mediating the H-reflex) and FMA-UE (r = 0.69, P = 0.013), which indicated that lower spasticity showed higher FMA-UE scores after stroke.

1.2.4 Dexterity

The dexterity is defined as the ability to precisely, quickly, adequately, and rationally to use the extremities and body to perform and solve motor tasks in daily life living (Canning et al., 2000). After stroke, the reduced dexterity accompanied by muscle weakness is considered a major disability of extremities (Canning et al., 2000; Fellows et al., 1994). The paretic upper extremity dexterity impairments, e.g., grasping, holding, manipulating objects deficits, remain up to 75% of people with stroke after 6 months post-stroke (Alon et al., 2007). The dexterity of the paretic hand, as measured by the Box and Block Test, can independently predict nearly 10% of the variance in the daily use of the paretic upper extremity in daily living activities, as assessed by the Motor Activity Log in people with stroke after one year post-stroke (Rand & Eng 2015).

After stroke, abnormal muscle activation characteristics may be the possible reason for dexterity impairment (Canning et al., 2000). Canning et al. (2000) demonstrated that people with stroke who exhibited lower dexterity performance was characterized by excessive biceps muscle activation (22.03 ± 15.54 vs. 8.44 ± 7.59, P = 0.002) and similar triceps muscle activation (6.56 ± 4.30 vs. 2.17 ± 1.31, P = 0.2) compared to those with higher dexterity

performance. Moreover, people with stroke who exhibited low dexterity showed significantly less coherence between net IEMG (combined biceps/triceps IEMG signal) and the motion of elbow flexion and extension (0.35 ± 0.28 vs. 0.61 ± 0.27, $P = 0.002$) compared to those with high dexterity performance (Canning et al., 2000). Parry et al. (2019) demonstrated that the overall duration of grasps of box was greater when using the paretic side arm compared with the non-paretic side arm in people with stroke (0.85 vs. 0.49, $P = 0.002$). Hence, these findings suggest that abnormal spatial and temporal muscle activation can impaire dexterity of upper extremity associated with low function of grapsing in people with stroke.

1.3 Phases of recovery of upper extremity motor function in stroke survivors

The recovery of upper extremity motor function in people with stroke can be divided into 3 phases, that is, the acute, sub-acute, and chronic (Wieloch & Nikolich, 2006). The acute stroke phase is the initial period following a stroke, lasting from a few hours to a few days (Mariana et al., 2023). During the critical period of the acute stroke phase, interventions of reperfusion or neuroprotection can minimize brain tissue damage and restore blood flow to the brain (Onose et al., 2022). Jørgensen et al. (1995) showed that the best neurological recovery was reached in 80% of people with stroke during the acute stroke phase (95% confidence interval: 4.0–5.0). Hence, people in the acute stroke phase are encouraged to begin rehabiliation strategies once their vital signs, e.g., blood pressure, have stabilized (Buma et al., 2013).

The sub-acute stroke phase is the period following the acute stroke phase, lasting from a few days to 6 months (Larsen et al., 2017). During the sub-acute stroke phase, the brain demonstrates a high level of plasticity, enabling it to adapt and change through functional cortical reorganization and the generation of new neurons (neurogenesis) (Aderinto et al.,

2023). Jørgensen et al. (1995) showed that the best neurological recovery was reached in 95% of people with sub-acute stroke within 11 weeks (95% confidence interval: 10.1–11.9). Moreover, the best functional recovery was reached in almost 80% of people with sub-acute stroke within 6 weeks (95% confidence interval: 5.3–6.7) and about 95% of people with sub-acute stroke within 13 weeks (95% confidence interval: 11.6–13.4) (Jørgensen et al., 1995). Hence, stroke rehabilitation interventions should take advantage of this increased neural plasticity to promote recovery of motor function during the sub-acute stroke phase.

The chronic stroke phase is the period following the sub-acute stroke phase, lasting from 6 months to several years, and represents the long-term phase of stroke recovery (Vive et al., 2022). Almost 45% of people with chronic stroke showed functional dependence at 1 year and about 41% showed functional dependence at 5 years post-stroke (Sennfält et al., 2019). Ferrarello et al. (2011) demonstrated that therapy-based rehabilitation had a favorable pooled effect size of 0.29 on all included outcome measures for recovery of motor function in people with stroke lasting more than 6 months (95% confidence interval: 0.14–0.45, $P < 0.001$) compared with no intervention. Hence, the recovery of motor function is still possible during the chronic stroke phase by increasing neural plasticity and creating new pathways for motor skill learning (Su & Xu, 2020).

1.4 Application of electrical stimulation for motor function in stroke survivors

Electrical stimulation has been widely used as a treatment to improve recovery of upper extremity motor function after stroke since 1980. Functional electrical stimulation is widely used to induce the muscle contraction due to muscle weakness (Hara et al., 2013) and TENS is

used as sensory electrical stimulation to improve performance of motor functions in people with stroke (van Dijk et al., 2002).

1.4.1 Functional electrical stimulation

Functional electrical stimulation is applied to targeted muscle groups to induce muscle contraction to generate functional movements (Eraifej et al., 2017) in order to improve recovery of motor function of paretic extremities in people with stroke. Pulses with an amplitude of 2 to 120 mA, a width of 100 to 350 μs, and a frequency of 20 to 40 Hz are commonly used for people with stroke to stimulate muscle contraction (Marquez-Chin & Popovic, 2020). Previous studies have shown that functional electrical stimulation can improve upper extremity motor function (Xie et al., 2024), upper extremity muscle strength (Naz et al., 2024) and reduce upper extremity spasticity (Ring & Rosenthal , 2005) in people with stroke.

1.4.2 Transcutaneous electrical nerve stimulation (TENS)

Traditionally, TENS is regarded as an effective non-invasive electrical stimulation for the primary treatment of pain (Wu et al., 2018). Two possible mechanisms for how TENS relieves pain have been proposed. First, Melzack & Wall (1965) proposed, based on gate control theory, that TENS can stimulate the large-diameter afferents, which can inhibit nociceptive responses to reduce the transmission of nociceptive information to the presynaptic input, thereby inhibiting pain. Second, Kalra et al. (2001) demonstrated that TENS applied to the extremities can decrease the activity of dorsal horn neurons to inhibit pain.

1.4.2.1 Different types of TENS

In clinical practice, three types of TENS are commonly used: conventional TENS, acupuncture-like TENS, and intense TENS. The details of the three types of TENS are summarized in Table 1.1 (modified from (Johnson, 2007)). Based on electrode placement, TENS can be categorized into unilateral and bilateral TENS. Unilateral TENS involves placing electrodes on the affected side of the limb, while bilateral TENS involves placing electrodes on both sides of the limb.

Table 1.1 Different types of TENS in clinical practice (modified from (Johnson, 2007)).

Parameters & Characteristics	Conventional TENS	Acupuncture-like TENS	Intense TENS
Frequency	High frequency with 50-100Hz	Low frequency with 2-4 Hz	High frequency up to 200 pps
Intensity	Low intensity with paraesthesia, but not painful	Higher intensity (tolerance threshold), longer pulse width (100-400 μs)	High intensity (tolerance threshold)
Targeted Fibers	Stimulate selectively large diameter	Stimulate selectively small diameter,	Stimulate small diameter
Clinical application	To induce a comfortable, non-painful paraesthesia to inhibit the activity in nociceptive transmission	To activate extrasegmental descending pain inhibitory pathways	To block nociceptive information transmission

1.4.2.2 TENS for recovery of upper extremity motor function in stroke survivors

The effects of TENS on recovery of upper extremity motor function in stroke survivors is summarized in Table 1.2. Three studies have applied TENS in sub-acute stroke survivors (Johansson et al., 2001; Klaiput & Kitisomprayoonkul, 2009; Tekeolu et al., 1998) while four studies have applied TENS in people with chronic stroke (Alwhaibi et al., 2021; Chen et al., 2022; Jung et al., 2017; Kim et al., 2013). The sample sizes of these studies ranged from 20 to 120. Five studies have investigated the effectiveness of TENS in people with stroke compared with Sham-TENS (Alwhaibi et al., 2021; Jung et al., 2017; Kim et al., 2013; Klaiput & Kitisomprayoonkul, 2009; Tekeolu et al., 1998). Only one study has investigated the effectiveness of bilateral TENS (Bi-TENS) in people with stroke compared with unilateral TENS (Uni-TENS) (Chen et al., 2022). Finally, one study investigated the effectiveness of high-intensity Uni-TENS in people with stroke compared with low-intensity Uni-TENS (Johansson et al., 2001).

Chen et al. (2022) showed that 20 sessions of 60-minute 100-Hz Bi-TENS over the median and radial nerve improved the FMA-UE scores by 14.8% while Sham-TENS only improved those scores by 5.4% in 60 stroke survivors. Kim et al. (2013) demonstrated that 20 sessions of 100-Hz TENS over the paretic side of the muscle belly of the triceps and wrist extensors combined with task-related training improved Box and Block Test scores by 21% while Sham-TENS combined with task-related training only improved those scores by 7.6% in 30 stroke survivors. Tekeolu et al. (1998) demonstrated that sensory-threshold TENS over the extensor muscles of the elbow improved quality of life, assessed by Barthel Index scores, by 90% while Sham-TENS only improved those scores by 35% in 60 stroke survivors.

In addition to the points summarized above, other meta-analyses have showed that the significant effectiveness of electrical stimulation in people with stroke (Yang et al., 2019). Yang et al. (2019) showed that electrical stimulation was superior to sham electrical stimulation in improving upper extremity motor function immediately, with an effect size of 0.67, by pooling data from 23 trials ($P < 0.001$), and at one-month follow-up, with an effect size of 0.66, by pooling data from 12 trials ($P < 0.001$).

Table 1.2 Summary of studies investigating effects of TENS in improving the recovery of upper extremity motor function in people with stroke

Study	Participants (TENS/ Control)	Post-stroke duration	Experimental group (EG)	Control group (CG)	Results
Chen et al., 2022	30/30/30	Chronic	Bi-TENS + Task-oriented training	Uni-TENS + Task-oriented training / Sham-TENS + Task-oriented training	FMA-UE: Bi-TENS ↑ > Uni-TENS ↑ > Sham-TENS ↑
Johansson et al., 2001	51/51	Sub-acute	Uni-TENS (High intensity with muscle contraction)	Uni-TENS (Low intensity without muscle contraction)	Rivermead Mobility Index: EG ↑ = CG ↑
Jung et al., 2017	23/23	Chronic	TENS + Task-related training	Sham-TENS + Task-related training	iEMG, Active Range of Motion, muscle strength, FMA-UE: EG ↑> CG↑

Kim et al., 2013	17/17	Chronic	TENS + Task-oriented training	Sham-TENS + Task-oriented training	FMA-UE, Manual Function Test, Box and Block Test: EG ↑> CG ↑ Modified Ashworth Scale: EG ↑, CG →
Klaiput & Kitisomprayoonkul 2009	10/10	Sub-acute	TENS	Sham-TENS	Lateral and tip pinch force: EG ↑> CG ↑ Action Research Arm Test: TENS →, Control →
Alwhaibi et al., 2021	20/20	Chronic	TENS + Task-specific training	Sham-TENS + Task-specific training	FMA-UE, Box and Block Test: EG ↑ = CG↑
Tekeoğlu et al., 1998	30/30	Sub-acute	TENS	Sham-TENS	Modified Ashworth Scale: EG ↓ > CG↓ Barthel Index: EG ↑ > CG ↑

Notes: ↑ indicates a significant improvement; ↓ indicates a significant decrease; → indicates no significant difference. TENS: Transcutaneous electrical nerve stimulation; EG: experimental group; CG: control group; Bi-TENS: bilateral transcutaneous electrical nerve stimulation; Uni-TENS: unilateral transcutaneous electrical nerve stimulation; FMA-UE: Fugl-Meyer Assessment-Upper Extremity; iEMG: integrated electromyography.

1.4.2.3 TENS for recovery of lower extremity motor function in people with stroke

The effects of TENS for recovery of lower extremity motor function in people with stroke is summarized in Table 1.3. All the included studies applied TENS in chronic stroke survivors (Cho et al., 2013; Jung et al., 2020; Kwong et al., 2018; Ng & Hui-Chan, 2007; Ng & Hui-Chan, 2009; Park et al., 2014). The sample sizes ranged from 34 to 109. Total five studies (Cho et al., 2013; Jung et al., 2020; Ng & Hui-Chan, 2007; Ng & Hui-Chan, 2009; Park et al., 2014) investigated the effectiveness of TENS in people with stroke compared with Sham-TENS. Only one study (Kwong et al., 2018) investigated the effects of Bi-TENS in people with stroke compared with Uni-TENS.

Kwong et al. (2018) demonstrated that 20 sessions of 60-minute 100-Hz Bi-TENS over the popliteal fossa and neck of the fibula combined with task-oriented training improved the paretic ankle dorsiflexion strength by 26% while Uni-TENS combined with task-oriented training only improved the paretic ankle dorsiflexion strength by 17% in 80 stroke survivors. Ng & Hui-Chan (2007) demonstrated that 20 sessions of 60-minute 100-Hz TENS over four acupuncture points (Zusanli, Taichong, Yanglingquan, and Kunlun) of the paretic lower extremity combined with task-related training decreased spasticity, assessed by the Composite Spasticity Scale, by 10% while Sham-TENS combined with task-related training only decreased spasticity by 8.9% in 44 people with stroke. Ng & Hui-Chan (2009) also demonstrated that 20 sessions of 60-minute 100-Hz TENS over the above-mentioned four acupuncture points of the paretic lower extremity combined with exercises improved lower extremity mobility by 27% while Sham-TENS combined with exercises only improved lower extremity mobility by 11% in 54 people with stroke. Park et al. (2014) demonstrated that 30 sessions of 30-minute 100-Hz TENS over the lateral and medial quadriceps and gastrocnemius of the paretic lower extremity

combined with 30-minute exercises improved gait velocity by 15% while Sham-TENS combined with exercises only improved gait velocity by 5.4% in 34 people with stroke.

In addition to the points summarized above, other meta-analyses have showed the significant effectiveness of electrical stimulation for improving the recovery of lower extremity motor function in people with stroke (Kwong et al., 2018; Lin et al., 2018). Kwong et al. (2018) demonstrated that TENS was superior to Sham-TENS in improving walking capacity, assessed by the Timed Up and Go Test, with an effect size of 0.392 (95% confidence interval: 0.178–0.606, $P < 0.001$) by pooling data from 9 trials after stroke. Lin et al. (2018) demonstrated that TENS was superior to Sham-TENS in reducing spasticity of the lower extremity, assessed by the Modified Ashworth Scale, with an effect size of 0.71 (95% confidence interval: 0.30–1.11, $P < 0.001$) by pooling data from 3 trials after stroke.

Table 1.3 Summary of studies investigating effects of TENS in improving the recovery of lower extremity motor function in people with stroke

Study	Participants Experiment/ Control)	Post-stroke duration	Experimental group (EG)	Control group (CG)	Results
Cho et al., 2013	22/20	Chronic	TENS + Physical therapy	Sham-TENS +Physical therapy	Modified Ashworth Scale: EG ↓ > CG ↓ Balance ability: EG ↑> CG ↑
Jung et al., 2020	20/20	Chronic	TENS + Heel-raise-lower exercise	Sham-TENS + Heel-raise-lower exercise	Postural sway distance: EG > CG ↓ Muscle strength (Hip extensor): EG ↑> CG↑ Composite Spasticity Scale: EG ↓ > CG ↓
Kwong et al., 2018	40/40	Chronic	Bi-TENS + Task-oriented training	Uni-TENS + Task-oriented training	Paretic ankle dorsiflexion strength: EG ↑ > CG ↑

					Timed Up and Go Test: EG ↓ > CG ↓
Ng & Hui-Chan 2007	22/22	Chronic	TENS + Task related training	Sham-TENS + Task related training	Composite Spasticity Score: EG ↓ > CG ↓ Peak ankle dorsiflexion torque: EG ↑ > CG ↑ Increased in peak plantarflexion torque: EG ↑ > CG↑ Gait velocity: EG ↑ > CG↑
Ng & Hui-Chan 2009	27/25/28	Chronic	TENS + exercise	Sham-TENS + exercise/ TENS	Gait velocity and 6 minute walk test: TENS + exercise ↑ > Sham-TENS ↑ > TENS ↑ Timed Up and Go Test: TENS + exercise ↓ > Sham-TENS ↓ > TENS ↓

Park et al., 2014	17/17	Chronic	TENS + Physical therapy	Sham-TENS + Physical therapy	Modified Ashworth Scale and Timed Up and Go Test: EG ↓ > CG ↓ Gait velocity: EG ↑ > CG ↑

Notes: ↑ indicates a significant improvement; ↓ indicates a significant decrease; → indicates no significant difference; TENS: Transcutaneous electrical nerve stimulation; EG: experimental group; CG: control group; Bi-TENS: bilateral transcutaneous electrical nerve stimulation; Uni-TENS: unilateral transcutaneous electrical nerve stimulation.

1.4.3 Proposed mechanisms of TENS for recovery of motor functions

The therapeutic effectiveness of Uni-TENS for recovery of motor function after stroke may be mediated via both peripheral (Chen et al., 2005; Hui-Chan & Levin, 1993; Levin & Hui-Chan, 1992) and central (Celnik et al., 2007; Lai et al., 2016) levels.

1.4.3.1 Proposed mechanisms of Uni-TENS for recovery of motor function

1.4.3.1.1 Decreased hyperexcitability of alpha motor neurons

Upper motor neuron deficits of the central nervous system are often caused by lesions of the primary motor and premotor cortex or the descending pathways (Adams et al., 1990; Sach et al., 2004) and are characterized by weakness associated with spasticity and Babinski signs of spinal reflex hyperactivity (Adams et al., 1990; Colebatch & Gandevia1989).

TENS has been demonstrated to activate the A alpha–beta range (Levin & Hui-Chan, 1993) with a reduction of the amplitude of H-reflexes to decrease the hyperactive stretch reflex to disinhibit alpha motor neurons (Levin & Hui-Chan, 1992). Levin &Hui-Chan (1993) demonstrated that one session of 45-minute high-frequency (99 Hz, sensory threshold) TENS with peroneal nerve stimulation could induce latency of the H-reflex of the soleus muscle by 50% after 1-hour stimulation in 21 healthy young people. Levin &Hui-Chan (1992) further demonstrated that after 15 sessions of 1-hour, high-frequency (99 Hz), low-intensity TENS, 10 people with stroke showed reductions of the stretch reflex by 31.2% in spastic ankle plantarflexors.

1.4.3.1.2 Reduction of short-interval intra-cortical inhibition (SICI)

SICI is assessed by measuring the relative amplitude reduction of motor evoked potentials (MEPs) when a subthreshold conditioning stimulus is delivered by using transcranial magnetic stimulation (TMS) (Ni & Chen, 2008). Previous evidence has demonstrated that TENS can improve recovery of motor function by reducing SICI in people with stroke (Celnik et al., 2007). Celink et al. (2007) demonstrated that 1-Hz TENS with 120-minute stimulation applied to the paretic ulnar and median nerves significantly reduced MEP-assessed SICI of the first dorsal interosseus muscle in the ipsilesionally hemisphere (79.83 mV vs. 48.62 mV, $P < 0.05$) compared with Sham-TENS in 9 people with stroke.

1.4.3.1.3 Increased corticospinal excitability

The corticospinal motor pathway is regarded as the primary anatomical structure for voluntary motor control in humans (Weavil & Amann, 2018), mainly including the motor cortex and spinal motor neurons (Weidner et al., 2001). TENS can increase the corticospinal excitability in healthy people as assessed by the MEPs of TMS. Chipchase et al. (2011) demonstrated that 30-minute electrical stimulation (30 Hz with muscle contraction) over the biceps brachii significantly increased the amplitude of corticomotor activation assessed by the MEPs (biceps brachii) of TMS by an average of 110%, compared with pre-intervention, in 10 healthy young people. Khaslavskaia et al. (2002) demonstrated that 30-minute motor threshold electrical stimulation with peroneal nerve significantly increased the MEPs by 104% (tibialis anterior muscle) in 10 healthy young people compared with pre-intervention.

1.4.3.1.4 Increased corticomuscular coherence

Corticomuscular coherence is regarded as a significant indicator for the synchronized interactions between the neural activity in the motor cortex and associated muscular activity (Liu et al., 2019) and is used to quantify the coupling between the motor cortex and corresponding muscle group by using electroencephalogram and corresponding electromyogram signals simultaneously (Siemionow et al., 2010). Xu et al. (2023) demonstrated that 12 people with stroke had significantly lower beta and gamma corticomuscular coherence compared with 15 age-matched healthy older people. The results also demonstrated that beta (r = 0.629, P = 0.028) and gamma (r = 0.619, P = 0.031) corticomuscular coherence had significant positive correlations with the impairment of lower extremity in 12 people with stroke (Xu et al., 2023).

Previous studies have demonstrated that TENS can improve recovery of motor function by increasing corticomuscular coherence after stroke (Lai et al., 2016; Pan et al., 2018). Lai et al. (2016) demonstrated that one session of 40-minute electrical stimulation (100 Hz, without muscle contraction) applied to the median nerve of the paretic side could significantly increase the peak gamma band of corticomuscular coherence by 48.6% from pre- (0.10 ± 0.02) to post- (0.15 ± 0.07) assessment in 15 stroke survivors. Pan et al. (2018) demonstrated that 8 sessions of 40-minute sensory electrical stimulation (100 Hz, without contraction) applied to the median nerve of the paretic side resulted in significantly higher corticomuscular coherence at 4 weeks, compared with sham electrical stimulation of the control group, in 12 people with stroke (0.45 vs. 0.09, P = 0.004).

1.4.3.2 Proposed mechanisms of Bi-TENS for recovery of motor function

The mechanisms of Bi-TENS are multifactorial and include all the effects initiated by Uni-TENS applied over paretic extremities as mentioned in Section 1.4.3.1. Compared with Uni-TENS, additional sensory input from the non-paretic extremity induced by Bi-TENS can be delivered to the contralesionally hemisphere. However, neurophysiological research on the mechanisms of Bi-TENS is lacking. Proposed mechanisms of Bi-TENS in stroke survivors on the basis of bilateral exercises include (1) recruitment of neural networks of the contralesionally hemisphere via uncrossed corticospinal projection; (2) rebalancing of interhemispheric inhibition via the transcallosal pathway.

1.4.3.2.1 Recruiting the neural networks of the contralesionally hemisphere via uncrossed corticospinal projection

The contralesionally hemisphere plays an important role in recovery of paretic upper extremity motor function in stroke survivors (Lotze et al., 2006) as about 10% of the corticospinal tract axons of the contralesionally hemisphere remain uncrossed and are projected to muscles of the ipsilaterally extremities (Lacroix et al., 2004; Lemon, 2008). Previous evidence (Chen et al., 2024; Schaechter & Perdue, 2008) has shown that bilateral upper extremity exercise training can induce significant activation of the contralesionally hemisphere. Schaechter et al. (2008) demonstrated that 10 people with stroke performing a bilateral hand motor task with gripping exercises exhibited significantly higher activation in the contralesionally primary motor cortex and primary somatosensory cortex compared with 10 age-matched healthy older people. Chen et al. (2024) demonstrated that bilateral coordinated fine motor skills training could induce significantly greater cortical activation of the contralesionally hemisphere by almost 88%, compared with unilateral paretic-side coordinated fine motor skills training, in 24 people with

stroke. Hence, Bi-TENS can improve the recovery of upper extremity motor function in stroke survivors by recruiting the neural networks of the contralesionally hemisphere.

1.4.3.2.2 Rebalancing interhemispheric inhibition via transcallosal pathway

Interhemispheric inhibition is regarded as a normal neurophysiological mechanism in which one primary motor cortex inhibits the opposite homologous primary motor cortex (Kirton et al., 2010). Interhemispheric inhibition is measured by applying a conditioning stimulus to one primary motor cortex, reducing the size of the MEPs assessed by TMS produced by the test stimulation of the opposite primary motor cortex (Daskalakis et al., 2002). After stroke, interhemispheric inhibition shows an imbalance in which the contralesionally primary motor cortex hemisphere with high excitability inhibits the ipsilesionally primary motor cortex hemisphere (Dodd et al., 2017). Murase et al. (2004) demonstrated that stroke survivors had abnormal interhemispheric inhibition from the contralesionally to the ipsilesionally primary motor cortex compared with age-matched healthy older people, assessed by the MEP amplitude of TMS (0.7 ± 0.2 vs. 1.3 ± 0.4, $P = 0.001$). The results also demonstrated that higher imbalance of interhemispheric inhibition from the contralesionally to the ipsilesionally primary motor cortex hemisphere was significantly associated with slower performance in the finger tapping task in 9 stroke survivors ($r = 0.9$, $P < 0.001$) (Murase et al., 2004).

Previous studies showed that bilateral electrical stimulation can reduce the inhibition of the ipsilesionally hemisphere by the contralesionally hemisphere to improve the recovery of paretic extremity motor function in stroke survivors (Cunningham et al., 2019). Cunningham et al. (2019) demonstrated that after bilateral, contralaterally controlled functional electrical stimulation with three 15-minute sets of bilateral hand exercises, the interhemispheric

inhibition of the ipsilesionally hemisphere was significantly reduced, compared with the same number of sessions of unilateral cyclic neuromuscular electrical stimulation with bilateral hand exercises, in 15 people with stroke (-9.5 ± -3.7% vs. + 4.5 ± 5.2%, $P = 0.049$). The results also showed that the upper extremity motor impairment assessed by the FMA-UE showed a significant correlation with the increase in ipsilesionally output following bilateral, contralaterally controlled functional electrical stimulation ($r = 0.78$, $P = 0.04$) in 15 people with stroke (Cunningham et al., 2019). Hence, compared with unilateral electrical stimulation, bilateral electrical stimulation can improve recovery of motor function by rebalancing interhemispheric inhibition from the contralesionally to the ipsilesionally primary motor cortex in people with stroke.

1.5 Mirror therapy for recovery of motor function in stroke survivors

During mirror therapy (MT), the movement of the non-paretic extremity creates the illusion of the movement of the paretic extremity (Deconinck et al., 2015; Ramachandran et al., 1995). MT has been used as sensory input to assist the recovery of upper and/or lower extremity motor function in stroke survivors based on visual stimulation (Feys et al., 2004).

1.5.1 MT for recovery of upper extremity motor function in stroke survivors

The effects of MT for enhancing recovery of upper extremity motor function in stroke survivors is summarized in Table 1.4. Total 13 studies (Antoniotti et al., 2019; Bai et al., 2019; Chan, 2018; Ding et al., 2019; Dohle et al., 2009; Invernizzi et al., 2013; Lee et al., 2012; Madhoun et al., 2020; Radajewska et al., 2013; Samuelkamaleshkumar et al., 2014; Thieme et al., 2013; Yavuzer et al., 2008; Zhuang et al., 2021) applied MT to improve the recovery of upper extremity motor function in sub-acute stroke survivors. Total 9 studies (Cho, 2015; Choi et al.,

2019; Colomer et al., 2016; Ehrensberger et al., 2019; Geller et al., 2022; Hsu et al., 2022; Michielsen et al., 2011; Park et al., 2015; Wu et al., 2013) applied MT to improve the recovery of upper extremity motor function in chronic stroke survivors. The sample sizes ranged from 15 to 60. Total 4 studies (Antoniotti et al., 2019; Cho et al., 2015; Choi et al., 2019; Park et al., 2015) investigated the effectiveness of MT combined with conventional therapy for improving the recovery of upper extremity motor function in people with stroke compared with Sham-MT combined with conventional therapy. Total 19 studies (Bai et al., 2019; Chan, 2018; Cho, 2015; Colomer et al., 2016; Ding et al., 2019; Dohle et al., 2009; Ehrensberger et al., 2019; Geller et al., 2022; Hsu et al., 2022; Invernizzi et al., 2013; Lee et al., 2012; Madhoun et al., 2020; Michielsen et al., 2011; Radajewska et al., 2013; Samuelkamaleshkumar et al., 2014; Thieme et al., 2013; Wu et al., 2013; Yavuzer et al., 2008; Zhuang et al., 2021) investigated the effectiveness of MT combined with conventional therapy for improving the recovery of upper extremity motor function in people with stroke compared with conventional therapy alone.

Bai et al. (2019) demonstrated that 20 sessions of 30-minute MT combined with 1-hour conventional therapy improved upper extremity impairment by 21%, while 1-hour conventional therapy alone only improved upper extremity impairment by 12.1%, in 34 stroke survivors. Cho & Cha (2015) demonstrated that 18 sessions of 20-minute MT combined with 20-minute transcranial direct current stimulation improved paretic upper extremity grip strength by 27%, while total sessions of 20-minute Sham-MT combined with 20-minute transcranial direct current stimulation only improved paretic upper extremity grip strength by 20%, in 27 stroke survivors. Chan & Au-Yeung(2018) demonstrated that 8 sessions of 30-minute MT combined with 30-minute conventional therapy improved upper extremity motor ability by 78%, while 30-minute conventional therapy alone only improved upper extremity

motor ability by 55%, in 41 stroke survivors. Madhoun et al. (2020) demonstrated that 25 sessions of 25-minute MT combined with 25-minute occupational therapy improved the quality of daily life by 32.5% while 25-minute occupational therapy alone only improved quality of daily life by 22% in 35 people with stroke.

In addition to the points summarized above, other systematic reviews and meta-analyses have demonstrated the effectiveness of MT for improving the recovery of upper extremity motor function in stroke survivors (Yang et al., 2018). Yang et al. (2018) demonstrated that MT combined with conventional therapy was superior to conventional therapy alone in improving the paretic upper extremity motor function in daily living activities with an effect size of 1.00 ($P < 0.05$), by pooling data from 11 trials in people with stroke.

Table 1.4 Summary of studies investigating effects of MT in improving the recovery of upper extremity motor function in people with stroke

Study	Participants (TENS/ Control)	Post-stroke duration	Experimental group (EG)	Control group (CG)	Results
Antoniotti et al., 2019	20/20	Sub-acute	MT + conventional therapy	Sham-MT + conventional therapy	FMA-UE:EG ↑ = CG ↑ Action Research Arm Test: EG ↑ = CG ↑ Functional Independence Measure: EG ↑ = CG ↑
Bai et al., 2019	23/11	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑ > CG ↑
Cho & Cha 2015	14/13	Chronic	MT + tDCS	Sham-MT + tDCS	FMA-UE: EG ↑ > CG ↑ Grip strength: EG ↑ > CG↑ Box and Block Test: EG ↑ > CG↑
Choi et al., 2019	24/12	Chronic	MT + conventional therapy	Sham-MT + conventional therapy	Manual Function Test: EG ↑ > CG↑

Colomer et al., 2016	17/17	Chronic	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑ > CG↑
Chan & Au-Yeung 2018	20/20	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑ = CG↑ Wolf Motor Function Test: EG ↑ = CG ↑
Ding et al., 2019	10/10	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑ >CG ↑ Functional Independence Measure: EG ↑ > CG ↑
Dohle et al., 2009	18/18	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG↑ > CG ↑ Action Research Arm Test: EG ↑ > CG ↑ Functional Independence Measure: EG ↑ > CG ↑
Ehrensberger et al., 2019	18/17	Chronic	MT + strength training	Strength training	Muscle strength: EG ↑ > CG↑ Modified Ashworth Scale: EG ↓ > CG ↓
Geller et al., 2022	17/8	Chronic	MT + occupational therapy	Occupational therapy	FMA-UE: EG↑= CG↑ Grip strength: EG↑= CG↑

					Stroke Impact Scale: EG ↑= CG ↑
Hsu et al.,2022	25/17	Chronic	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑= CG↑ Modified Ashworth Scale: EG ↓= CG↓ Box and Block Test: EG ↑= CG↑ Motor Activity Log: EG↑= CG↑
Invernizzi et al., 2013	13/13	Sub-acute	MT + conventional therapy	Conventional therapy	Motricity index: EG↑> CG↑ Action Research Arm Test: EG↑> CG↑ Functional Independence Measure: EG↑> CG↑
Lee et al., 2012	14/14	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑> CG↑ Brunnstrom motor recovery stages: EG ↑> CG↑
Madhoun et al., 2020	18/17	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑> CG↑ Barthel Index: EG↑> CG↑
Michielsen et al., 2011	20/20	Chronic	MT + conventional therapy	Conventional therapy	FMA-UE: EG↑= CG↑ Grip strength: EG ↑= CG↑ Tardieu Scale: EG ↓= CG↓

Park et al., 2015	15/15	Chronic	MT + conventional therapy	Sham-MT + conventional therapy	FMA-UE: EG ↑> CG↑ Box and Block Test: EG ↑> CG↑ Functional Independence Measure: EG ↑> CG↑
Radajewska et al., 2013	30/30	Sub-acute	MT + conventional therapy	Conventional therapy	Frenchay arm test: EG ↑> CG↑
Samuelkamaleshkumar et al., 2014	10/10	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑> CG↑ Modified Ashworth Scale: EG ↓> CG↓ Brunnstrom Arm and Hand: EG ↓> CG↓
Thieme et al.,2013	39/21	Sub-acute	MT + conventional therapy	Conventional therapy	Modified Ashworth Scale (finger): EG ↓> CG↓
Wu et al., 2013	16/17	Chronic	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑> CG↑
Yavuzer et al., 2008	20/20	Sub-acute	MT + conventional therapy	Conventional therapy	Modified Ashworth Scale: EG ↓> CG↓
Zhuang et al., 2021	18/18	Sub-acute	MT + conventional therapy	Conventional therapy	FMA-UE: EG ↑> CG↑ Box and Block Test: EG ↑> CG↑ Functional Independence Measure: EG ↑> CG↑

Notes: ↑ indicates a significant improvement; ↓ indicates a significant decrease; EG: experimental group; CG: control group; MT: Mirror therapy; FMA-UE: Fugl-Meyer Assessment-Upper Extremity; tDCS: transcranial direct current stimulation.

1.5.2 MT for recovery of lower extremity motor function in stroke survivors

The effects of MT in people with stroke is summarized in Table 1.5. Total two studies (Ji & Kim, 2015; Mohan et al., 2013) applied MT in sub-acute stroke survivors. Total two studies (Arya et al., 2019; Simpson et al., 2019) applied MT in chronic stroke survivors. The sample sizes ranged from 22 to 36. Total three studies (Arya et al., 2019; Mohan et al., 2013; Simpson et al., 2019) investigated the effectiveness of MT combined with conventional therapy in people with stroke compared with conventional therapy, while only one study (Ji & Kim, 2015) investigated the effectiveness of MT combined with conventional therapy in people with stroke compared with Sham-MT combined with conventional therapy.

Arya et al. (2019) demonstrated that 30 sessions of 60-minute MT combined with 30-minute conventional therapy improved lower extremity motor function by 20% while 1-hour dosage of matched conventional therapy alone only improved lower extremity motor function by 1.6% in 36 stroke survivors. Simpson et al. (2019) demonstrated that 12 sessions of MT combined with strength training improved lower extremity mobility by 3% while strength training alone improved lower extremity mobility by 2.4% in 31 stroke survivors. Simpson et al. (2019) also demonstrated that 12 sessions of MT combined with strength training improved walk ability by 11% while strength training alone only improved walk ability by 3.8% in 31 people with stroke.

In addition to the points summarized above, other meta-analyses have demonstrated the effectiveness of MT in stroke survivors (Broderick et al., 2018; Li et al., 2018; Louie et al., 2019). Broderick et al. (2018) demonstrated that MT was superior to Sham-MT in improving lower extremity motor impairment with an effect size of 0.59 ($P < 0.001$), by pooling data from

5 trials in stroke survivors. Li et al. (2018) demonstrated that MT was superior to Sham-MT in improving balance of the lower extremity with an effect size of 0.66 ($P < 0.001$), by pooling data from 6 trials in stroke survivors. Louie et al. (2019) demonstrated that MT was superior to Sham-MT in improving lower extremity gait speed, with an effect size of 1.04 ($P < 0.001$), by pooling data from 6 trials in people with stroke.

Table 1.5 Summary of studies investigating effects of MT in improving the recovery of lower extremity motor function in people with stroke

Study	Participants (TENS/ Control)	Post-stroke duration	Experimental group (EG)	Control group (CG)	Results
Arya et al., 2019	19/17	Chronic	MT + conventional therapy	Conventional therapy	FMA-LE: EG↑ > CG↑ Rivermead visual gait assessment: EG ↓ > CG↓
Ji & Kim 2015	17/17	Sub-acute	MT + conventional therapy	Sham-MT + conventional therapy	Gait ability (Single stance, step length, and stride length):EG ↓ > CG ↓
Mohan et al., 2013	11/11	Sub-acute	MT + conventional therapy	conventional therapy	FMA-LE: EG↑ > CG ↑ Brunnel Balance Assessment: EG ↑ > CG ↑ Functional Ambulation Categories: EG ↓ > CG↓
Simpson et al., 2019	16/15	Chronic	MT + strength training	Strength training	Modified Ashworth Scale: EG ↓ > CG ↓ Timed Up and Go Test: EG↓ > CG ↓ 10 Minute Walk Test: EG ↑ > CG ↑

Notes: ↑ indicates a significant improvement; ↓ indicates a significant decrease; MT:Mirror therapy; FMA-LE: Fugl-Meyer Assessment-Lower Extremity.

1.5.3 The proposed mechanisms of MT for recovery of motor function in people with stroke

The therapeutic effects of MT in people with stroke may be mediated via (1) the activation of the mirror neuron system, (2) increased functional connectivity between the ipsilesionally and contralesionally primary motor cortex, and (3) increased attention processing.

1.5.3.1 The activation of mirror neuron system

The mirror neuron system, visuomotor neurons, is associated with action observation and execution in humans (Iacoboni & Mazziotta, 2007). Compared with age-matched healthy older people, people with stroke show a lower fractional amplitude of low-frequency fluctuation values in the mirror neuron system of the ipsilesionally hemisphere, e.g., inferior frontal gyrus and superior temporal gyrus (Zhang et al., 2024).

Results of previous study demonstrated that MT could induce the activation of a partly mirror neuron system in stroke survivors. For example, Zhang et al. (2024) demonstrated that after 20 sessions of MT training combined with conventional therapy of the upper extremity, significant activation was observed in the ipsilesionally inferior frontal gyrus and contralesionally superior temporal gyrus of the mirror neuron system compared with pre-intervention, and the activation of the contralesionally superior temporal gyrus of the mirror neuron system had a significant correlation ($r = 0.44$, $P = 0.008$) with FMA-UE scores in 16 people with stroke.

Zhang et al. (2024) further demonstrated that MT combined with conventional therapy could induce significantly greater activations in ipsilesionally superior temporal gyrus and ipsilesionally superior frontal gyrus of mirror neuron system when compared with

conventional therapy alone. The activation of those two regions had significantly correlations with FMA-UE score in MT group in 16 people with stroke ($r = 0.49$, $P = 0.003$ and $r = 0.34$, $P = 0.04$, respectively).

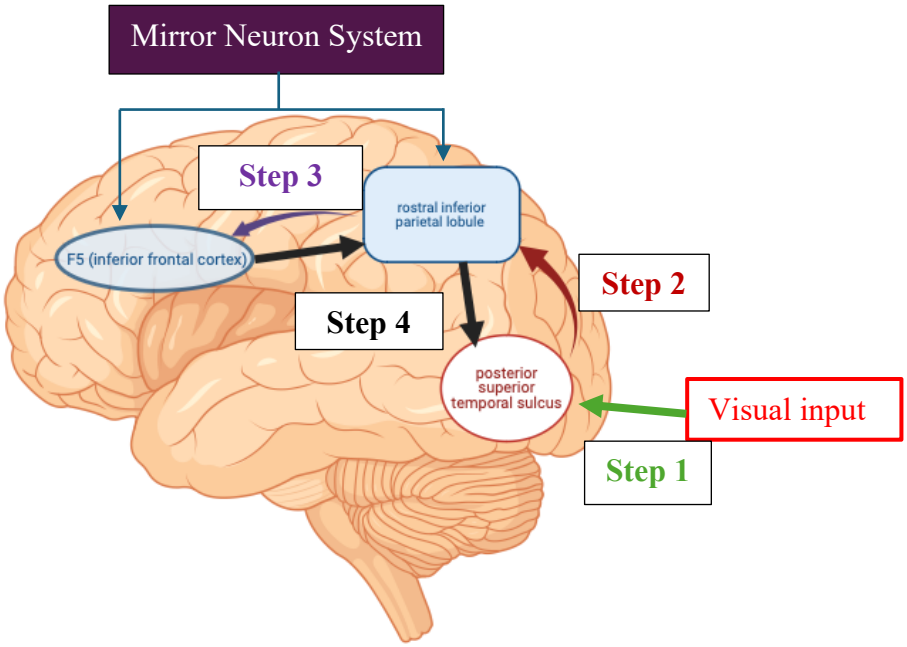


Figure 1.1 The Mirror Neuron System

This figure was created by using the online BioRender (modified from (Iacoboni & Dapretto, 2006)). Three parts form the core circuit for sensorimotor integration involving in the Mirror Neuron System.

Step 1: the green arrow indicates the visual input to the superior temporal gyrus

Step 2: the red arrow indicates the information flow from the superior temporal gyrus to parietal mirror neuron system, concerning about motoric description of action.

Step 3: The purple arrow indicates information flow from parietal mirror neuron system to frontal mirror neuron system, concerning about the goal of action.

Step 4: The black arrows indicate the copies of motor imitative commands sent back to superior temporal gyrus to match the visual input of observed action.

1.5.3.2 The increased functional connectivity between ipsilesionally and contralesionally primary motor cortex

The “functional connectivity” refers to the temporal correlation between the fluctuations in the cerebral blood flow of the two primary motor cortexes (Palmer et al., 2019). Zhang et al. (2024) showed that a decreased interhemispheric functional connectivity between the ipsilesionally and contralesionally primary motor cortex in people with stroke compared with age-matched healthy older people. The decreased interhemispheric functional connectivity between two primary motor cortexes had a significant positive correlation ($r = 0.62$, $P < 0.05$) with the impairment of upper extremity in stroke survivors (Grefkes et al., 2008).

MT can improve recovery of upper extremity motor function in people with stroke by increasing activation of both the ipsilesionally and contralesionally primary motor cortex and re-establishing the functional connectivity between them. Zhang et al. (2024) demonstrated that compared with pre-intervention, total 3-week (20 sessions) of MT combined with conventional therapy of upper extremity significantly induced the activations of two primary motor cortexes in 16 people with stroke, respectively. The results also showed that the interhemispheric functional connectivity between the ipsilesionally and contralesionally primary motor cortex was significantly increased after 3 weeks (20 sessions) of MT combined with conventional therapy in the MT group, compared with conventional therapy alone, in 35 stroke survivors (Zhang et al., 2024). Increase in interhemispheric functional connectivity between two primary motor cortexes from pre- to post-intervention in the MT group had a significant positive correlation with FMA-UE improvement ($r = 0.7$, $P = 0.005$) in 16 people with stroke (Zhang et al., 2024).

1.5.3.3 The increased attention processing

MT could improve the recovery of motor function in people with stroke by increasing the attention processing on the paretic side (Zhang et al., 2024). During MT training, people with stroke are required to look into a mirror and imagine the non-paretic-side movements are paretic-side movements while they perform bilateral exercises (Deconinck et al., 2015). Previous studies (Michielsen et al., 2011; Zhang et al., 2024) have demonstrated that MT can induce significant activation in the ipsilesionally and contralesionally sides of the precuneus, which are associated with attention network interaction (Luo et al., 2020) in people with stroke.

Uisng fMRI, Michielsen et al. (2011) demonstrated that compared with pre-intervention, the ipsilesionally and contralesionally precuneus could be significantly activated during mirror condition while practising bimanual hands movements in 20 people with stroke. Zhang et al. (2024) demonstrated that both the ipsilesionally and contralesionally precuneus could be significantly activated after 3 weeks (20 sessions) of MT combined with conventional therapy of the upper extremity in the MT group, compared with conventional therapy, in 35 people with stroke. The results also showed that the fractional amplitude of low-frequency fluctuation changes of the ipsilesionally and contralesionally precuneus from pre- to post-intervention had a significant correlation with FMA-UE scores ($r = 0.439$, $P = 0.008$) in the mirror condition in 35 people with stroke (Zhang et al., 2024).

1.6 Summary

The incidence of stroke is on the rise globally. Motor impairment in the upper extremity is the most common aftereffect in stroke survivors, often requiring prolonged rehabilitation and resulting in significant economic burdens for individuals, their families, and society as a whole.

Bi-TENS is effective in improving the recovery of upper extremity motor function in people with both sub-acute and chronic stroke. MT is effective in improving the recovery of upper extremity motor function in people with both sub-acute and chronic stroke. Hence, these findings indicate that MT combined with Bi-TENS can recruitment additional corticospinal pathways for improving the recovery of upper extremity motor function in stroke survivors.

CHAPTER TWO

Overview of Dissertation

2.1 Research Gaps Identified

Bilateral transcutaneous electrical nerve stimulation (Bi-TENS) could improve the recovery of upper extremity motor function stroke survivors (Chen et al., 2022). Mirror Therapy (MT) is an effective adjunct treatment to improve the recovery of upper extremity motor function in people with stroke by creating reflective visual illusions of the paretic extremity with the reflection of the non-paretic extremity (Gygax et al., 2011). Hence, MT combined with Bi-TENS could possibly exert synergistic effects to improve the recovery of upper extremity motor function in stroke survivors. Based on the review of previous literature related to the recovery of upper extremity motor function in people with stroke in Chapter 1, several research gaps were identified.

First, previous evidence showed the significant effects of TENS alone or MT alone in improving the recovery of upper extremity motor function in stroke survivors. However, no consistent evidence to show the synergistic effect of MT combined with electrical stimulation in improving the recovery of upper extremity motor function in people with stroke. An updated review is necessary to investigate the synergistic effects of MT combined with ES for improving the recovery of upper extremity motor function in people with stroke. **Second,** compared with objective outcome measures, the subjective outcome measures can provide insights into patients' views of their physical symptoms, functional abilities, and overall psychosocial wellbeing related to their health status. While previous study (Lieshout et al., 2020) investigated role of objective outcome measures in stroke recovery and health-related quality of life, the role of subjective self-perceived upper extremity motor function and its relationship with health-related quality of life have not been explored in stroke survivors. **Third,** although the Upper Extremity Functional Index has been validated in people with

musculoskeletal disorders (Chesworth et al., 2014) and SATIS-Stroke has been translated into Portuguese (Pereira et al., 2019) and English (Bouffioulx, et al., 2008) in people with stroke, these two outcome measures have not been culturally adapted in Chinese people with stroke. **Fourth**, Bi-TENS alone or MT alone is known to effectively improve the recovery of upper extremity motor function in stroke survivors, respectively. However, no study has investigated whether MT combined with Bi-TENS could exert synergistic effect in improving the recovery of upper extremity motor function in stroke survivors. Moreover, it is not known whether this synergistic effect would consequently improve self-perceived upper extremity performance in activities of daily living and social participation in this population.

2.2 Null Hypothesis

The null hypothesis (main study) was that the effects of MT + Bi-TENS was not superior to Sham-MT + Bi-TENS in terms of improving upper extremity impairment, motor function, and level of social participation in people with sub-acute and chronic stroke.

2.3 Aims & Targets

The target of this thesis was to explore compared with Sham-MT + Bi-TENS, MT + Bi-TENS would have earlier and greater significant effects in improving upper extremity impairment and other outcome measures in stroke survivors. Four phases were divided according to this research project. **Phase 1** targeted to bridge the knowledge gap that TENS and MT might exert the synergistic effects for improving the recovery of upper extremity motor function in stroke survivors. **Phase 2** targeted to bridge the knowledge gap that whether a treatment targeting on the self-perceived upper extremity motor function in activity of daily living could improve

health-related quality of life in stroke survivors. **Phase 3** aimed at reviewing reliable and valid outcome measures used in the main study. **Phase 4** targeted at addressing the research question that whether the combined MT and Bi-TENS is superior to combined Sham-MT and Bi-TENS in improving the recovery of upper extremity motor function, self-perceived upper extremity performance in activities of daily living and level of social participation in stroke survivors.

Several objectives of this thesis were presented as follows:

1. To review the effects of MT combined with electrical stimulation simultaneously on the recovery of upper extremity motor function in people with stroke;

2. To determine whether self-perceived upper extremity motor function independently predicts health-related quality of life in stroke survivors;

3. To culturally adapt the contents of the English version of Upper Extremity Functional Index into the Chinese (Cantonese) language; report an initial validation of Chinese version of Upper Extremity Functional Index, including the test-retest reliability, and content validity in Chinese stroke survivors;

4. To culturally adapt the contents of the English version of SATIS-Stroke into the Chinese (Cantonese) language; report an initial validation of Chinese version of SATIS-Stroke, including the test-retest reliability, and content validity in Chinese people with stroke;

5. To investigate whether MT + Bi-TENS is superior to Sham-MT + Bi-TENS for improving the upper extremity impairment and level of social participation in both sub-acute and chronic stroke.

2.4 Outline of Dissertation

This thesis mainly targeted to present the results of the effects of MT + Bi-TENS compared with Sham-MT + Bi-TENS in stroke survivors. All the studies are presented in this thesis from Chapter 3 to Chapter 7.

2.4.1 Chapter 3: The synergistic effects of mirror therapy combined with electrical stimulation for recovery of upper extremity motor function in people with stroke: a systematic review and meta-analysis

Total 18 clinical randomised controlled trials investigated the synergistic effects of mirror therapy combined with electrical stimulation in terms of improving the recovery of upper extremity motor function in stroke survivors.

2.4.2 Chapter 4: The predictive roles of self-perceived upper extremity motor function, objective upper extremity motor impairment, and objective function ability in health-related quality of life in chronic stroke survivors

This chapter investigates the roles of self-perceived upper extremity motor function, objective upper extremity motor impairment, and objective function ability as predictors of the level of health-related quality of life in chronic stroke survivors.

2.4.3 Chapter 5: Psychometric properties of outcome measures used in the main studies

Chapter 5 described the studies of investigating the psychometric property of Chinese version of Upper Extremity Functional Index and Chinese version of SATIS-Stroke in Chinese people with stroke, which were used as outcome measures in our main randomised controlled trials.

2.4.4 Chapter 6: Randomized controlled trial of upper extremity training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper extremity motor functions in sub-acute stroke survivors

This chapter reported the results of the main study including 30 sub-acute stroke survivors with post-stroke duration from 3 weeks to 6 months. It was a randomized, sham-controlled clinical trial which compared the effects of MT + Bi-TENS with those of Sham-MT + Bi-TENS in terms of upper extremity impairment and other outcome measures in sub-acute stroke survivors.

2.4.5 Chapter 7: Randomized controlled trial of upper extremity training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper extremity motor functions in chronic stroke survivors

This chapter reported the results of the main study including 60 chronic stroke survivors with post-stroke duration from more than 6 months to 10 years. It was a randomized, sham-

controlled clinical trial which compared the effects of MT + Bi-TENS with those of Sham-MT + Bi-TENS in terms of upper extremity impairment and other outcome measures in chronic stroke survivors.

2.4.6 Chapter 8: Summary, limitation and conclusion of the thesis

The final chapter presented the summary, limitation, clinical implication, and final conclusion.

CHAPTER THREE

The Synergistic Effects of Mirror Therapy Combined with Electrical Stimulation for Upper Extremity Motor Function in People with Stroke: A Systematic Review and Meta-Analysis

The study in this chapter has been published in a peer-reviewed journal.

Pan Hong, Liu TW, Ng SSM, Chen PM, Chung RCK, Lam SSL, Li CSK, Chan CCC, Lai CWK, Ng WWL, Tang MWS, Hui E, Woo J (2024). Effects of mirror therapy with electrical stimulation for upper limb recovery in people with stroke: a systematic review and meta-analysis. *Disability and Rehabilitation*, 46(24):5660-5675. (Appendix 3.1)

Parts of content have been presented at one international conference.

Pan Hong, Liu TW, Ng SSM. Synergistic effects of mirror therapy combined with electrical stimulation simultaneously for motor recovery of upper limb in people with stroke: a meta-analysis, *12th Pan-Pacific Conference on Rehabilitation*, 27-28 November, 2021, Hong Kong, China. (Appendix 3.2)

3.1 Abstract

Previous studies have determined the benefits of Mirror Therapy (MT) and Electrical Stimulation (ES) alone for improving the recovery of upper extremity motor function in stroke survivors. However, as stated in Chapter 2, one of the research gaps is that there was inconsistent evidence about the MT combined with ES for improving the recovery of upper extremity motor function in stroke survivors. Due to the emergence of new studies, in this chapter, we reported an updated review to summarize clinical trials investigating the synergistic effects of MT combined with ES simultaneously for improving the recovery of upper extremity motor function in stroke survivors based on the International Classification of Functioning, Disability, and Health framework.

This systematic review begun with a search in English (Medline, Embase, Cochrane Library, Web of Science, Scopus, Physiotherapy Evidence Database) and Chinese (China Biology Medicine, China National Knowledge Infrastructure, Wan Fang, VIP) databases. The ClinicalTrials.gov and Chinese Clinical Trial Registry were also searched for forward citation check of unpublished trials. Total 18 randomized controlled trials met the inclusion criteria, including 848 people with subacute and chronic stroke.

MT with ES and conventional therapy (CT) was effective in improving upper extremity impairment assessed by Fugl-Meyer Assessment-Upper Extremity (FMA-UE) compared with CT alone (Standard Mean Difference (SMD) 1.49, 95% Confidence Interval (CI) 0.77 to 2.22). MT with ES and CT was effective in improving the FMA-UE compared with ES and CT (SMD 0.34, 95% CI 0.02 to 0.66). MT with ES and CT was effective in improving the FMA-UE compared with MT and CT (SMD 0.40, 95% CI 0.05 to 0.75). There were no significant effects

in reducing spasticity assessed by Modified Ashworth Scale with MT with ES and CT compared with CT alone (Mean Difference (MD) -0.76, 95% CI -1.86 to 0.34), and MT and CT (MD 0.00, 95%CI -0.18 to 0.18). MT with ES and CT is effective in improving upper extremity gross gripping function assessed by Action Research Arm Test compared with MT and CT (MD 0.57, 95% CI 1.35 to 10.05). There was no significant effect in improving Action Research Arm Test with MT with ES and CT compared with ES and CT (MD 2.17, 95% CI -2.75 to 7.09).

There were no significant effects in improving upper extremity gross dexterity assessed by Box and Block Test with MT with ES and CT compared with CT alone (SMD -0.05, 95% CI -0.58 to 0.49). There were no significant effects in improving upper extremity gross dexterity assessed by Box and Block Test with MT with ES and CT compared with ES and CT (SMD 0.43, 95% CI -0.06 to 0.92). There were no significant effects in improving upper extremity gross dexterity assessed by Box and Block Test with MT with ES and CT compared with MT and CT (SMD 0.32, 95% CI -0.07 to 0.70). MT with ES and CT was effective in improving activity of daily living compared with CT alone (SMD 0.84, 95% CI 0.31 to 1.36). There were no significant effects in improving activity of daily living with MT with ES and CT compared with ES and CT (SMD 0.49, 95% CI 0.00 to 0.97). There were no significant effects in improving activity of daily living with MT with ES and CT compared with MT and CT (SMD 0.40, 95% CI -0.08 to 0.88). We conclude that MT combined with ES effectively improves the recovery of upper extremity motor function in stroke survivors.

3.2 Introduction

Up to 80% of stroke survivors have motor impairments of upper extremity (Nakayama et al., 1994). Almost 66% of people with stroke are unable to regain the recovery of motor function of the paretic upper extremity after 6 months post-stroke (Kwakkel et al., 2003). The impaired upper extremity motor function may lead to reduced ability of activities of daily living and impaired social functioning, which would further cause the reduced social community integration (Pollock et al., 2014) in people with stroke. Hence, the recovery of upper extremity motor function becomes one of the most important goals for stroke rehabilitation.

MT is an effective adjunct intervention for recovery of upper extremity motor function in people with stroke (Selles et al., 2014). MT could creat the visual illusion that the paretic arm has the same and normal movement pattern as the non-paretic arm to improve the paretic arm recovery of motor function in stroke survivors (Ding et al., 2019). ES has been used as effective modality for stroke rehabilitation (Stoykov & Madhavan, 2015). ES could stimulate the motor or sensory nerves, or activate muscle responses to improve recovery of upper extremity motor function in stroke survivors (Yang et al., 2019). Previous study (Zeng et al., 2018) showed that MT with CT was significantly improving the recovery of upper extremity motor impairment assessed by FMA-UE (effect size = 0.51, 95% CI 0.29-0.73, $P < 0.001$) compared with CT alone in people with stroke. Previous meta-analysis (Yang et al., 2019) demonstrated that ES was superior than Sham-ES in improving the recovery of upper extremity motor impairment assessed by FMA-UE (effect size = 0.67, 95% CI 0.51-0.84, $P < 0.001$) in people with stroke.

Two recent systematic reviews provided initially evidence about the MT combined with ES, as a new combination priming technique, on the recovery of upper extremity motor function in people with stroke (Luo et al., 2020; Saavedra-García et al., 2021). The meta-analysis (Luo et al., 2020) had shown that MT combined with ES had significant synergistic effects for

improving recovery of upper extremity motor function in people with stroke compared with CT alone. The subgroup analysis of two randomized controlled trials (Kim et al., 2014; Schick et al., 2017) had shown that MT with electromyography triggered ES (muscle contraction) and CT significantly markedly improved upper extremity motor impairment assessed by FMA-UE (MD, 10.14; 95% CI, 5.67-15.01) in people with subacute stroke compared with CT alone (Luo et al., 2020). However, the subgroup analysis of two studies (Lee et al., 2015; Lin et al., 2014) had shown that MT with mesh glove-afferent ES (sensory input) and CT could not improve upper extremity motor impairment assessed by FMA-UE score in chronic stroke survivors compared with CT alone (Luo et al., 2020).

In contrast to the study by Luo et al. (2020), Saavedra-García et al. (2021) shown that MT with ES and CT was not superior to CT alone, MT and CT, or ES and CT in improving upper extremity motor impairment assessed by FMA-UE, upper extremity motor function assessed by Action Research Arm Test, upper extremity gross manual dexterity assessed by Box and Block Test in people with stroke from pooled results of 7 trials (Kim et al., 2014; Kim & Lee, 2015; Lin (a) et al., 2014; Lin (b) et al., 2014; Mathieson et al., 2018; Nagapattinam et al., 2015; Schick et al., 2017). This discrepancy may be that Saavedra-García et al. (2021) pooled the data from people with subacute and chronic stroke, while Luo et al. (2020) analysed the data from people with subacute and chronic stroke separately. Hence, the differences in the synergistic effects of MT combined with ES in people with sub-acute and chronic stroke should be investigated in future studies.

Although two studies by Luo et al. (2020) and Saavedra-García et al. (2021) provided a preliminary understanding of the synergistic effects of MT combined with ES on the recovery of upper extremity motor function in people with stroke, three research questions remain

unanswered. First, there is no meta-analysis about the effects of MT combined with ES in improving upper extremity impairment and upper extremity motor function based on International Classification of Functioning, Disability, and Health framework according to different post-stroke phases (acute/subacute compared with chronic). Second, whether MT combined with ES could improve the participation level in activities of daily living in people with stroke remains unanswered. Third, there are many different types of ES, current studies did not include transcutaneous electrical nerve stimulation. Hence, this systematic review and meta-analysis aims to provide updated evidence from newly published randomized control trials from their inception until April 2024 about the synergistic effects of MT combined with ES for the recovery of upper extremity motor function in people with stroke.

Therefore, the specific objectives of this study were to (1) examine whether MT with ES and CT (MT + ES + CT) is more effective in improving recovery of upper extremity motor function in people with stroke compared with CT alone, ES and CT (ES + CT), or MT and CT (MT + CT) based on the International Classification of Functioning, Disability, and Health framework; (2) identify the differences on the effects of MT combined with ES for recovery of upper extremity motor function in people with acute/subacute and chronic stroke.

3.3 Method

3.3.1 Protocol and registration

This study followed the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis statement (Page et al., 2021). The review protocol was registered in the PROSPERO database of systematic review (CRD42020212070).

3.3.2 Eligibility Criteria

The inclusion criteria were used to identify the studies that: (1) the articles were published in English and Chinese peer-reviewed journals; (2) were participants with different phase of stroke and one or multiple history of stroke; (3) investigated the net effects of MT combined with ES (MT + ES + CT vs. CT alone), the net effects of ES (MT + ES + CT vs. MT + CT), or net effects of MT (MT + ES + CT vs. ES + CT); (4) were randomized controlled trials or crossover designs with period one data. The exclusion criteria included if the studies: (1) were conference abstract; (2) were thesis; (3) case reports; (4) reporting data that could not be extracted from figure or graphs by using the software WebPlotDigitizer; (5) in which all groups using MT combined with ES; (6) in which MT was in comparison to Sham-MT or ES was in comparison to Sham-ES.

3.3.3 Search strategy

Several databases were systematically searched from their inception until April 2024: MEDLINE, Embase, Cochrane Library, Web of Science, Scopus, Physiotherapy Evidence Database, China Biology Medicine, China National Knowledge Infrastructure, Wan Fang, VIP. The search strategies are presented in Appendix 3.3.

3.3.4 Study Selection and Data Extraction

All of the full-text were screened and extracted by two reviewers independently (HP and CCCC). Full texts were assessed based on the inclusion and exclusion criteria to identify the

articles and extracted by using a standardized form. Any disagreements were solved by discussion and consulted from the corresponding author. The International Classification of Functioning, Disability, and Health framework was used to evaluate the upper extremity impairment, recovery of motor function, and participation in stroke survivors.

3.3.5 Methodological Quality (Risk of Bias Assessment)

The included trials were appraised by two independently authors (HP and CCCC) by using the version 2 of the Cochrane tool for assessing risk of bias in randomized trials (Sterne et al., 2019). The overall quality of evidence was assessed by the GRADE assessment (Guyatt et al., 2011).

3.3.6 Statistical Analyses

All the data analyses were presented by the software of Review Manager version 5.3 (Copenhagen, Denmark: The Nordic Cochrane Center, Cochrane Collaboration). The means and standard deviation (SD) for experimental and control groups at the post-time point were extracted for data analysis. If the studies had several different time points, e.g., 3, 6, or 9 weeks, only the longest time point was considered for data analysis as it was regarded to have greater clinical significance (Monte-Silva et al., 2019). If the raw data were presented as median values or interquartile ranges, the data analysis only included the normally distributed data and the median values were regarded equal to the mean values. For the SD of interquartile ranges, it was calculated according to following formula (Higgins et al., 2011):

$$SD = (\text{upper limit} - \text{lower limit}) / 1.35.$$

The software of WebPlotDigitizer (https://apps.automeris.io/wpd/) was used to extract the data from the figures or graphs (Drevon et al., 2017), if the continuous data were presented as figures or graphs. The random-effects models with mean difference (MD) and 95% Confidence intervals (CIs) were used to calculate the effect size for the same outcome measures while random-effects models with standardized mean difference (SMD) and 95% CIs were used to calculate the effect size for the different outcome measures. The SMD could be calculated according to the following formulas (Higgins et al., 2011):

$$\text{SMD} = \frac{\text{MD}}{\text{SD(pooled)}}, \quad \text{SD (pooled)} = \sqrt{\frac{SDc^2 + SDe^2}{2}}.$$

The effect sizes were defined as small (< 0.2), moderate (0.2 to < 0.5), large (0.5 to < 0.8), or very large (> 0.8) (Goff et al., 2021; Liu et al., 2018; Higgins et al., 2011).

3.3.7 Testing Homogeneity

P value less than 0.05 of Chi- squared test was regarded that the heterogeneity was statistically significant. The I^2 value was used to indicate the degree of heterogeneity and 25%, 50%, and 75% of I^2 value prompt low, moderate, and high degree of heterogeneity, separately (Higgins et al., 2011).

3.3.8 Subgroup Analysis

The phases after stroke were categorized as acute (< 3 weeks), subacute (3 weeks to 6 months), or chronic (≥ 6 months) (Monte-Silva et al., 2019). A predefined subgroup analysis would be conducted according to the chronicity of stroke (acute/subacute vs. chronic).

3.3.9 Sensitivity Analysis

Sensitivity analysis was conducted by removing studies rated as high risk assessed by the version 2 of the Cochrane tool for assessing risk of bias to find the source of heterogeneity.

3.3.10 Meta-Regression Analysis

The duration of each training session, weekly frequency, and number of weeks were extracted for dosage calculation (Yang & Butler, 2020). The training dosage was calculated as the duration of each training session multiplied by the frequency and the number of weeks. A meta-regression analysis was calculated by using the STATA 15.0 (College Station, Texas 77845 USA) software to explore the relationship between the training dosage and effect size in more than 10 trails (Higgins et al., 2011).

3.3.11 Publication Bias

The Egger's test was used to detect the probability of publication bias if more than 10 trials were included while the Fail-Safe N analysis was be applied for outcome measures to detect the probability of publication bias if less than 10 trials were included (Liu et al., 2018).

3.4 Results

3.4.1 Search Results

All the details of the inclusion producers of studies were presented in Figure 3.1. A total of 2893 citations were retrieved from the electronic databases, registry centres, and reference lists searches and 1300 studies were removed as duplicates. After screened the titles and abstract according to the inclusion and exclusion criteria, the full texts of the 97 publications were assessed. Finally, total 18 studies were included in this study.

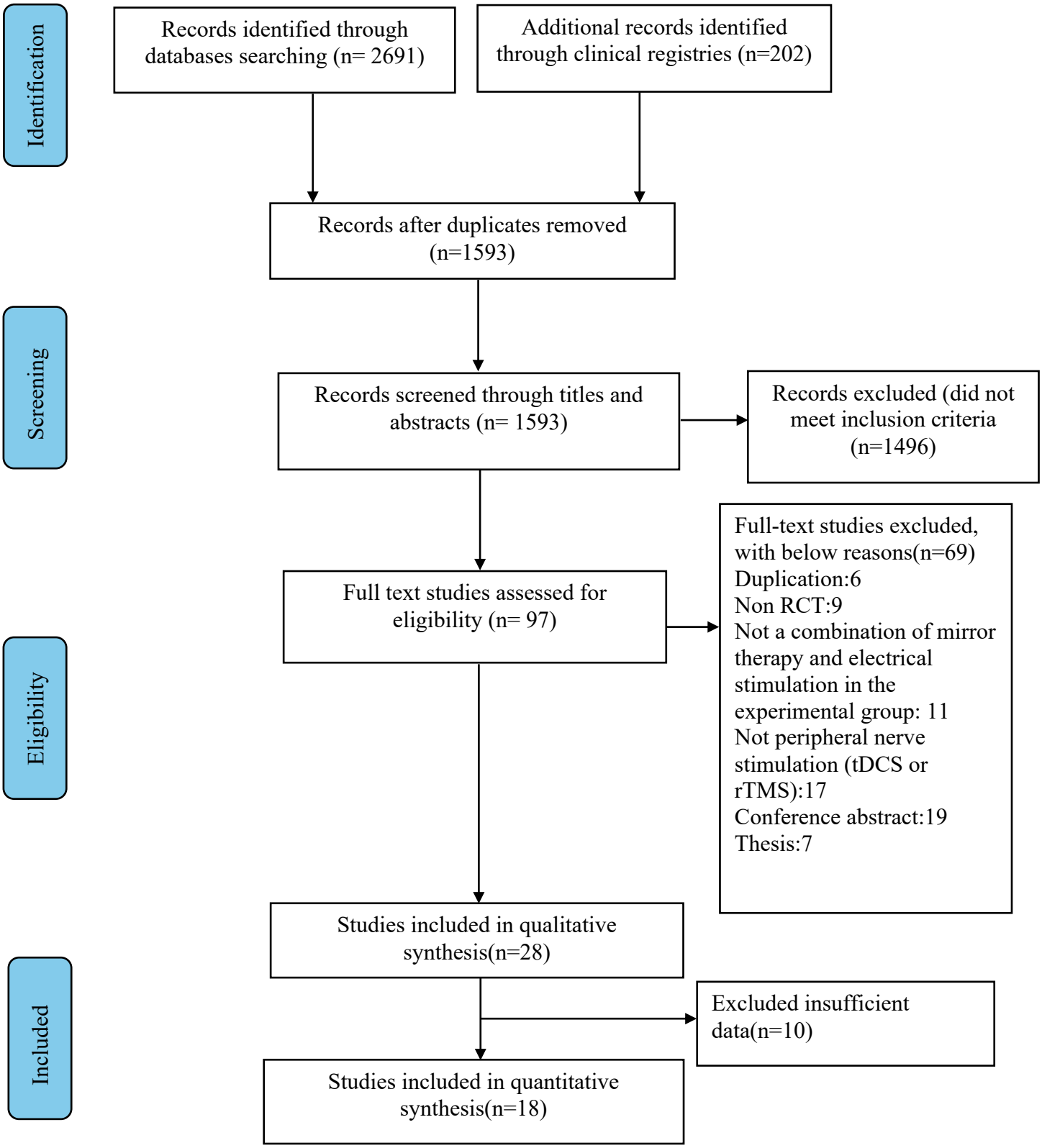


Figure 3.1 The Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram for this study (This figure was modified from the published paper (Pan et al., 2023))

3.4.2 Study characteristics

The descriptive information of the included studies in this systematic review and meta-analysis were presented in Table 3.1.

3.4.2.1 Participants

The studies reviewed 18 articles (Kim et al., 2014; Kim, 2015; Kim et al., 2023; Lee et al., 2015; Lin(a) et al., 2014; Lin (b) et al., 2014; Mathieson et al., 2018; Nagapattinam et al., 2015; Chen et al., 2014; Schick et al., 2017; Yun et al., 2011; Zhang et al., 2023; Feng et al., 2021; Lu et al, 2018; Zhou et al., 2021; Yao et al., 2016; Xu et al., 2020; Wang et al., 2015), including a total 848 people with stroke. The sample size ranged from 16 to 90 people with stroke and the mean age of people with stroke was between 44 and 75 years. Total 12 studies were conducted in people with acute / subacute stroke (Kim et al., 2014; Mathieson et al., 2018; Nagapattinam et al., 2015; Chen et al., 2014; Schick et al., 2017; Yun et al., 2011; Zhang et al., 2023; Lu et al., 2018; Zhou et al., 2021; Yao et al., 2017; Xu et al., 2020; Wang et al., 2015) while total 6 studies investigated in people with chronic stroke (Kim, 2015; Kim et al., 2023; Lee et al., 2015; Lin(a) et al., 2014; Lin (b) et al., 2014; Feng et al., 2021). The upper extremity impairment levels ranged from severe (FMA-UE < 30) (12 studies, 628 people with stroke) (Kim et al., 2014; Mathieson et al., 2018; Chen et al., 2014; Schick et al., 2017; Yun et al., 2011; Zhang et al., 2023; Feng et al., 2021; Lu et al., 2018; Zhou et al., 2021; Yao et al., 2017; Xu et al., 2020; Wang et al., 2015) to moderate (30 < FMA-UE < 50) (4 studies, 131 people with stroke) (Kim et al., 2023; Lee et al., 2015; Lin(a) et al., 2014; Lin (b) et al., 2014) in

severity according to the assessment of initial FMA-UE score. No information about the FMAUE score were provided in two studies (Kim, 2015; Nagapattinam et al., 2015).

3.4.2.2 Interventions

The experimental group of all included studies was MT with ES and CT. For MT, total nine studies (Chen et al., 2015; Feng et al., 2021; Kim et al., 2014; Kim et al., 2015; Kim et al., 2023; Lin(a) et al.,2014; Yao et al., 2017; Yun et al., 2011; Zhang et al., 2023) used movement MT. A total of nine studies (Lee et al., 2015; Lin (b) et al., 2014; Lu et al., 2018; Mathieson et al., 2018; Nagapattinam et al., 2015; Schick et al., 2017; Wang et al., 2015; Xu et al., 2020; Zhou et al., 2021) used task MT. The total training session of MT ranged from 20 to 60 minutes, the duration of MT ranged from 3 to 8 weeks, and the training frequency of MT ranged from 5 to 7 days per week.

Different types of ES were included in this study. These modalities include functional electrical stimulation (Kim et al., 2014; Kim et al., 2015; Kim et al., 2023; Lu et al, 2018; Mathieson et al., 2018; Nagapattinam et al., 2015; Zhang et al., 2023; Zhou et al., 2021), neuromuscular electrical stimulation (Yao et al, 2017; Yun et al., 2011), EMG-triggered biofeedback electrical stimulation (Chen et al., 2015; Schick et al., 2017; Wang et al., 2015; Xu et al., 2020), somatosensory electrical stimulation (Lee et al., 2015; Lin(a) et al., 2014; Lin (b) et al., 2014), and transcutaneous electrical nerve stimulation (Feng et al., 2021). The stimulated muscles were extensor digitorum communis and extensor carpi radialis. The intensity ranged from 0 to 90 mA, the frequency ranged from 20 to 60 Hz, and pulse width ranged from 100 to 500 μs. Total three studies (Kim, 2015; Schick et al., 2017; Zhang et al., 2023) applied bilateral ES and remaining studies applied unilateral ES. The total training session of ES ranged from 20 to 60

minutes, the duration of ES ranged from 3 to 8 weeks, and the training frequency of ES ranged from 5 to 7 days per week.

Total twelve studies used the physical therapy and occupational therapy (Chen et al., 2015; Feng et al., 2021; Kim et al., 2014; Kim et al., 2023; Lu et al., 2018; Schick et al., 2017; Wang et al., 2015; Xu et al., 2020; Yao et al., 2017; Yun et al., 2011; Zhang et al., 2023; Zhou et al., 2021) as the treatment components of CT. A total of two studies only used the physical therapy (Kim, 2015; Mathieson et al., 2018), and four studies in total (Lee et al., 2015; Lin (a) et al., 2014; Lin (b) et al., 2014; Nagapattinam et al., 2015) only used occupational therapy as the treatment component of CT, respectively. The total training session of CT ranged from 20 to 240 minutes. The duration and training frequency of CT ranged from 3 to 8 weeks and 4 to 6 days per week, respectively.

For the control groups, three types of comparator were included in this study. A total of 9 studies used the MT with CT as the comparator (Lin (a) et al., 2014; Lin (b) et al., 2014; Mathieson et al., 2018; Nagapattinam et al., 2015; Yun et al., 2011; Zhang et al., 2023; Lu et al., 2018; Zhou et al., 2021; Xu et al., 2020). Total 10 studies used ES and CT as the comparator (Kim et al., 2014; Kim et al., 2023; Mathieson et al., 2018; Nagapattinam et al., 2015; Chen et al., 2015; Schick et al., 2017; Zhang et al., 2023; Zhou et al., 2021; Yao et al., 2017; Wang et al., 2015). 8 studies in total used CT alone as the comparator (Kim, 2015; Lee et al., 2015; Lin (b) et al., 2014; Yun et al., 2011; Zhang et al., 2023; Feng et al., 2021; Yao et al., 2017; Wang et al., 2015). In general, the experimental and control groups had the similar training session, frquency, duration, and dosage.

3.4.2.3 Outcome measures

A total of 15 (Chen et al., 2015; Feng et al., 2021; Kim et al., 2014; Kim et al., 2023; Lee et al., 2015; Lin (b) et al., 2014; ; Lu et al, 2018; Mathieson et al., 2018; Schick et al., 2017; Wang et al., 2015; Xu et al., 2020; Yao et al., 2017; Yun et al., 2011; Zhang et al., 2023; Zhou et al., 2021) and total 4 (Feng et al., 2021; Kim, 2015; Lin (a) et al., 2014; Yun et al., 2011) studies assessed the upper extremity motor impairment and spasticity by FMA-UE and Modified Ashworth Scale, respectively, on the Body Structure and Function domain. A total of 4 (Lin (a) et al., 2014; Mathieson et al., 2018; Nagapattinam et al., 2015; Zhang et al., 2023) and total 7 (Kim et al., 2014; Kim, 2015; Lee et al., 2015; Lin (a) et al., 2014; Lin (b) et al., 2014; Schick et al., 2017; Zhou et al., 2021) studies assessed the upper extremity gross gripping function and dexterity by Action Research Arm Test, Block and Box Test, separately, on the Activity domain. Total 6 (Feng et al., 2021; Kim et al., 2023; Lu et al., 2018; Schick et al., 2017; Xu et al., 2020; Zhang et al., 2023) and total 5 (Kim, 2015; Lee et al., 2015; Lin (a), et al., 2014; Mathieson et al., 2018; Yao et al., 2017) studies assessed the functional mobility and daily life living assessed by Modified Barthel Index and by Functional Independent Measure, respectively, on the Activity domain. Hobart et al. (2001) demonstrated that Functional Independent Measure and Modified Barthel Index had the similar psychometric in the evaluation of physical disability. Therefore, this systematic review and meta-analysis pooled the Functional Independent Measure and Modified Barthel Index together as one outcome measure to assess the daily life living in people with stroke. Only two studies reported the outcome measures on the participation domain of difficulty level of paretic upper extremity use in daily life living and health-related quality of life assessed by Motor Activity Log (Lin (b) et al., 2014) and Stroke-Specific Quality of Life Scale (Kim, 2015), respectively.

Table 3.1 Characteristics of included studies (Pan et al., 2023)

Study	Participants	Intervention	Parameters of Electrical stimulation	Outcome measures
Chen 2015[#] (China), Unfunded	EG:30 patients; 58.13yrs; 2.0 Mo (Subacute); fugl-meyer assessment:7.45(Severe). CG: 30 patients; 57.35yrs; 2.0 Mo (Subacute); fugl-meyer assessment: 7.63 (Severe).	EG:MT+EMG-BF-ES+CT; 80min;5D/W;8(W). CG: EMG-BF-ES+CT; 50min;5D/W;8(W).	MS: ECR; EDC.PW: NA. Threshold: Motor.ET: Surface electrodes. Frequency: NA. Intensity: NA. Unilateral.	Fugl-meyer assessment
Feng 2021[#] (China), Unfunded	EG:38 patients; 61.58yrs; 3.2 Mo (Chronic); fugl-meyer assessment: 13.18(Severe). CG: 39 patients; 63.15yrs;3.4 Mo (Chronic); fugl-meyer assessment:12.71(Severe).	EG: TENS+MT+CT; 110min,6D/W;6(W). CG: CT; 50min; 80min, 6D/W;6(W).	MS: ECRB; PW: NA. Threshold: Sensory.ET: Surface electrodes. Frequency: NA. Intensity: ST. Unilateral.	Fugl-meyer assessment, Modified ashworth scale, Modified barthel index
Kim 2023[#] (Korea), Funded	EG: 12 patients; 75.9 yrs; > 6 Mo (Chronic); fugl-meyer assessment: 24.9 (Moderate) CG: 12 patients; 74.9 yrs; > 6 Mo (Chronic); fugl-meyer assessment:25.5 (Moderate)	EG:MT+FES+CT; 30 min; 5D/W; 4 (W). CG:MT+CT; 30 min; 5D/W; 4 (W).	MS:ECR;PW:NA. Threshold Sensory: Motor. ET: Surface electrodes. Frequency: NA. Intensity: MC. Unilateral.	Fugl-meyer assessment, Modified barthel index
Kim 2014[#] (Korea), Unfunded	EG:12 patients; 55.92yrs;1.1 Mo (Subacute); fugl-meyer assessment: 11.08(Severe). CG:11 patients; 55.64yrs;1.2 Mo (Subacute); fugl-meyer assessment: 9.46(Severe)	EG: MT+FES+CT; 90min;5D/W;4(W). CG: FES+CT; 90min;5D/W;4(W).	MS: ECR; EDC.PW: 300μs. Threshold: Motor.ET: Surface electrodes. Frequency: 20Hz. Intensity: MC. Unilateral.	Fugl-meyer assessment, Box and block test

Kim 2015[#]	EG1: 10 patients; 58.1yrs; 10.2 Mo (Chronic); fugl-meyer assessment: NA.	EG1: MT+EMG-BF-FES+CT; 60min;5D/W;4(W).	MS: ECR; EDC.PW: NA. Threshold: Motor.ET: Surface electrodes. Frequency: NA. Intensity: NA.	Modified ashworth scale, Box and block test, Functional independent measure, Stroke specific quality of life
	EG2: 10 patients; 53.2yrs; 16.4 Mo (Chronic); fugl-meyer assessment: NA.	EG2: MT+FES+CT; 60min;5D/W;4(W).	Bilateral.	
(Korea), Unfunded	CG: 9 patients; 62.11yrs; 13.9 Mo (Chronic); fugl-meyer assessment: NA.	CG: CT; 30min;5D/W;4(W).		
Lee 2015[#]	EG: 15 patients; 52.50yrs; 22 Mo (Chronic); fugl-meyer assessment: 35.87(Moderate).	EG: MT+MGAS+CT; 90min;5D/W;4(W).	MS: Elbow Joint. PW: 300μsecs. Threshold: Sensory. ET: Mesh glove. Frequency: 50Hz. Intensity: NA.	Fugl-meyer assessment, Box and block test, Functional independent measure
	CG1:16 patients; 49.10yrs; 23.3 Mo (Chronic); fugl-meyer assessment: 36(6.99) (Moderate).	CG1: MT+ Placebo MGAS+CT; 90min;5D/W;4(W).	Unilateral.	
(Korea), Unfunded	CG2:17 patients; 56.64yrs; 17.7 Mo (Chronic); fugl-meyer assessment: 40.71(9.66) (Moderate).	CG2: MT+CT; 90min;5D/W;4(W).		
Lin 2014(a)[#]	EG: 8 patients; 56.31yrs; 8.9 Mo (Chronic); fugl-meyer assessment: 45.38 (Moderate).	EG: MT+MGAS+CT; 90min;5D/W;4(W).	MS: Palmar; Dorsal. PW: NA. Threshold: Sensory. ET: Mesh glove. Frequency: NA.	Modified ashworth scale, Action research arm test, Box and block test, Functional independent measure
(Korea),Funded	CG: 8 patients; 54.97yrs;23.4 Mo (Chronic); fugl-meyer assessment: 44.25(Moderate).	CG: MT+CT; 90 min;5D/W;4(W).	Intensity: ST. Unilateral.	
Lin 2014 (b)[#]	EG: 14 patients; 55.79yrs; 22.71 Mo (Chronic); fugl-meyer assessment: 45.43(Moderate).	EG: MT+MGAS+CT; 90 min; 5D/W;4(W).	MS: Palmar; Dorsal. PW: NA. Threshold: Sensory.ET: Mesh glove. Frequency: NA.	Fugl-meyer assessment, Box and block test, Motor activity log
(China),Funded	CG1: 14 patients; 56.01yrs; 18.50 Mo (Chronic); fugl-meyer assessment: 44.21(Moderate).	CG1: MT+CT; 90 min; 5D/W;4(W).	Intensity: ST. Unilateral.	

	CG2: 15 patients; 53.34yrs; 17.80 Mo (Chronic); fugl-meyer assessment: 43.80(Moderate).	CG2: CT; 90 min; 5D/W;4(W).		
Lu 2018[#]	EG: 20 patients; 62.89yrs; 0.33 Mo (Acute); fugl-meyer assessment: 21.7(Severe).	EG:MT+FES+CT; 30min, 5D/W;4(W).	MS: NA. PW: 200μs. Threshold: Motor. ET: Surface electrodes. Frequency: 60 Hz.	Fugl-meyer assessment, Modified barthel index
(China),Unfunded	CG: 20 patients; 61.25yrs; 0.34 Mo (Acute); fugl-meyer assessment: 20.2(Severe).	CG: MT+CT; 30min, 5D/W;4(W).	Intensity: 0-60μmA. Unilateral.	
Mathieson 2018[#]	EG: 23 patients; 73.35yrs; Acute. fugl-meyer assessment: 12.74 (Severe).	EG: MT+FES+CT; 120 min; 5D/W;3(W).	MS: ED; EPB. PW: 200μs. Threshold: Motor.ET: Surface electrodes. Frequency: 45Hz.	Fugl-meyer assessment, Action research arm test, Functional independent measure
(New Zealand), Unfunded.	CG1:15 patients; 66.07yrs; Acute; fugl-meyer assessment: 10.57 (Severe).	CG1: MT+CT;120 min; 5D/W;3(W).	Intensity: NA. Unilateral.	
	CG2: 12 patients; 72.42yrs; Acute; fugl-meyer assessment: 10.38 (Severe).	CG2: FES+CT; 120 min; 5D/W;3(W).		
Navaratnam 2015[#]	EG: 20 patients; 45.75yrs; Subacute. fugl-meyer assessment: NA.	EG: MT+FES+CT; 60min; 3D/W;2(W).	MS: EDC; ECRB; ECRL. PW: 250μs. Threshold: Motor.ET: Surface electrodes. Frequency: 35Hz. Intensity: 90mA. Unilateral.	Action research arm test
(India),Unfunded.	CG1:20 patients; 44.65yrs; Subacute; fugl-meyer assessment: NA.	CG1: MT+CT; 60min; 3D/W;2(W).		
	CG2: 20 patients; 44.15yrs; Subacute; fugl-meyer assessment: NA.	CG2: FES+CT; 60min; 3D/W;2(W).		
Schick 2017[#]	EG: 15 patients; 62yrs; Subacute; fugl-meyer assessment: 16.47(Severe).	EG:MT+EMG-BF-ES+CT; 30min; 5D/W;3(W).	MS: ECRL; ECRB; FDS. PW: 300μs. Threshold: Motor.ET: Surface electrodes.	Fugl-meyer assessment, Box and block test, Modified barthel index
(Austria),Unfunded	CG: 17 patients; 63yrs; Subacute; fugl-meyer assessment: 28.22 (Severe).	CG: EMG-BF-ES+CT; 30min; 5D/W;3(W).	Frequency: 30-35Hz. Intensity: 16-18mA. Bilateral.	

Wang 2015[#] (China),Funded.	EG:30 patients; 64.68yrs; 2.1 Mo (Subacute); fugl-meyer assessment: 17.51 (Severe). CG1: 30 patients; 65.16yrs; 2.1 Mo (Subacute); fugl-meyer assessment: 17.67 (Severe). CG2: 30 patients; 64.87yrs; 2.1 Mo (Subacute); fugl-meyer assessment: 17.46 (Severe).	EG:(MT+EMG-BF-ES) +CT; 90min; 6D/W;8(W). CG1: EMG-BF-ES+CT; 80min; 6D/W;8(W). CG2: CT; 60min; 6D/W;8(W).	MS: Deltoid, Triceps, Forearm extensor. PW: 500μs,200μs. Threshold: Motor. ET: Surface electrodes. Frequency: 35Hz. Intensity: NA. Unilateral.	Fugl-meyer assessment
Xu 2020[#] (China),Unfunded	EG: 20 patients; 62.4yrs; 0.65 Mo (Acute); fugl-meyer assessment: 10.0 (Severe). CG: 20 patients; 60.8yrs; 0.61 Mo (Acute); fugl-meyer assessment: 10.6(Severe).	EG: MT+EMG-BF-ES+CT; 30min; 5D/W;4(W). CG: MT+CT; 30min; 5D/W;4(W).	MS: ECR. PW: NA. Threshold: Motor.ET: Surface electrodes. Frequency: NA. Intensity: 0-35 mA. Unilateral.	Fugl-meyer assessment, Modified barthel index
Yao 2016[#] (China),Unfunded	EG: 15 patients; 59.73yrs; 0.6 Mo (Acute); fugl-meyer assessment: 22.67(Severe). CG1: 15 patients; 57.60yrs; 0.6 Mo (Acute); fugl-meyer assessment: 22.60(Severe). CG2: 15 patients; 59.27yrs; 0.7 Mo (Acute); fugl-meyer assessment: 25.07(Severe).	EG: (MT+EMG-BF-NMES) +CT; 65min; 6D/W;4(W). CG1: EMG-BF-NMES+CT; 65min; 6D/W;4(W). CG2: CT; 45 min; 6D/W;4(W).	MS: Wrist, Finger Extensor. PW: NA. Threshold: Motor.ET: Surface electrodes. Frequency: NA. Intensity: NA. Unilateral.	Fugl-meyer assessment, Functional independent measure
Yun 2011[#] (Korea), Unfunded	EG: 20 patients; 65.9yrs; 0.85 Mo (Acute); fugl-meyer assessment: 4.3 (Severe). CG1: 20 patients; 63.1yrs; 0.80 Mo (Acute); fugl-meyer assessment: 5.3 (Severe). CG2: 20 patients; 61yrs; 0.94 Mo (Acute); fugl-meyer assessment: 5.3 (Severe).	EG: MT+NMES+CT; 30 min; 5D/W;3(W). CG1: MT+CT; 30min; 5D/W;3(W). CG2: NMES+CT; 30 min; 5D/W;3(W).	MS: ED; EPB. PW: 250μs. Threshold: Motor.ET: Surface electrodes. Frequency: 35Hz. Intensity:30-70mA. Unilateral.	Fugl-meyer assessment, Modified ashworth scale

Zhang 2023[#] (China), Funded	EG:12 patients; 62.3 yrs; 0.77 Mo (Aute); fugl-meyer assessment: 15.2 (Severe). CG1:12 patients; 58.6 yrs; 0.5 Mo (Acute); fugl-meyer assessment: 14.8 (Severe). CG2:14 patients; 60.4 yrs; 0.83 Mo (Acute); fugl-meyer assessment: 13.0 (Severe). CG3:13 patients; 54.5 yrs; 1.1 Mo (Subacute); fugl-meyer assessment: 17.0 (Severe).	EG: MT+FES+CT; 200 min; 5D/W; 3(W) CG1: MT+CT;200 min; 5D/W; 3(W) CG2: FES+CT;200 min; 5D/W; 3(W) CG3: CT;180 min; 5D/W; 3(W)	MS: ECR. PW: 100μs. Threshold: Motor. ET: Surface electrodes. Frequency:: NA. Intensity:0-80mA. Bilateral.	Fugl-meyer assessment, Action research arm test, Modified barthel index
Zhou 2021	EG: 20 patients; 56.65yrs; 0.88 Mo (Acute); fugl-meyer assessment: 13.8(Severe). CG1: 20 patients; 58.9yrs; 0.79 Mo (Acute); fugl-meyer assessment: 12.8(Severe). CG2: 20 patients; 59.3yrs; 0.81 Mo (Acute); fugl-meyer assessment: 14.75 (Severe).	EG: MT+FES+CT; 20min; 5D/W;4(W). CG1: FES+CT; 20min; 5D/W;4(W). CG2: MT+CT; 20min; 5D/W;4(W).	MS: NA. PW: NA. Threshold: Motor.ET: Surface electrodes. Frequency: NA. Intensity: NA. Unilateral.	Fugl-meyer assessment, Box and block test

Abbreviation:

EG: experimental Group; yrs: years; Mo: month; CG: control group; MT: mirror therapy; EMG-BF-ES: electromyographic biofeedback electrical stimulation; CT: Conventional Therapy; Min: minute; D: day; W: week; MS: Muscle stimulation; ECR: extensor carpi radialis; EDC: extensor digitorum communis; PW: pulse width; NA: not available; ET: Electrode type; TENS: Transcutaneous electrical nerve stimulation; ECRB: extensor carpi radialis brevis; ST: sensory

threshold; FES: functional electrical stimulation; MC: muscle contraction; EMG-BF-FES: electromyographic biofeedback functional electrical stimulation; MGAS: mesh glove afferent stimulation; FDS: flexor digitorum superficialis; ED: extensor digitorum; EPB: extensor polliics brevis; ECRL: extensor carpi radialis longus; EMG-BF-NMES: electromyographic biofeedback neuromuscular electrical stimulation; NMES: neuromuscular electrical stimulation.

Note: # Location of therapy in hospital (Inpatient).

3.4.3 Methodological quality

The methodological quality of included studies is presented in Table 3.2. All 18 included studies showed the items of “missing outcome data” and “measurement of the outcome” with low risk of bias. Total 10 studies (Feng et al., 2021; Kim et al., 2023; Lin (b) et al., 2014; Lu et al., 2018; Mathieson et al., 2018; Nagapattinam et al., 2015; Schick et al., 2017; Xu et al., 2020; Zhang et al., 2023; Zhou et al., 2021) were assessed low risk of bias about the randomization process and remaining studies (Chen et al., 2015; Kim et al., 2014; Kim et al., 2014; Kim, 2015; Lin (a) et al., 2014; Wang et al., 2015; Yao et al., 2017; Yun et al., 2011) showed some concerns. Total two studies (Kim et al., 2014; Kim, 2015) had high risk of bias about the evaluation item of “deviations from the intended interventions” and remaining studies showed low risk of bias. Only one study (Schick et al., 2017) was assessed low risk of bias about the selection of the reported result and remaining studies showed some concerns. Only one study (Schick et al., 2017) was assessed low risk of bias, total two studies (Kim et al., 2014; Kim, 2015) were assessed high risk of bias about the overall quality of included studies, and remaining showed some concerns.

Table 3.2 The methodological quality as assessed by using the version 2 of the Cochrane risk of bias tool (RoB 2) (Pan et al., 2023)

Study ID	Randomization Process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Chen 2015	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns
Feng 2021	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Kim 2023	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Kim 2014	Some concerns	High risk	Low risk	Low risk	Some concerns	High risk
Kim 2015	Some concerns	High risk	Low risk	Low risk	Some concerns	High risk
Lee 2015	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Lin 2014(a)	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns
Lin 2014 (b)	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Lu 2018	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Mathieson 2018	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Nagapattinam 2015	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Schick 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Wang 2015	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns
Xu 2020	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Yao 2016	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns
Yun 2011	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns
Zhang 2023	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Zhou 2021	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns

3.4.4 Quantitative analysis

3.4.4.1 Comparing the effects of MT with ES and CT with CT alone on the body function, activity, and participation domain outcomes

Total 6 studies (Feng et al., 2021; Kim, 2015; Lin (b) et al., 2014; Wang et al., 2015; Yao et al., 2017; Zhang et al., 2023) investigated the effects of MT with ES and CT on recovery of upper extremity motor function and health-related quality of life in people with stroke compared with CT alone (Figure 3.2). The results of GRADE assessment for this comparison were presented in Table 3.3. The GRADE assessment was downgraded one level for serious risk of bias, heterogeneity, and imprecision, respectively. The certainty of the evidence for the outcome measures varied from very low to low according to the GRADE assessment.

A large significant effect was observed favouring MT with ES and CT for improving upper extremity impairment assessed by FMA-UE compared with CT alone (SMD 1.49, 95% CI 0.77-2.22, $P < 0.001$) with moderate heterogeneity ($I^2 = 78\%$, $P = 0.004$). A sensitivity analysis was conducted by moving one trial (Zhang et al., 2023), and a similar significant result was got with no heterogeneity (SMD 1.89, 95% CI 1.52-2.26, $P < 0.001$, $I^2 = 0\%$). No significant effects were observed favouring MT with ES and CT in comparison to CT alone (MD -0.76,95% CI -1.86-0.34, $P = 0.17$, $I^2 = 42\%$) for spasticity assessed by Modified Ashworth Scale in people with stroke. No significant effects were achieved to favour the MT with ES and CT for upper extremity dexterity assessed by Block and Box Test in people with stroke compared with CT alone (SMD -0.05, 95% CI -0.58-0.49, $P = 0.86$, $I^2 = 0\%$). A large significant effect size was achieved to favour MT with ES and CT for activity of daily living in stroke in comparison to CT alone (SMD 0.84, 95% CI 0.31-1.36, $P = 0.002$) with significant heterogeneity (I^2=61%, P

= 0.04). A sensitivity analysis was conducted by moving one study (Yao et al., 2017), and a similar significant result was got with low heterogeneity (SMD 0.81, 95% CI 0.28-1.34, P = 0.003, I^2 = 29%).

One study (Lin (b) et al., 2014) reported the improvement of MT with ES and CT in the difficulty level of the paretic upper extremity in daily life living use assessed by Motor Activity Log in comparison to CT alone (SMD 0.08, 95% CI -0.65 to 0.81 for Amount of Use and SMD 0.04, 95% CI -0.69 to 0.77 for Quality of Movement, respectively). Another study (Kim, 2015) reported the improvement of MT with ES and CT in health-related quality of life assessed by Stroke Specific Quality of Life compared with CT alone (SMD 0.47, 95% CI -0.32 to 1.27).

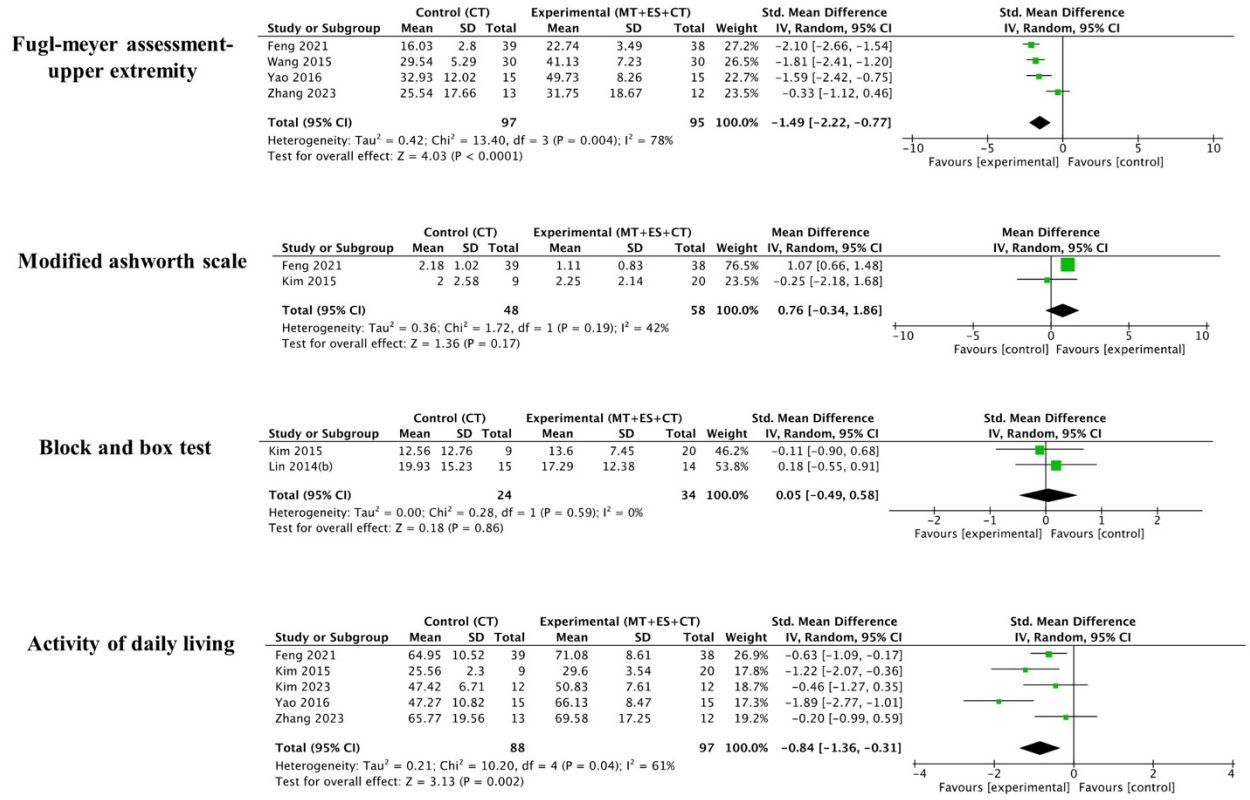


Figure 3.2 Meta-analyses of the effects of MT with ES and CT vs. CT alone group on Fugl-Meyer Assessment-Upper Extremity, Modified Ashworth Scale, Block and Box test, and Activity of Daily Living based on the International Classification of Functionality, Disability, and Health in people with stroke at the end of treatment

Table 3.3 Quality of Evidence (Grading of Recommendations Assessment, Development, and Evaluation) (MT + ES + CT vs. CT alone)

MT+ES + CT vs. CT alone							
Number of studies (patients)	SMD (95%CI)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of Evidence
			Fugl-Meyer Assessment-Upper Extremity				
4(192)	1.49 (0.77-2.22) *	Serious[a]	Not serious	Not serious	Serious[c]	Not serious	⊕⊕⊕O Low
			Modified Ashworth Scale				
2(106)	-0.76 (-1.86-0.34)	Serious[a]	Serious[b]	Not serious	Serious[c]	Not serious	⊕OOO Very Low
			Box and Block Test				
2(58)	0.05 (0.58-0.49)	Serious[a]	Not serious	Not serious	Serious[c]	Not serious	⊕⊕OO Low
			Activities of Daily Living				
5(185)	0.84 (0.31-1.36) *	Serious[a]	Not serious	Not serious	Serious[c]	Not serious	⊕⊕OO Low

*: Statistically significant ($p < 0.05$); a: downgraded one level for serious risk of bias; b: downgraded one level for heterogeneity; c: downgraded one level for serious imprecision.

3.4.4.2 Comparing the effects of MT with ES and CT with ES and CT on body function, activity, and participation domain outcomes

Total 9 studies (Chen et al., 2015; Kim et al., 2014; Mathieson et al., 2018; Nagapattinam et al., 2015; Schick et al., 2017; Yao et al., 2017; Yun et al., 2011; Zhang et al., 2023; Zhou et al., 2021) investigated the effects of MT with ES and CT on the recovery of upper extremity motor function and health-related quality of life in people with stroke compared with ES and CT (Figure 3.3). The results of GRADE assessment for this comparison is presented in Table 3.4. The GRADE assessment were downgraded one level for serious risk of bias and imprecision, respectively. The certainty of the evidence for the outcomes varied from low to moderate according to the GRADE assessment.

Moderate significant effects were observed to favour MT with ES and CT for upper extremity impairment assessed by FMA-UE in people with stroke compared to ES and CT (SMD 0.34, 95% CI 0.02 - 0.66, P = 0.04, I^2 = 43%). Only one study (Yun et al., 2011) reported the improvement in the spasticity assessed by Modified Ashworth Scale with MT with ES and CT compared with ES and CT in people with stroke (SMD -0.15, 95% CI -0.77 to 0.47). No significant effects were observed to favour MT with ES and CT for upper extremity gross gripping function assessed by Action Research Arm Test in stroke survivors compared to ES and CT (MD 2.17, 95% CI -0.75 - 7.09, P = 0.39, I^2 = 0%). No significant effects were observed to favour MT with ES and CT for upper extremity dexterity assessed by Block and Box Test in people with stroke compared to ES and CT (SMD 0.43, 95% CI -0.06-0.92, P = 0.08, I^2 = 28%). No significant effects were observed to favour MT with ES and CT for Activity of Daily Living in people with stroke compared with ES and CT (SMD 0.49, 95% CI 0.0-0.97, P = 0.05) with low heterogeneity (I^2 = 41%, P = 0.17).

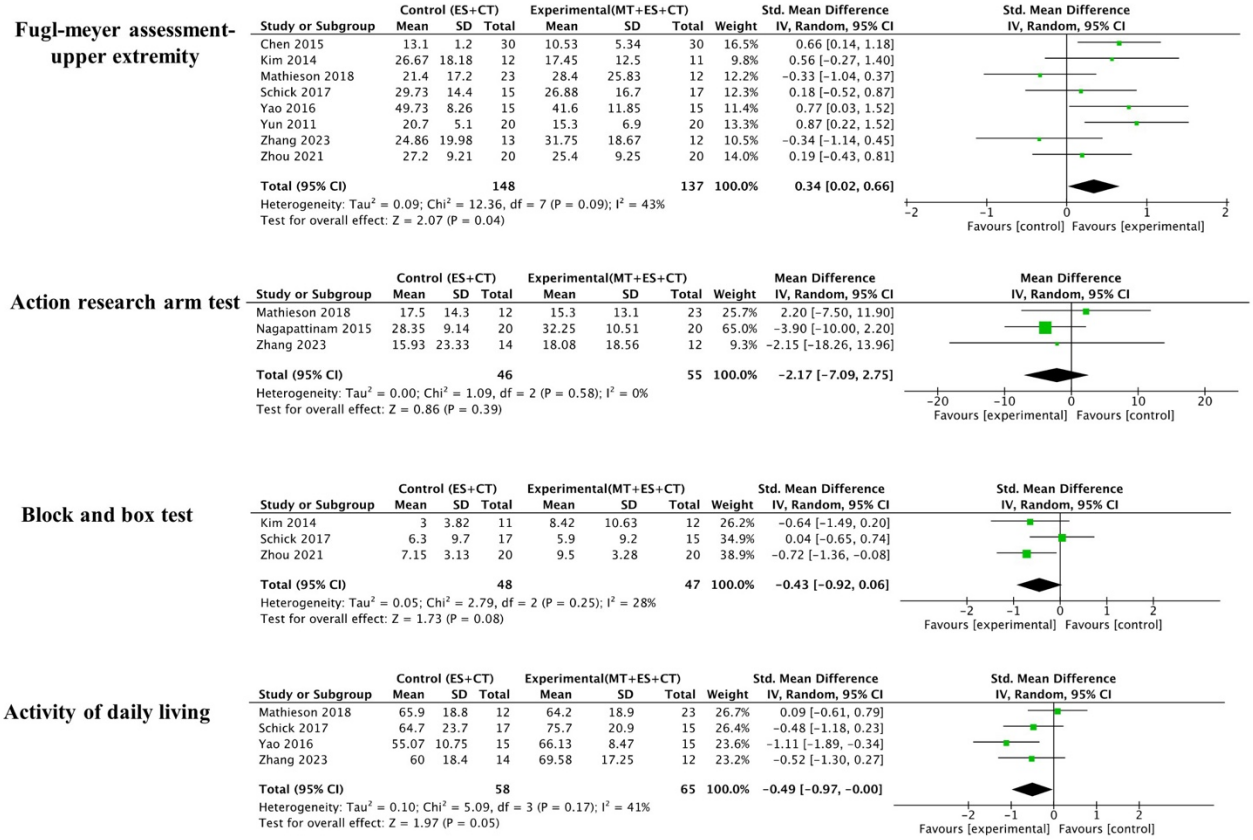


Figure 3.3 Meta -analyses of the effects of MT with ES and CT vs. ES and CT on Fugl-Meyer Assessment-Upper Extremity, Action Research Arm Test, Block and Box Test, and Activity of Daily Living based on International Classification of Functionality, Disability, and Health in people with stroke at the end of treatment.

Table 3.4 Quality of Evidence (Grading of Recommendations Assessment, Development, and Evaluation) (MT + ES + CT vs. ES + CT)

MT+ES + CT vs. ES + CT							
Number of studies (patients)	SMD (95%CI)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of Evidence
Fugl-Meyer Assessment-Upper Extremity							
8(285)	0.34 (0.02-0.66) *	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕⊕O Low
Action Research Arm Test							
3(101)	2.17 (-2.75-7.09)	Not serious	Not serious	Not serious	Serious[b]	Not serious	⊕⊕⊕O Moderate
Box and Block Test							
3(95)	0.43 (-0.06-0.92)	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low
Activities of Daily Living							
4(123)	0.49 (0.00-0.97)	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low

*: Statistically significant ($p < 0.05$); a: downgraded one level for serious risk of bias; b: downgraded one level for serious imprecision.

3.4.4.3 Comparing the effects of MT with ES and CT with MT and CT on body function, activity, and participation domain outcomes

Total 11 studies (Kim et al., 2023; Lee et al., 2015; Lin (a) et al., 2014; Lin (b) et al., 2014; Lu et al., 2018; Mathieson et al., 2018; Nagapattinam et al., 2015; Xu et al., 2020; Yun et al., 2011; Zhang et al., 2023; Zhou et al., 2021) investigated the effects of MT with ES and CT on the recovery of upper extremity motor function and health-related quality of life in people with stroke compared with MT and CT (Figure 3.4). The results of GRADE assessment for this comparison are presented in Table 3.5. The GRADE assessment was downgraded one level for serious risk of bias and imprecision, respectively. The certainty of the evidence for outcomes were assessed with low according to the GRADE assessment.

Moderate significant effects were observed to favour MT with ES and CT for upper extremity impairment assessed by FMA-UE in people with stroke compared to MT and CT (SMD 0.4, 95% CI 0.05-0.75, $P = 0.02$, $I^2 = 57\%$). A sensitivity analysis was conducted by moving one trial (Yun et al., 2011), and significant effect was yielded to favour the MT with ES and CT for upper extremity impairment compared with MT and CT (SMD 0.27, 95% CI 0.01-0.52, $P = 0.04$, $I^2 = 9\%$) with low heterogeneity. No significant effects were observed to favour MT with ES and CT for spasticity assessed by Modified Ashworth Scale in people with stroke compared with MT and CT (MD 0.00, 95% CI -0.18-0.18, $P = 1.0$, $I^2 = 0\%$). Significant effects were observed to favour MT with ES and CT for upper extremity gross gripping function assessed by Action Research Arm Test in people with stroke compared with MT and CT (MD 5.7, 95% CI 1.35-10.05, $P = 0.01$, $I^2 = 0\%$). No significant effects were observed to favour MT with ES and CT for upper extremity dexterity assessed by Block and Box Test in people with stroke compared with MT and CT (SMD 0.32, 95% CI -0.07-0.7, $P = 0.11$, $I^2 = 13\%$).

No significant effects were observed to favour MT with ES and CT for Activity of Daily Living in people with stroke compared with MT and CT (SMD 0.40, 95% CI -0.08-0.88, $P = 0.10$, $I^2 = 67\%$) with high significant heterogeneity ($P = 0.006$). Sensitivity analysis was conducted by moving two trials (Lin (a) et al., 2014; Lu et al., 2018), and opposite significant effect was yielded to favour MT with ES and CT for Activity of Daily Living in people with stroke compared with MT and CT (SMD 0.4, 95% CI 0.08-0.72, $P = 0.02$, $I^2 = 8\%$) with low heterogeneity. Only one study (Lin (b) et al., 2014) reported the improvement of MT with ES and CT in the difficulty level of the paretic upper extremity use in daily life living assessed by Motor Activity Log in comparison to MT and CT ((SMD -0.2, 95%CI - 0.94 to 0.55) for Amount of Use and (SMD -0.34, 95%CI -1.09 to 0.41) for Quality of Movement, respectively).

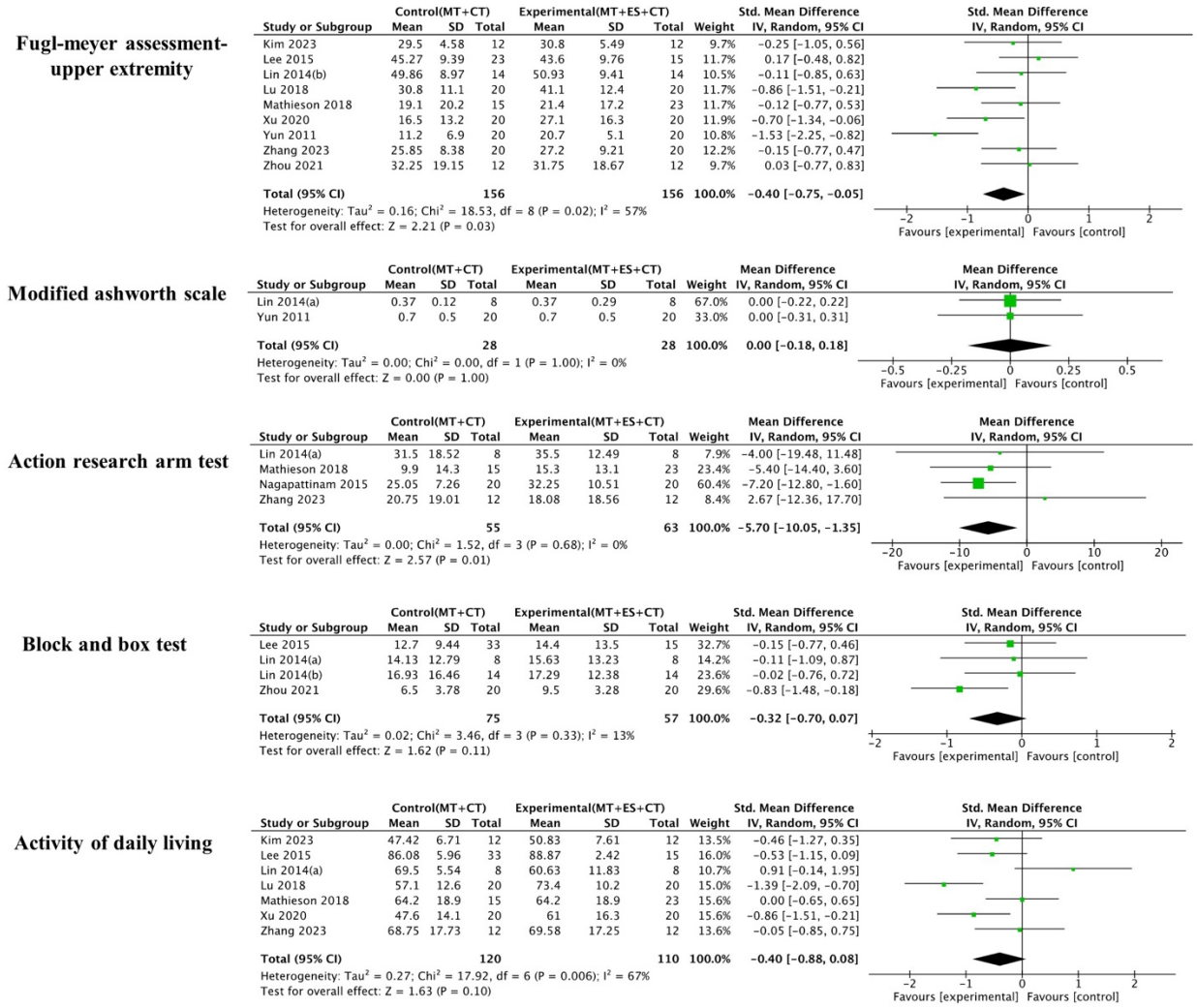


Figure 3.4 Meta-analyses of the effects of MT with ES and CT vs. MT and CT on Fugl-Meyer Assessment-Upper Extremity, Modified Ashworth Scale, Action Research Arm Test, Block and Box Test, and Activity of Daily Living based on International Classification of Functionality, Disability, and Health in people with stroke at the end of treatment.

Table 3.5 Quality of Evidence (Grading of Recommendations Assessment, Development, and Evaluation) (MT + ES + CT vs. MT + CT)

MT+ES + CT vs. MT + CT							
Number of studies (patients)	SMD (95%CI)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of Evidence
Fugl-Meyer Assessment-Upper Extremity							
9(312)	0.40(0.05-0.75) *	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low
Modified Ashworth Scale							
2(56)	0.00(-0.18-0.18)	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low
Action Research Arm Test							
4(118)	5.7(1.35-10.05) *	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low
Box and Block Test							
4(132)	0.32(-0.07-0.7)	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low
Activities of Daily Living							
7(231)	0.40(-0.08-0.88)	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low

*: Statistically significant ($p < 0.05$); a: downgraded one level for serious risk of bias; b: downgraded one level for serious imprecision.

3.4.5 Subgroup analysis

Figure 3.5 demonstrated that MT with ES and CT had a moderate significant effect for upper extremity impairment assessed by FMA-UE in acute/subacute (SMD 0.56, 95% CI 0.1-1.01, $P = 0.02$, $I^2 = 63\%$), but not chronic stroke (SMD 0.03, 95% CI -0.39-0.45, $P = 0.88$, $I^2 = 0\%$) compared with MT and CT. A sensitivity analysis was conducted by moving one trial (Yun et al., 2011) and similar significant effect was achieved to favour MT with ES and CT for upper extremity impairment assessed by FMA-UE in people with acute/subacute stroke (SMD 0.38, 95% CI 0.04-0.72, $P = 0.03$) with low heterogeneity ($I^2 = 22\%$, $P = 0.27$) compared with MT and CT. The results of GRADE assessment for this subgroup analysis is presented in Table 3.6. The GRADE assessment were downgraded one level for serious risk of bias and imprecision, respectively. The certainty of the evidence for outcomes with low according to the GRADE assessment.

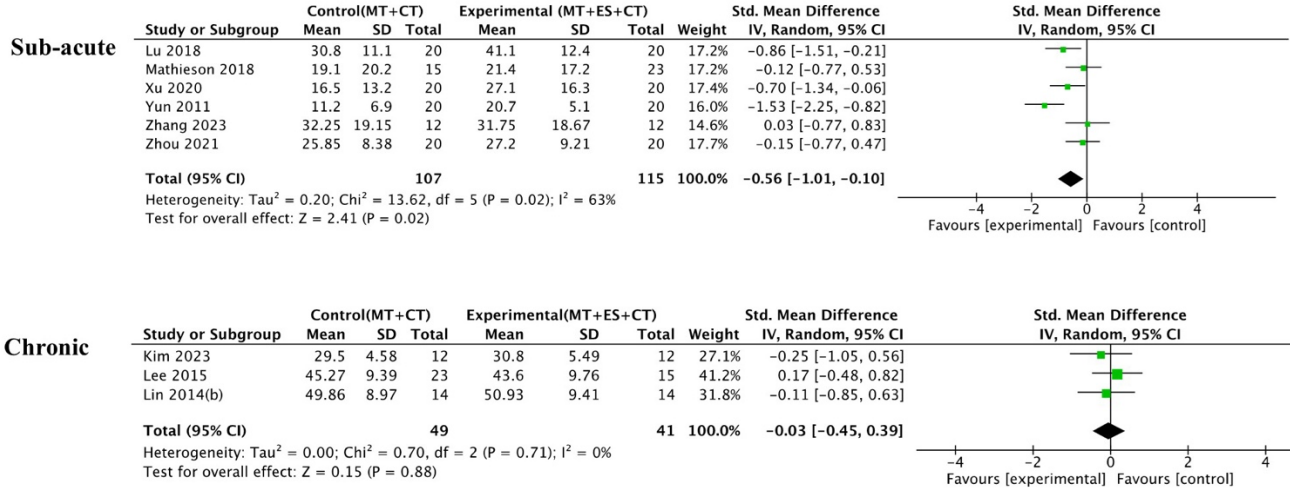


Figure 3.5 Subgroup meta-analysis of the effects of MT with ES and CT vs. MT and CT group on Fugl-Meyer Assessment-Upper Extremity in people with subacute and chronic stroke at the end of treatment

Table 3.6 Quality of Evidence (Grading of Recommendations Assessment, Development, and Evaluation) (MT + ES + CT vs. MT + CT)

(Subgroup analysis)

Number of studies (patients)	SMD (95%CI)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of Evidence
Subgroup analysis- Fugl-Meyer Assessment-Upper Extremity -Acute/Subacute Phase							
5(198)	0.66(0.17-1.15) *	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low
Subgroup analysis- Fugl-Meyer Assessment-Upper Extremity -Chronic phase							
2(66)	-0.05(-0.54-0.44)	Serious[a]	Not serious	Not serious	Serious[b]	Not serious	⊕⊕OO Low

*: Statistically significant ($p < 0.05$); a: downgraded one level for serious risk of bias; b: downgraded one level for serious imprecision

3.4.6 Meta-regression analysis

Only the FMA-UE outcome variable had sufficient number of studies (n = 15) to perform the meta-regression analysis. The result demonstrated that training dosage of combined MT and ES had no significantly correlation with the pooled effect size for the FMA-UE outcome measure in people with stroke (r = 0.48, P = 0.07).

3.4.7 Sensitivity analysis

The results of sensitivity analysis are presented in Table 3.7. Five sensitivity analyses were conducted by removing studies to explore the source of homogeneity. All the results of the sensitivity analysis favour the effects of MT combined with ES for upper extremity motor impairment assessed by FMA-UE and Activity of Daily Living in people with stroke with low to no homogeneity.

Table 3.7 The results of sensitivity analysis

Comparisons	Outcome measure	SMD and 95% CI	Heterogeneity	Results	Excluded studies
MT+ES + CT vs. CT	Fugl-Meyer Assessment-Upper Extremity	1.89 (1.52-2.26)	I^2 = 0%	Similar significant effect	Zhang 2023
MT+ES + CT vs. CT	Activity of Daily Living	0.81 (0.28-1.34)	I^2 = 29%	Similar significant effect	Yao 2017
MT+ES + CT vs. CT	Activity of Daily Living	0.4 (0.08-0.72)	I^2 = 8%	Opposite significant effect	Chen 2014, Lu 2018
MT+ES + CT vs. CT	Fugl-Meyer Assessment-Upper Extremity	0.27 (0.01-0.52)	I^2 = 9%	Similar significant effect	Yun, 2011
MT+ES + CT VS. MT + CT (Acute/Subacute stroke)	Fugl-Meyer Assessment-Upper Extremity	0.38 (0.04-0.72)	I^2 = 22%	Similar significant effect	Yun 2011

3.4.8 Publication bias

As the FMA-UE with sufficient number of studies (n = 15), we used the FMA-UE to explore the publication bias by the Egger's regression test and the result demonstrated that no significant publication bias was detected (coefficient = 1.23, 95% CI = - 4.97 - 7.21, P = 0.48) in this systematic review and meta-analysis.

3.5 Discussion

We conducted an updated systematic review and meta-analysis to investigate the synergistic effects of MT combined with ES on improving recovery of upper extremity motor function and health-related quality of life based on International Classification of Functioning, Disability, and Health framework in people with stroke. The results demonstrated that MT with ES and CT was superior to CT alone, ES and CT, and MT and CT for improving upper extremity impairment assessed by FMA-UE based on the impairment level. MT with ES and CT was superior to CT alone to improve activity of daily living performance assessed by Functional Independent Measure and Modified Barthel Index, and MT and CT to improve upper extremity gross gripping function assessed by Action Research Arm Test based on the activity level. MT with ES and CT was significantly superior to MT and CT for improving the upper extremity impairment assessed by FMA-UE in people with acute/subacute stroke but not chronic stroke.

3.5.1 Comparing the effects of MT + ES + CT with CT alone

MT with ES and CT was superior to CT alone to improve the upper extremity impairment assessed by FMA-UE and Activity of Daily Living assessed by Functional Independent Measure and Modified Barthel Index in people with stroke on Body Function and Activity domain, respectively. MT with the illusion that paretic hand with normal movement of non-paretic hand during bimanual movement could significantly induce the activation of contralesionally and ipsilesionally sensorimotor cortex in people with stroke (Hamzei et al., 2020). ES with sensory afferent input could also induce the ipsilesionally primary motor cortex and contralesionally sensorimotor cortex in people with stroke (Guo et al., 2022). MT combined with ES simultaneously could increase the activation of sensorimotor cortex representation in stroke survivors (Saavedra-García et al., 2021). The plasticity of sensorimotor cortex had been demonstrated significantly correlated with motor learning (Ostry et al., 2010). Hence, MT combined with ES could statically significant improve upper extremity impairment in this study. However, the upper extremity impairment improvement did not reach a minimal clinically important change (10 points of FMA-UE for sub-acute stroke (Lundquist & Maribo, 2017) and 4 points of FMA-UE for chronic stroke (Ghaziani et al., 2018)) in this study. The possible reason may be that CT alone could have additional effects in improving upper extremity impairment in people with stroke in this study, which may lead to additional effects of MT with ES could not reach the minimal clinically important change in people with stroke in this study.

Our study also shown that MT with ES and CT could improve the Activity of Daily Living performance assessed by Functional Independent Measure and Modified Barthel Index in people with stroke compared with CT alone. CT training could add the effects in improving the performance of daily life activity tasks in people with stroke through increasing muscle strength and range of motion of upper extremity in people with stroke. On top of above reason,

MT combined with ES could augment the additional effects in improving the performance of daily life activities in people with stroke. Moreover, MT combined with ES with visual stimulation and cutaneous sensory input simultaneously could increase the accuracy of task-relevant sensory information gathering and increase the confidence of performing the motor tasks in daily life living activities in stroke survivors (Wolpert et al., 2011). Hence, the improvement of upper extremity impairment by MT combined with ES and CT could transfer to improve the ability in daily life tasks in people with stroke in this study.

3.5.2 Comparing the effects of MT + ES + CT with ES + CT

MT with ES and CT was only superior to ES and CT to improve the upper extremity impairment assessed by FMA-UE on the Body domain in people with stroke in our study. MT could induce mirror neuron system (e.g., inferior parietal lobule and inferior frontal gyrus) in human (Iacoboni et al., 1999), which has been proposed to be an important neural substrate to prime motor cortex for actions of understanding, imitation, and motor learning (Pineda, 2008). Hence, the addition of MT may provide additional benefits for recovery of upper extremity impairment in people with stroke. However, the addition of MT could not improve the activity of daily living performance assessed by Functional Independent Measure and Modified Barthel Index in people with stroke in this study. The possible reason may be the improvements in the upper extremity impairment may not be sufficient to improve the performance of activity daily living as it requires the coordination of different joints, e.g., motor control of trunk and balance ability of lower limb, in people with stroke.

3.5.3 Comparing the effects of MT + ES + CT with MT + CT

MT with ES and CT was superior to MT and CT to improve the upper extremity impairment assessed by FMA-UE and gross gripping function assessed by Action Research Arm Test on Body Function and Activity domain, respectively, in people with stroke in this study. The ES with cutaneous sensory input could significantly induce the activation of sensory-motor cortex in people with stroke (Guo et al., 2022), which plays an important role in motor learning and execution. Meanwhile, the cutaneous sensory inputs induced by ES could give information to monitor the body position in space, which could give benefits for upper extremity motor control (Wu et al., 2005). Hence, the addition of ES could provide additional benefits for recovery of upper extremity impairment in people with stroke. Moreover, this benefits could transfer into the improvement of upper extremity gross gripping function assessed by Action Research Arm Test in stroke survivors. The possible reason may be that the addition of ES applied to the elbow or wrist of the paretic arm with direct stimulation could induce the motor intension to perform voluntary movements (Shen et al., 2015), which could promote the motor relearning in stroke survivors (Guo et al., 2022).

3.5.4 Subgroup analysis

For the subgroup analysis, MT with ES and CT had significant effects in the upper extremity impairment assessed by FMA-UE in people with acute/subacute but not chronic stroke compared with MT and CT. Hakon et al. (2018) shown that multisensory stimulation could induce significant more resting-state functional connectivity of different distinct brain regions, which could lead to a fast recovery of brain function and improvements in impairment of tactile and proprioceptive function in a mouse model of early two days after stroke. Hence, this

subgroup analysis suggested that multiple sensory stimulation has an important clinical significance for people with acute/subacute stroke.

3.5.5 Meta-regression analysis

This is the first study to explore the relationship between the effect size and therapy dosage of MT combined with ES in people with stroke. The meta-regression analysis shown that there is no significant linear correlation between the pooled effect size of FMA-UE and the dosage of MT combined with ES (total duration of each training session multiplied by the frequency and the number of weeks) in this study. The limited number of included studies (n = 15) may have lacked sufficient power to detect a significant correlation and to recalculate the dosage response based on different dosage groups. Moreover, the total training sessions may be not the best parameter to explore the significant correlations between the pooled effect size and the dosage of MT combined with ES.

3.5.6 Limitations

First, an optimal training protocol may be very important for achieving maximum treatment effects (Guyatt et al., 2011), however, limited number of included studies and lack of sufficient training details about the ES parameters (e.g., frequency or intensity of ES) would hinder an optimal training protocol identification. Second, the sequence of priming would be important to determine the interaction direction between MT and ES (Stoykov, 2015). However, limited information of the application sequence of MT and ES, and MT combined with ES simultaneously in major included studies hinder an optimal sequence of application of MT and ES for the recovery of upper extremity motor function in people with stroke. Third, major

included studies were assessed with high risk of bias and very low certainty of evidence, which may decrease the accuracy of the results with over-estimate the true effects and false positive effects. Fourth, some reporting data could not be extracted from the graphs or figures or obtained the raw data from the authors , resulting in the missing of relevant information and a limited sample size for this meta-analysis. Therefore, future research should incorporate a larger number of studies to provide more robust evidence on the effects of MT combined with ES for the recovery of upper extremity motor function in people with stroke. Fifth, the CT were included in this study. However, the duration of CT in this study varied across all included studies. Moreover, the effects of CT intervention was not the focus in this study. Hence, the CT effects alone could not be determined in this study.

3.6 Conclusion

In conclusion, MT with ES and CT was superior to CT alone, ES and CT, and MT and CT for improving upper extremity impairment assessed by FMA-UE based on the impairment level. MT with ES and CT was superior to CT alone to improve activity of daily living performance assessed by Functional Independent Measure and Modified Barthel Index, and MT and CT to improve upper extremity gross gripping function assessed by Action Research Arm Test based on the activity level. MT with ES and CT was significant superior to MT and CT for improving the upper extremity impairment assessed by FMA-UE in people with acute/subacute stroke but not chronic stroke. This systematic review and meta-analysis provided overall significant effects of MT combined with ES as an effective priming technique on the improvement of recovery of upper extremity motor function in people with stroke, especially for people with sub-acute stroke. However, high-quality studies with larger sample sizes are warranted to

clarify the uncertain effects of MT combined with ES on different aspects of recovery after stroke in this study.

CHAPTER FOUR

Self-Perceived Upper Extremity Motor Function Predicts Health-Related Quality of Life in People with Chronic Stroke

The study in this chapter has been published in a peer-reviewed journal.

Pan Hong, Ng SSM, Liu TW, Lam SSL, Chan CCC, Li CSK, Chung RCK, Lai CWK, Ng WWL, Tang MWS, Hui E, Woo J (2024). Self-perceived upper extremity motor function predicts health-related quality of life in chronic stroke survivors. *Disability and Rehabilitation*, 47(1):186-193. (Appendix 4.1)

Parts of content has been presented at one international conferences.

Pan Hong, Liu TW, Ng SSM. Self-perceived upper extremity motor function predicts health-related quality of life after stroke in people with chronic stroke, *Rehabilitation Medicine Society of Australia and New Zealand 6th Annual Scientific Meeting*, *2023,* Hobart. (Appendix 4.2)

4.1 Abstract

Upper extremity motor function plays a critical role in the execution of daily life activities and contributes to the dexterity of daily activity tasks and health-related quality of life (HRQOL) in stroke survivors. Upper extremity motor functions can be evaluated using both observation-based and self-perceived outcome measures. The self-perceived upper extremity function may reflect the subjective views of the upper extremity motor function level to help the clinicians to design and prescribe personalized intervention to improve the effects of stroke rehabilitation. However, the relationship between self-perceived upper extremity function and HRQOL in stroke survivors remains uncertain. This study aimed to investigate the independently relative contributions of self-perceived upper extremity function to HRQOL in stroke survivors.

Total 95 chronic stroke survivors aged more than 50 years were included. For all people with stroke, the self-perceived upper extremity function and HRQOL were assessed by Upper Extremity Functional Index (UEFI) and Stroke Impact Scale (SIS), respectively. Other outcome measures used in the predictive model in this study include paretic hand grip strength, Fugl-Meyer Upper Extremity Assessment (FMA-UE), Wolf Motor Function Test (WMFT).

The correlation analysis showed that the UEFI score, a measure of self-perceived upper extremity function, had the strongest significant positive correlation with the SIS scores among all tested outcome variables. The analysis showed that objective outcome measures, FMA-UE and WMFT, were not significant predictors for SIS scores. The final regression model based on the age, using walking aids, paretic side grip strength, FMA-UE score, WMFT score, and UEFI score predicted 63.1% of the variance of SIS score.

The findings suggest that self-perceived upper extremity function was the best significant predictor of HRQOL in people with stroke, accounting 18.8% independently change of the variance. The self-perceived upper extremity motor function involving in daily life tasks is a crucial component to be included in stroke rehabilitation to enhance the quality of life and participation in stroke survivors.

4.2 Introduction

Previous chapter 3 had shown that mirror therapy combined with electrical stimulation could significantly improve upper extremity impairment and recovery of motor function in people with sub-acute stroke. As HRQOL is substantially impaired (Chen et al., 2015), to improve the overall health status of stroke survivors in various life domains is an important goal of stroke rehabilitation. However, the application of mirror therapy combined with transcutaneous electrical nerve stimulation mainly focus on improving upper extremity impairment and recovery of motor function, and it does not directly have effects on the HRQOL in people with chronic stroke survivors. To hypothesize that the use of mirror therapy combined with transcutaneous electrical nerve stimulation could improve the level of HRQOL, the research gap about the roles of upper extremity motor function play in the HRQOL in chronic stroke survivors should be filled.

The upper extremity motor function plays an important role in the daily life activity execution, contributing significantly to the daily life manual dexterity for specific task (Lieshout et al., 2020), which could induce more involvement in improving the HRQOL and social participation (Morris et al., 2013). Previous study had identified that observation-based outcome measure of upper extremity functional status assessed by FMA-UE was a significant

predictor of HRQOL, accounting for about 40% of the variances, in people with stroke (Chen et al., 2015). However, compared with observation-based assessments, the self-report assessments for the upper extremity motor function could provide additional values that it can reflect the subjective feeling of people with stroke about their views of current recovery level of upper extremity motor function (Reeves et al., 2018). Moreover, Essers et al. (2021) demonstrated that up to almost 23% people with stroke show high level observed upper extremity motor function corresponds to low level self-perceived recovery of motor function even at 12-month post stroke phase, which shows that the observation-based upper extremity motor function does not match the self-perceived upper extremity motor function level. Hence, evaluation of self-perceived upper extremity motor function could be more precise to reflect the effects of interventions and the upper extremity motor function status in stroke survivors.

The SIS, compared with other self-reported questionnaires (e.g., 36-Item Short-Form Survey (Zhang et al., 2012), covers more life domains, e.g., cognitive function, which is essential for the daily life activity execution, and is used widely to assess HRQOL in acute (Duncan et al., 2003), subacute (MacIsaac et al., 2016), and chronic (Zhang et al., 2012) stroke survivors. Hence, the SIS could be more precise to evaluate the HRQOL in people with stroke. The UEFI had been demonstrated excellent reliability and validity in people with stroke as a self-perceived upper extremity motor function assessment tool (Pan et al., 2023). Compared with another self-perceived questionnaire evaluating unilateral recovery of paretic upper extremity motor function, e.g., Motor Activity Log, the UEFI involves in more bilaterally upper extremity motor function on daily life living activities, which could reflect actual amount use of the paretic arm in daily life living activity. Hence, the UEFI is used to measure the self-perceived bilateral upper extremity motor function in chronic stroke survivors.

Therefore, this study aimed to explore whether the self-perceived upper extremity motor function assessed by UEFI makes an independent contribution to HRQOL assessed by SIS; and to quantify its relative contribution to HRQOL when observation-based outcome measures of upper extremity motor function were also included in this study in chronic stroke survivors.

4.3 Method

4.3.1 Study Design

The study protocol was approved by the Departmental Research Committee of the Hong Kong Polytechnic University (approval number: HSEAR2021011002) and conducted in accordance with the Declaration of Helsinki (1975 and its revision in 1983) for human experimentation.

4.3.2 Participants

The assessment venue of this trial was a university-based rehabilitation centre. People with stroke were recruited from local self-help groups or a community rehabilitation network through poster advertisements. People with stroke survivors were included in this study if they were aged between 50 and 80 years; had experienced one single stroke, confirmed by magnetic resonance imaging, or computerized tomography, with at least 1 year stroke history; scored more than 7 on the Chinese version of the Abbreviated Mental Test (Hodkinson, 1972); could have a good command of Cantonese; could initiate at least minimal anti-gravity movement in their paretic arm shoulder; and could independently walk for at least 10 m with or without an assistive device. People with stroke were excluded if they had any other unstable medical conditions (e.g., angina pectoris of cardiovascular, or arthritis of musculoskeletal disease) or

other conditions with medications (e.g., Parkinson's disease or Multiple Sclerosis) that potentially affect the upper limb motor function and had any aphasia or hearing impairment that could affect the accurate data collection.

4.3.3 Demographic Data

Several demographic data were collected: (1) characteristics data, e.g., age, gender, living arrangements, body mass index; (2) stroke-related variables, e.g., stroke duration, cause of stroke, hemiplegic side, and using of walking aids; (3) stroke mobility-related outcome measures, e.g., paretic maximal grip strength, FMA-UE, WMFT, UEFI, and SIS.

4.3.4 Outcome Measures

4.3.4.1 Paretic maximal grip strength

The maximum grip strength is an appropriate measurement to quantify upper extremity weakness and recovery in older adults (Abizanda et al., 2012) and stroke survivors (Bertrand et al., 2015). The maximum grip strength was evaluated using a dynamometer to squeeze the dynamometer with full strength for 5 seconds in each of three times with standardised sitting position (Abizanda et al., 2012; Innes, 1999). The non-paretic hand was assessed first. The mean non-paretic and paretic hand grip strength was calculated from three trials used for data analysis. The maximal paretic grip strength assessment has previously demonstrated excellent test–retest reliability (ICC = 0.91-0.99) for the paretic hand in stroke survivors (Boissy et al., 1999).

4.3.4.2 Fugl-Meyer Assessment for Upper Extremity (FMA-UE)

The FMA-UE, one of the most widely used quantitative outcome measure, assesses the upper extremity motor impairment from the proximal to the distal part in stroke survivors (Fugl-Meyer et al., 1975). The FMA-UE comprises 33 items on an ordinal scale, with total score of 66. The FMA-UE has been demonstrated excellent inter-rater (ICC = 0.93-0.992) and intra-rater reliability (ICC = 0.995- 0.996) in stroke survivors (Duncan et al., 1983).

4.3.4.3 Wolf Motor Function Test (WMFT)

The WMFT is used to assess the upper extremity motor ability and functional tasks in stroke survivors(Wolf et al., 2005). The functional ability score is rated using a 6-point ordinal scale on 15 items, with a maximum score of 75. The WMFT functional ability score has been demonstrated excellent inter-rater reliability (ICC = 0.93) and internal consistency in stroke survivors (Morris et al., 2001).

4.3.4.4 Upper Extremity Functional Test (UEFI)

The Chinese version of UEFI (C-UEFI) is used to assess the self-perceived difficulty in the performance of upper extremity motor function in daily life activity in stroke survivors (Pan et al., 2023). The total score of C-UEFI ranges from 0 to 59, with a higher score indicating better self-perceived upper extremity motor function in people with stroke. The C-UEFI had been demonstrated good test-retest reliability ($ICC_{3,1}$= 0.87) and excellent internal consistency (Cronbach's $\alpha = 0.92$) in stroke survivors (Pan et al., 2023).

4.3.4.5 Stroke Impact Scale (SIS)

The SIS is used to assess the subjective level of disability and health-related quality of life in people with stroke (MacIsaac et al., 2016). The SIS includes 59 items in eight domains and an extra question on stroke recovery. The total scores were generated for each domain (Mulder & Nijland, 2016) with the ranging from 0 to 100. The average score of total 9 domains was calculated (Norouzi-Gheidari et al., 2019). The higher scores indicate better self-reported HRQOL. The SIS has been demonstrated good to excellent test-retest reliability (ICC = 0.7 - 0.92) and internal consistency (Cronbach's $\alpha = 0.90$) in stroke survivors (Mulder & Nijland, 2016).

4.3.5 Statistical Analysis

The SPSS software version 26.0 was used to analysis the data. The data normality was tested by using Shapiro–Wilk Test. The significance level was set at $\alpha = 0.05$ (two-tailed). For the multiple regression analysis, as five outcome measures were tested on the same participants, the Bonferroni-corrected threshold was calculated ($0.05/5 = 0.01$) to decrease the risk of a type I error. Descriptive statistics were used for demographic data. Pearson's and Spearman's correlation coefficients for normally and non-normally distributed data, respectively, were calculated for the correlation between SIS scores and other outcome measures. In order to control the sociodemographic parameters, e.g., age, gender, living arraignments, body mass index, stroke duration, cause of stroke, hemiplegic side, and the use of walking aids, partial correlation coefficients were calculated to test the correlation between SIS scores and other stroke-related outcome measures. A forced entry method of multiple linear regression was used to determine the proportion of variability in HRQOL (SIS scores) explained by the four independent variables (paretic maximal grip strength, FMA-UE, WMFT, and C-UEFI scores).

The analysis was calculated to identify the variable with most predictive power for HRQOL assessed by SIS scores, which was indicated by the largest standardized regression coefficients.

4.3.6 Sample Size Calculation

A linear regression model was used to calculate the sample size (Guan et al., 2023). Four predictors (independent outcome measures e.g., paretic maximal grip strength, FMA-UE, WMFT, C-UEFI) were included in this linear regression model. The effect size (*d*) was selected as 0.6 corresponding to about an effect size (*f*) of 0.4 and the power of analysis was selected as 0.8. Hence, 85 stroke survivors were needed for this predication analysis. Considering 10% dropout rate, at least 95 stroke survivors were needed.

4.4 Results

4.4.1 Characteristics of stroke survivors

The characteristics of the stroke survivors were presented in Table 4.1. Total 53 (56%) males and 42 (44%) females were included in this study. Total 65 ischemic strokes (68%) and 30 haemorrhagic strokes (32%) were included in this study. The mean age and average stroke duration of people with stroke were 63.84 ± 6.4 and 6.66 ± 4.35 years, respectively. Total 45 left hemiplegia (47%) and 50 right hemiplegia (53%) were included in this study. The body mass index was 25.24±11.51 kg/m^2, with the range from 18.66 to 132.67. About 69 (73%) of people with stroke needed the use of walking aids for their daily life living. Total 85 (89%) people with stroke lived with their family members, carers, or friend and 10 (11%) people with stroke lived alone.

For the included outcome measures, the mean (SD) score of paretic hand grip strength was 14.34 (8.24) kg, which indicates that the participants had muscle weakness of hand and forearm in their chronic phase after stroke (Ademoyegun et al., 2022). The mean (SD) FMA-UE, WMFT, and C-UEFI scores were 44.59 (18.12), 51.68 (21.20), and 46.02 (11.22), respectively, which indicates that the people with stroke had limited capacity of full recovery of upper extremity motor function (Hoonhorst et al., 2015). The mean (SD) score of SIS was 59.77 (17.58), which indicates that the people with stroke perceived overall moderate health impact on their daily life living (Duncan et al., 1999; Guidetti et al., 2014).

Table 4.1 Characteristics of the people with stroke (n = 95)

Characteristics	**Mean ± SD (range) or No. (%)**
Age (Years)	63.84±6.4 (50-76)
Sex (Male/ Female)	53 (56%)/42 (44%)
Living arrangement (Alone/With family members, carer, or friend)	10 (11%)/85 (89%)
Body mass index (kg/m^2)	25.24±11.51 (18.66-132.67)
Stroke duration (Years)	6.66±4.35 (0.58-23.17)
Cause of stroke (Ischemic/haemorrhagic/Unknown or mixed)	65 (68%)/30 (32%)/0 (0%)
Hemiplegic side (Left/ Right)	45 (47%)/50 (53%)
Use of walking aids (Yes/No)	69 (73%)/26 (27%)
Grip Strength (Paretic Side) (kg)	14.34±8.24 (2.95-39.3)
Fugl-Meyer Upper Extremity Assessment (FMA-UE) (Total score)	44.59±18.12 (4-66)
Wolf Motor Function Test (WMFT) (Paretic Side) (Total score)	51.68±21.20 (1-75)
Upper Extremity Functional Index (UEFI) (Total score)	46.02±11.22 (14-60)
Stroke Impact Scale (SIS) (Total Score)	59.77±17.58 (15.35-93.75)

4.4.2 Relations between SIS scores and other variables

The correlations and partial correlations of SIS scores and other outcome measures were presented in Table 4.2 and 4.3, respectively. Without control the demographic characteristics, the results shown that only age (r = - 0.276, P = 0.007) and use of walking aids (r = - 0.324, P = 0.001) had significantly correlations with SIS scores. The paretic hand grip strength, FMA-UE, WMFT of paretic hand, and C-UEFI had significant positive moderate to strong correlation with SIS scores, with the r from 0.544 to 0.687 (P < 0.001). By controlling the demographic characteristics, the partial correlation results shown that the paretic hand grip strength, FMA-UE, WMFT of paretic hand, and C-UEFI had significant positive fair to strong correlation with SIS scores, with the r from 0.439 to 0.629 (P < 0.001).

Table 4.2 Correlations between SIS Scores and other variables (n = 95)

Variables	Spearman r	P Value
Age	-0.276**	0.007
Sex	-0.012	0.911
Body mass index (kg/m^2)	-0.088	0.394
Years since stroke	-0.036	0.728
Type of stroke (Ischemic/Hemorrhagic/Unknown or Mixed)	-0.033	0.748
Paretic side (Left/ Right)	0.241	0.019
Use of walking aids (Yes/No)	-0.324**	0.001
Living arrangement (Alone/With family members, carer, or friend)	0.139	0.178
Grip Strength (Paretic Side)	0.577**	<0.001
Fugl-Meyer Upper Extremity Assessment (FMA-UE) score	0.565**	<0.001
Wolf Motor Function Test (WMFT) (Paretic Side) score	0.544**	<0.001
Upper Extremity Functional Index (UEFI) score	0.687**	<0.001

Notes: **. Correlation is significant at the 0.01 level (2-tailed).

Table 4.3 Partial correlation coefficients (after controlling for age, affected side, and use of walking aids) between SIS and other variables (n = 95)

Variables	Partial correlation Coefficients with SIS	*P* Value
Grip Strength (Paretic Side)	0.594**	<0.001
Fugl-Meyer Upper Extremity Assessment (FMA-UE)	0.471**	<0.001
Wolf Motor Function Test (WMFT) (Paretic Side)	0.439**	<0.001
Upper Extremity Functional Index (UEFI)	0.629**	<0.001

Notes:

**. Correlation is significant at the 0.01 level (2-tailed).

4.4.3 C-UEFI and SIS scores

The multiple linear regression model results were presented in Table 4.4. The total regression model could predict 60.3% of the variance in SIS scores (6, 81 = 23.06, $P < 0.001$). The paretic hand grip strength and C-UEFI scores were identified as significant predictors for SIS score in this study. Among those two significant predictors, the C-UEFI score was the best predictor of SIS score as indicated by the magnitude of the standardised regression coefficient ($\beta = 0.487$), with *P* value less than 0.001. The statistics of Variance Inflation Factor (VIF) were ranged from 1.100 (Age) to 6.808 (FMA-UE) for all variables, which indicated that there was no redundancy among all included variables.

Table 4.4 Multiple linear regression analyses (forced entry) relating SIS and other variables ($n = 95$)

Model No.	Independent Variables	*B*	*β*	*P* value	R^2 (R^2 Adjusted)	R^2 Change

Model 1	Age	-0.443	-0.171	0.044	0.431 (0.41)	0.431
	Using Walking Aids	-5.699	-0.161	0.061		
	Grip Strength (Paretic Side)	1.143	0.581	<0.001**		
Model 2	Age	-0.51	-0.197	0.024	0.443 (0.416)	0.012
	Using Walking Aids	-4.278	-0.121	0.18		
	Grip Strength (Paretic Side)	0.96	0.487	<0.001**		
	FMA-UE	0.16	0.155	0.181		
Model 3	Age	-0.505	-0.195	0.027	0.443 (0.417)	0
	Using Walking Aids	-4.162	-0.118	0.198		
	Grip Strength (Paretic Side)	0.971	0.493	<0.001**		
	FMA-UE	0.214	0.208	0.336		
	WMFT	-0.054	-0.061	0.772		
Model 4	Age	-0.436	-0.168	0.02	0.631 (0.603)	0.188
	Using Walking Aids	0.578	0.016	0.833		
	Grip Strength (Paretic Side)	0.707	0.359	<0.001**		
	FMA-UE	0.282	0.274	0.124		
	WMFT	-0.138	-0.154	0.372		
	C-UEFI	0.719	0.487	<0.001**		

Notes:

**. Correlation is significant at the 0.01 level (2-tailed).

Abbreviations: B, unstandardized regression coefficient; ß, standardized regression coefficient.

4.5 Discussion

This is the first study to show that the C-UEFI scores can independently predict their SIS scores in chronic stroke survivors. The finding highlights that the roles of self-perceived upper extremity motor function in daily life living in HRQOL in chronic stroke survivors. The clinical

implication is that improving self-perceived upper extremity motor function in daily life activities could be helpful in promoting better HRQOL in people with chronic stroke.

4.5.1 C-UEFI scores independently predict SIS scores

The C-UEFI scores had good significant positive correlation with SIS scores in people with chronic stroke. The possible reason may be that self-perceived difficulty of upper extremity motor function in daily life living could precisely reflect the actual ability and usage of upper extremity in daily life activity and tasks in people with chronic stroke (Pan et al., 2023).

The final regression model explained total 60.3% of the variance in the SIS scores. The self-perceived difficulty of upper extremity motor function in daily life living was the best independent predictor of SIS scores, accounting for almost 18.8% of the variance in chronic stroke survivors. The C-UEFI includes the evaluation of both basic and instrumental daily life living activities (Ghaffari et al., 2021; Pan et al., 2023). Both basic and instrumental daily life living activities in the C-UEFI require specific skills and abilities to manage daily life living physical needs to live independently at home or community, e.g., dressing, grooming, housekeeping (Juniper & Connor, 2022), maintaining balance (Khan et al., 2022), and body transferring (Lamberti et al., 2017). Engaging in that daily life living activities and regaining the mobility would contribute a lot for the independent living in the participation and improvement in quality of life in people with chronic stroke. Hence, higher performance in daily life living tasks may lead to higher HRQOL and participation in people with chronic stroke. Thus, the score of UEFI can independently predict the SIS score in chronic stroke survivors.

4.5.2 The correlations of SIS score and other outcome variables

For the demographic characteristics, the age and using of walking aids had significant negative correlations with SIS scores. For other outcome measures, the paretic hand grip strength, FMA-UE scores, and WMFT scores had significant positive moderate to strong correlations with SIS scores.

Consistent with previous studies (Bagg et al., 2002; Sturm et al., 2004), the age shown fair negative significant correlation with SIS scores in people with chronic stroke. The possible reason may be that the old age may associated with low physical functioning and slow recovery of motor function with low tolerance and involvement in rehabilitation programme (Bagg et al., 2002). The use of walking aids had fair negative significant correlation with SIS scores. The possible reasons may be that the greater usage of walking aids (e.g., cane) for long period could induce reduced complex motor performance and proprioceptive sense perception of the non-paretic upper extremity in chronic stroke survivors (Son et al., 2012). Son et al. (2012) demonstrated that compared with no cane using group, the people with stroke using cane group shown decreased proprioceptive joint sense (7.35± 2.62 vs. 5.03 ± 2.98, $P = 0.013$), and motor dexterity (27.74 ± 5.07 vs. 21.30 ± 5.9, $P = 0.001$) of the non-paretic upper extremity. Hence, the decreased motor function of the non-paretic upper extremity after a long period of cane usage would impede the bilateral upper extremity activity in daily life tasks in people with chronic stroke. Hence, the age and use of walking of aids may be significant negative correlated with SIS scores in chronic stroke survivors.

The decreased paretic hand grip strength has been demonstrated to associate with a reduce in physical functioning assessed by Timed Up and Go Test (Coefficient = 2.3, 95% confidence

interval = 1.63-3.01, $P < 0.001$) (Chen et al., 2022), which may induce low independence of the involvement in daily life activity and tasks in chronic stroke survivors. The FMA-UE and WMFT mainly evaluate the paretic upper extremity motor control and ability in stroke survivors (Edwards et al., 2012), which are essential for daily life living activity and tasks (Lundquist, 2017). Hence, improving the paretic upper extremity strength, motor control, and motor ability could improve upper extremity daily life performance and health-related status in activity of daily living.

4.5.3 Limitations

This study has several limitations that should be addressed in the future. First, as the regression model only explained 60.3% of the variance in SIS scores and almost 40% of the variance remained unexplained. Hence, future research should investigate other relevant factors, e.g., lower extremity motor function in daily life living and cognition function, to better explain variations in SIS scores. Second, the causal relationship between the improvement of self-perceived upper extremity motor function in daily life living activities and HRQOL in people with chronic stroke could not be built in this cross-sectional study design. Hence, future research should be conducted in controlled clinical trials to investigate the causal relationship. Third, the people with stroke in this study were recruited by local self-help group with a relatively better motor function and high motivation in participating in various activities, which may lead to low generalizability to less able people with chronic stroke. Hence, future research should verify whether these findings can be applicable to lower upper extremity motor function of people with chronic stroke. Fourth, the results indicate that upper extremity daily life activities significantly contributed to HRQOL in chronic stroke survivors. However, C-UEFI contains basic and instrumental activity daily living, whether basic or instrumental activity

daily living have a greater impact on HRQOL in these individuals remains unclear. Thus, future studies should quantify the significant contributions of basic and instrumental activity daily living to HRQOL in chronic stroke survivors.

4.6 Conclusion

Self- perceived upper extremity motor function in daily life living activities assessed by UEFI is a significantly independent predictor, explaining 18.8% variance of HRQOL assessed by SIS scores in people with chronic stroke, while other observational outcome measures, e.g., FMA-UE and WMFT are not. Therefore, the clinical implication of this study is that the training of bilateral upper extremity motor function in daily life living activities as stroke rehabilitation strategy should exert the strongest therapeutic effects in the improvement in the HRQOL in people with chronic stroke.

CHAPTER FIVE

Psychometric Properties of Outcome Measures used in the Main Studies

Parts of content have been published in two peer-reviewed journals.

Pan Hong, Ng SSM, Liu TW, Tsoh J, Wong TWL (2023). Psychometric properties of the Chinese (Cantonese) version of the Upper Extremity Functional Index in people with chronic stroke. *Frontiers in Neurology*. 14:989403. (Appendix 5.1)

Pan Hong, Liu TW, Ng SSM, Tsoh J, Wong TWL, Lam SSL, Li CSK, Chan CCC, Lai CYY (2024). Testing the psychometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke. *Disability and Rehabilitation*. 46(1): 159-169. (Appendix 5.2)

Parts of content have been presented at one international conferences.

Pan Hong, Liu TW, Lam SSL, Chan CCC, Li CSK, Ng SSM. Testing the psychrometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke, *10th World Congress for Neurorehabilitation*, 14-17 December 2022, Vienna, Austria. (Appendix 5.3)

5.1 Abstract

There is a need to develop and establish reliable and valid upper extremity patient-report outcome measures to assess paretic upper extremity activity functional recovery and monitor the progress of the effects of the interventions in stroke survivors. Moreover, it is important to develop an outcome measure to assess the subjective satisfaction of the patients and clearly inform physiotherapists of the needs of people with stroke. The main objective of this study was to translate and validate the Upper Extremity Functional Index (UEFI) and SATIS-Stroke in Chinese people with stroke, which were used in the main studies (Chapter 6 and Chapter 7) of this PhD study. A cross-sectional study was conducted to determine the reliability and validity of these two outcome measures for assessing self-perceived functional recovery of upper extremity activity (UEFI) and subjective satisfaction with daily life activity and social life (SATIS-Stroke) in people with stroke, respectively.

The results demonstrated that the Chinese UEFI (C-UEFI) assessing the self-perceived functional recovery of upper extremity in daily life activity had good test–retest reliability (intraclass correlation coefficient $[ICC]_{3,1}$ = 0.87) and excellent internal consistency (Cronbach's α = 0.92) in stroke survivors. The mean scores of the C-UEFI had significant fair to excellent correlations (r = 0.217 to 0.759) with the mean scores of the Fugl-Meyer Assessment-Upper Extremity (FMA-UE), Wolf Motor Function Test (WMFT), Motor Activity Log (MAL), Stroke Impact Scale (SIS), and Community Integration Measure (CIM) (r = 0.217 to 0.759) in stroke survivors. The Chinese version of the SATIS-Stroke (C-SATIS-Stroke) had excellent internal consistency (Cronbach's α = 0.96) and test–retest reliability ($ICC_{3,1}$ = 0.91) in people with stroke. The mean scores of the C-SATIS-Stroke had fair to good significant correlations (r = 0.27 to 0.53) with the mean scores of the SIS and CIM in people with stroke.

5.2 Introduction

The Chapter 1 (review) demonstrated that, when applied for stroke rehabilitation, mirror therapy alone and transcutaneous electrical nerve stimulation alone have beneficial effects. Chapter 2 presented the overall outline of the PhD study. The Chapter 3 further demonstrated that mirror therapy combined with electrical stimulation and conventional therapy was more effective in improving upper extremity motor control, as assessed using the Fugl-Meyer Assessment-Upper Extremity (FMA-UE) (Standard Mean Difference (SMD), 1.89; 95% Confidence Interval (CI), 1.52–2.26), and the ability to perform activities of daily living (SMD, 1.17; 95% CI, 0.42–1.93) than conventional therapy alone. Mirror therapy combined with electrical stimulation and conventional therapy was more effective in improving upper extremity motor control, as assessed using the FMA-UE, than electrical stimulation and conventional therapy (SMD, 0.42; 95% CI, 0.11–0.73). Mirror therapy combined with electrical stimulation and conventional therapy was more effective in improving upper extremity motor control, as assessed using the FMA-UE (SMD, 0.47; 95% CI, 0.04–0.89), and the upper extremity gross gripping function, as assessed using the Action Research Arm Test (SMD, 0.53; 95% CI, -0.11–0.94), than mirror therapy and conventional therapy. These results indicate that mirror therapy combined with electrical stimulation and conventional therapy is an effective intervention for improving recovery of upper extremity motor function compared with conventional therapy alone, electrical stimulation and conventional therapy, and mirror therapy and conventional therapy in stroke survivors. The results of the regression model reported in Chapter 4 showed that after adjustment for demographic factors and stroke-related impairments, the C-UEFI scores still independently predicted the SIS scores, accounting for 18.8% of the variance, with the entire model explaining 60.3% of the variance in the SIS scores.

This study indicates that self-perceived upper extremity motor function is a crucial component to be included in the rehabilitation program aimed at enhancing quality of life and social participation among stroke survivors.

Patient-report outcome measures could provide clinical value in terms of screening, monitoring progress, and facilitating patient-centered care by assessing the patients' views of their impairments, and motor functional abilities (Moloney et al., 2023; Stewart & Cramer, 2013). A 15-item English version of the UEFI was used to assess the functional recovery of upper extremity activity. This version showed excellent test–retest reliability (ICC = 0.94) in people with upper extremity musculoskeletal disorders (Chesworth et al., 2014; Hamilton, 2013).

Moreover, assessing the subjective satisfaction of people with stroke with their daily life and social activities in their actual environment is crucial as it could reveal their perception of their actual performance in daily life and social activities and inform whether the intervention is effective in achieving their goals (Bouffioulx et al., 2008). Hence, a reliable and valid outcome measure to assess subjective satisfaction could provide physiotherapists with clear information to identify the needs of people with stroke and accordingly plan, prescribe, and adjust interventions to improve their functional capacity and performance in daily life and social activities (Bouffioulx et al., 2008). In this study, the SATIS-Stroke was used as an outcome measure of satisfaction perceived by people with stroke with their performance and participation in life activities and situations (Bouffioulx et al., 2010).

However, the UEFI and SATIS-Stroke had not previously been translated into Chinese and culturally adapted for the Chinese stroke population. Moreover, their reliability and validity and their correlations with other stroke-related outcome measures remain to be examined in

Chinese stroke survivors. Hence, the objective of this cross-sectional study was to translate and culturally adapt the UEFI and SATIS-Stroke into Chinese (Cantonese) (C-UEFI and C-SATIS-Stroke) for assessing upper extremity functional activity level in daily life and the level of satisfaction with activity and participation in Chinese chronic stroke survivors. Hence, the study reported in this chapter mainly investigated the psychometric properties of these two outcome measures used in the main study, which compared with the effects of Mirror Therapy + Bilateral Transcutaneous Electrical Nerve Stimulation + Conventional Therapy and Sham-Mirror Therapy + Bilateral Transcutaneous Electrical Nerve Stimulation + Conventional Therapy in people with sub-acute stroke (reported in Chapter 6) and the effects of Mirror Therapy + Bilateral Transcutaneous Electrical Nerve Stimulation and Sham-Mirror Therapy + Bilateral Transcutaneous Electrical Nerve Stimulation in chronic stroke survivors (reported in Chapter 7).

5.3 Method

5.3.1 Subjects

In this cross-sectional study, 101 people with chronic stroke were recruited from a local self-help group in Hong Kong via poster advertisements. Potential people with stroke were recruited if they (1) were between 50 and 80 years old; (2) had suffered a single stroke, as confirmed by MRI or CT, at least 1 year before the start of the study; (3) had a score higher than 7 on the Chinese version of the Abbreviated Mental Test (Hodkinson, 1972), (4) could speak Chinese (Cantonese); (5) could demonstrate at least minimal anti-gravity movement in the shoulder of their paretic arm and at least 5° of wrist extension; and (6) could walk independently for at least 10 m with or without an assistive device. People with stroke were excluded if they (1) had

any other unstable medical condition (e.g., angina pectoris or arthritis) or other conditions requiring medication (e.g., Parkinson's disease or multiple sclerosis) that could potentially affect the upper extremity motor function or (2) had aphasia or hearing impairment that could affect accurate data collection. The studies involving human participants were reviewed and approved by the Departmental Research Committee of Hong Kong Polytechnic University (Approval number: HSEARS20210110002).

Fifty age-matched healthy older adults with stable health condition were recruited as the control group. Those with neurological defects or cardiovascular disease that could affect proper assessment were excluded.

5.3.2 Outcome measures

5.3.2.1 Upper Extremity Functional Index (UEFI)

The UEFI was used to assess the self-perceived upper extremity functional recovery in daily life activity in stroke survivors (Pan et al., 2023). The 15-item UEFI has the same rating scale as the 20-item UEFI for all items except item 9, "doing up buttons," which was modified to a scale from 0 to 3 points (Chesworth et al., 2014). Total score of UEFI is 59, with higher score indicating better upper extremity motor ability in daily life activity.

5.3.2.2 SATIS-Stroke

The SATIS-Stroke is used to assess the level of satisfaction of people with stroke with activity and social participation in their environments (Bouffioulx et al., 2010). This questionnaire has

36 items, and each item is rated on a 4-point scale, ranging from “0 = very dissatisfied” (individuals unable to perform activities with assistance) to “3 = very satisfied” (individuals who can perform activities easily and independently) (Bouffioulx et al., 2008). The activities and life situations not encountered in the previous 30 days can be marked “not applicable” or scored “0” (Pereira et al., 2021). In this study, the total SATIS-Stroke raw score (range: 0–108) was transformed into a linear measure on a unidimensional scale expressed in “logits” (-5.11 to 5.08) using the Rasch model to avoid measurement errors and increase the reliability of the general measure of satisfaction (Bouffioulx et al., 2010; Pereira et al., 2021). A higher value in logits corresponds to a higher degree of satisfaction with activity and social participation. In addition, the transformation table provided by Pereira was used to identify which values in logits should be considered to obtain raw SATIS-Stroke scores (Pereira et al., 2021).

5.3.2.3 Fugl-Meyer Assessment (FMA)

The FMA is considered one of the most comprehensive quantitative assessment tools for evaluating motor function impairment in the upper and lower extremities of people with stroke (Fugl-Meyer et al., 1975). The motor domain of the FMA comprises 50 items that measure the reflex, movement, and coordination of the shoulder, elbow, forearm, wrist, hand, hip, knee, and ankle (Gladstone et al., 2002). Each item is scored on a 3-point scale ranging from 0 to 2, with maximum possible scores of 66 and 34 for the upper and lower limbs, respectively (Gladstone et al., 2002). The FMA has shown excellent intra-rater reliability (total score ICC = 0.98–0.99; upper extremity motor sub-score ICC = 0.995–0.996; lower extremity motor sub-score ICC = 0.96) and inter-rater reliability (total score ICC = 0.96; upper extremity motor sub-score ICC = 0.97; lower extremity motor sub-score ICC = 0.92) in people with chronic stroke (Gladstone et al., 2002).

5.3.2.4 Wolf Motor Function Test (WMFT)

The WMFT is a quantitative outcome measure that includes timed and functional tasks to assess the upper extremity motor ability of stroke survivors (Wolf et al., 2005). The WMFT yields three scores: a time score to quantify the speed of the performance, a functional ability score to quantify the quality of performance, and a paretic grip strength score. As people with stroke were too weak to undergo the weight to box assessment, this assessment was excluded in this study. Hence, only 15 function-related tasks and paretic grip strength were included. The functional ability score is obtained from 15 items rating by a 6-point ordinal scale, with a maximum score of 75. The WMFT functional ability score has shown excellent inter-rater reliability (ICC = 0.93) in stroke survivors (Edwards et al., 2012; Morris et al., 2001). The detailed protocol of the WMFT is provided in Appendix 5.9. The functional ability score was only calculated for paretic upper extremity functional ability according to the below criteria, based on a comparison with the unaffected upper extremity:

(1) 0 score: no movement of the paretic hand.
(2) 1 score: the paretic hand only shows muscle activation, and even with the help of the nonparetic hand, it is impossible to complete the motor function exercises.
(3) 2 score: the paretic hand can complete the motor function exercises with the help of the nonparetic hand.
(4) 3 score: the paretic hand takes 5 seconds longer to complete the motor function exercises than the nonparetic hand.
(5) 4 score: the difference in the test completion time between the paretic hand and nonparetic hand is 2–5 seconds.

(6) 5 score: the difference in the test completion time between the paretic hand and nonparetic hand is less than 2 seconds.

5.3.2.5 Six-minute Walk Test (6MWT)

The 6MWT is commonly used as a standardized outcome measure of walking endurance following stroke. It has also been shown to be a significant predictor of community ambulation and integration in individuals with stroke (Liu et al., 2008; Macchiavelli et al., 2021). Participants are instructed to walk back and forth along a 20-m corridor, covering the maximum distance possible in 6 min and taking rest as needed. The maximum distance covered is then recorded (Liu et al., 2008). The 6MWT has shown good intra-rater reliability (ICC = 0.78) and interrater reliability (ICC = 0.75) and excellent test–retest reliability ($ICC_{2,1}$ = 0.98) in stroke survivors (Liu et al., 2008; Macchiavelli et al., 2021).

5.3.2.6 Five Times Sit-to Stand (FTSTS) Test

The FTSTS test is used to assess functional lower extremity muscle strength in people with chronic stroke (Mong et al., 2010). It measures the time taken to complete five repetitions of the sit-to-stand action. All sit-to-stand actions are performed on a chair nearly 43 cm in height and 47.5 cm in depth, without an armrest. The average of three measurements is considered for analysis. The FTSTS test has shown excellent intra-rater reliability (ICC = 0.97–0.98), inter-rater reliability (ICC = 0.99), and test–retest reliability (ICC = 0.98–0.99) in people with chronic stroke (Mong et al., 2010).

5.3.2.7 Timed Up and Go Test (TUGT)

The TUGT is an objective clinical measurement used to assess functional mobility (Ng & Hui Chan, 2005). Individuals are instructed to rise from a chair, walk 3 m, turn, walk back, and sit down. The time (in seconds) taken to complete the task is measured in two trials with a stopwatch. The mean time of two trials is calculated and recorded. The TUGT has shown excellent reliability (ICC = 0.95) in people with chronic stroke (Ng & Hui Chan, 2005).

5.3.2.8 Berg Balance Scale (BBS)

The BBS measures functional balance in older adults and people with various disorders, including stroke (Hiengkaew et al., 2012). The BBS comprises 14 items, scored from 0 to 4, with total scores between 0 and 56. A higher score indicates better balance. The BBS has shown excellent inter-rater reliability (ICC = 0.95) and test-retest reliability ($ICC_{3,1}$ = 0.98) in people with stroke (Hiengkaew et al., 2012).

5.3.2.9 Motor Activity Log (MAL)

The MAL was used to assess the Amount of Use and Quality of Movement of the paretic upper extremity function of stroke survivors during ADLs, as indicated in a semi-structured interview (van der Lee et al., 2004). Each item of the Amount of Use and Quality of Movement is rated on a scale from 0 to 5, with the total scores of 150 (van der Lee et al., 2004). The MAL has previously demonstrated excellent internal consistency for the Amount of Use (Cronbach's α = 0.88) and Quality of Movement (Cronbach's α = 0.91) and good test–retest reliability for the

Amount of Use (r = 0.70–0.85) and Quality of Movement (r = 0.61–0.71) in stroke survivors (Uswatte et al., 2006; van der Lee et al., 2004).

5.3.2.10 Activity-Specific Balance Confidence (ABC) Scale

The ABC scale is a 16-item outcome measure used to assess subjective balance confidence in daily activities (Mak et al., 2007). The items are rated from 0 to 100. A score of 0 represents no confidence, and a score of 100 represents complete confidence. The total ABC score for each participant is calculated by summing the scores of individual items and then dividing the total by the number of items (Botner et al., 2005). The ABC scale has shown good test–retest reliability (ICC = 0.85) and high internal consistency (Cronbach's α = 0.97) in people with stroke (Botner et al., 2005).

5.3.2.11 Lawton Instrumental Activities of Daily Living (IADL) Scale

The Lawton IADL scale (van der Lee et al., 2004) is used to assess the more complex ADLs necessary for living in a community (Landis & Koch, 1977). The Lawton IADL scale measures nine function items with a total scores of 27. The Lawton IDAL scale has demonstrated excellent inter-rater reliability ($ICC_{2,1}$ = 0.99) in older adults (van der Lee et al., 2004).

5.3.2.12 Survey of Activities and Fear of Falling in the Elderly (SAFFE)

The SAFFE was developed to assess the effect of fear of falling on activity restriction in older adults (Lachman et al., 1998). It assesses the respondent's fear of falling while performing 11 activities. Each activity is rated on a 4-point Likert scale (0 = not at all worried, 1 = slightly

worried, 2 = somewhat worried, and 3 = extremely worried). The total score is an unweighted sum of these 11 items, ranging from 0 to 33, with a higher score indicating greater fear (Chou et al., 2005; Lachman et al., 1998). The SAFFE has shown good internal consistency (Cronbach's $\alpha = 0.95$) in older Chinese adults (Chou et al., 2005; Lachman et al., 1998).

5.3.2.13 Stroke Impact Scale (SIS)

The SIS is a self-reported questionnaire used to assess the subjective level of disability and health-related quality of life in people with stroke (MacIsaac et al., 2016). The SIS includes 59 items and an extra question. Each item is rated on a 5-point Likert scale. The summative scores range from 0 to 100, and the average score of nine domains is also calculated (Norouzi-Gheidari et al., 2019). Higher scores indicate better self-reported health. The SIS has demonstrated good-to-excellent test–retest reliability (ICC = 0.7–0.92) in stroke survivors (Mulder, 2016).

5.3.2.14 Community Integration Measure (CIM)

The Cantonese version of the CIM (C-CIM) was used to assess the level of community integration in stroke survivors, with the total scores of 50 (Liu et al., 2014). The C-CIM has demonstrated good test–retest reliability (ICC = 0.84) in stroke survivors (Liu et al., 2014).

Permissions to translate the original English UEFI and SATIS-Stroke into Chinese were obtained from the authors. The five procedures of UEFI and SATIS-Stroke translation are delineated in Figure 5.1. The procedures of this study are shown in Figure 5.2.

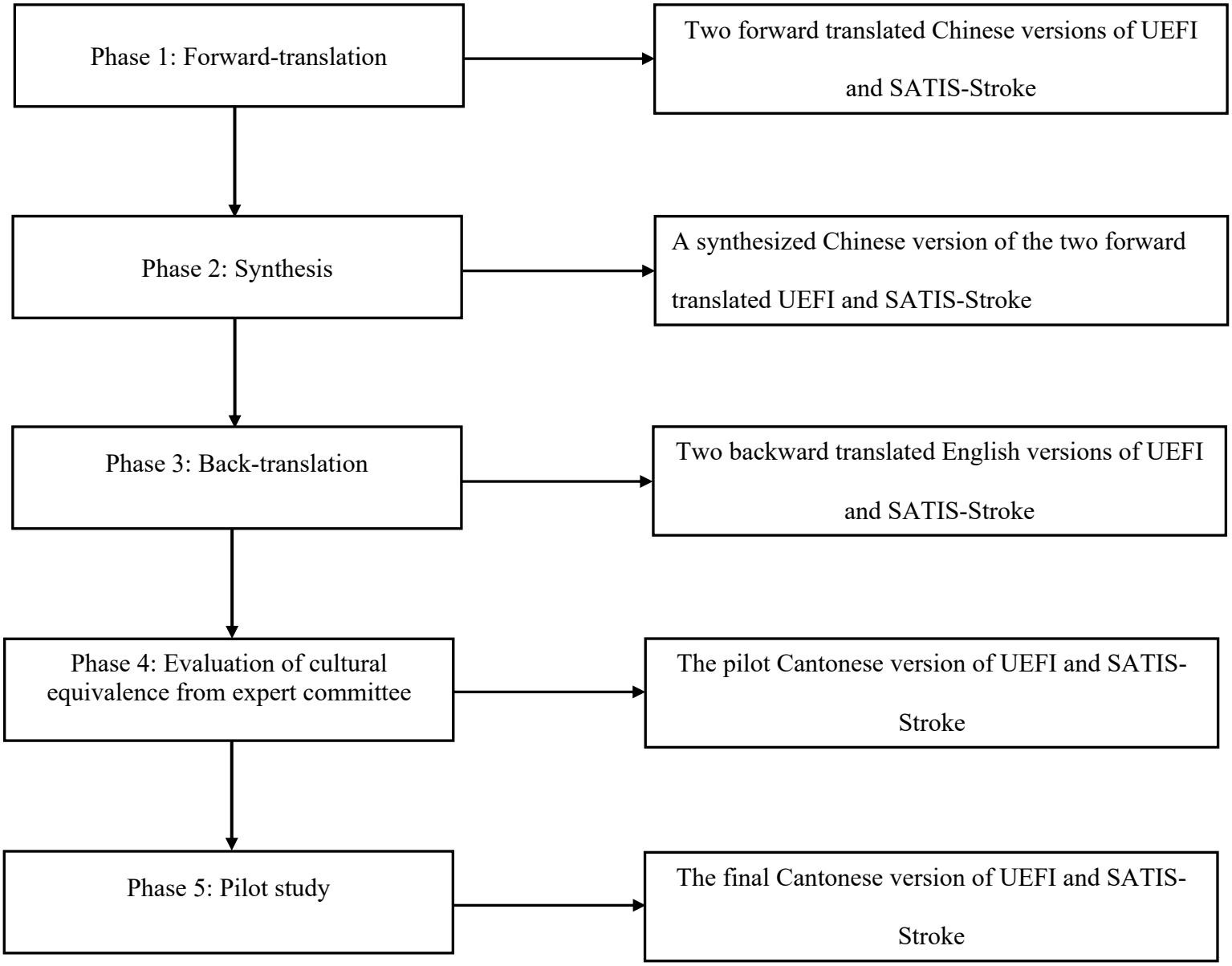


Figure 5.1 Translation and cross-cultural adaptation process

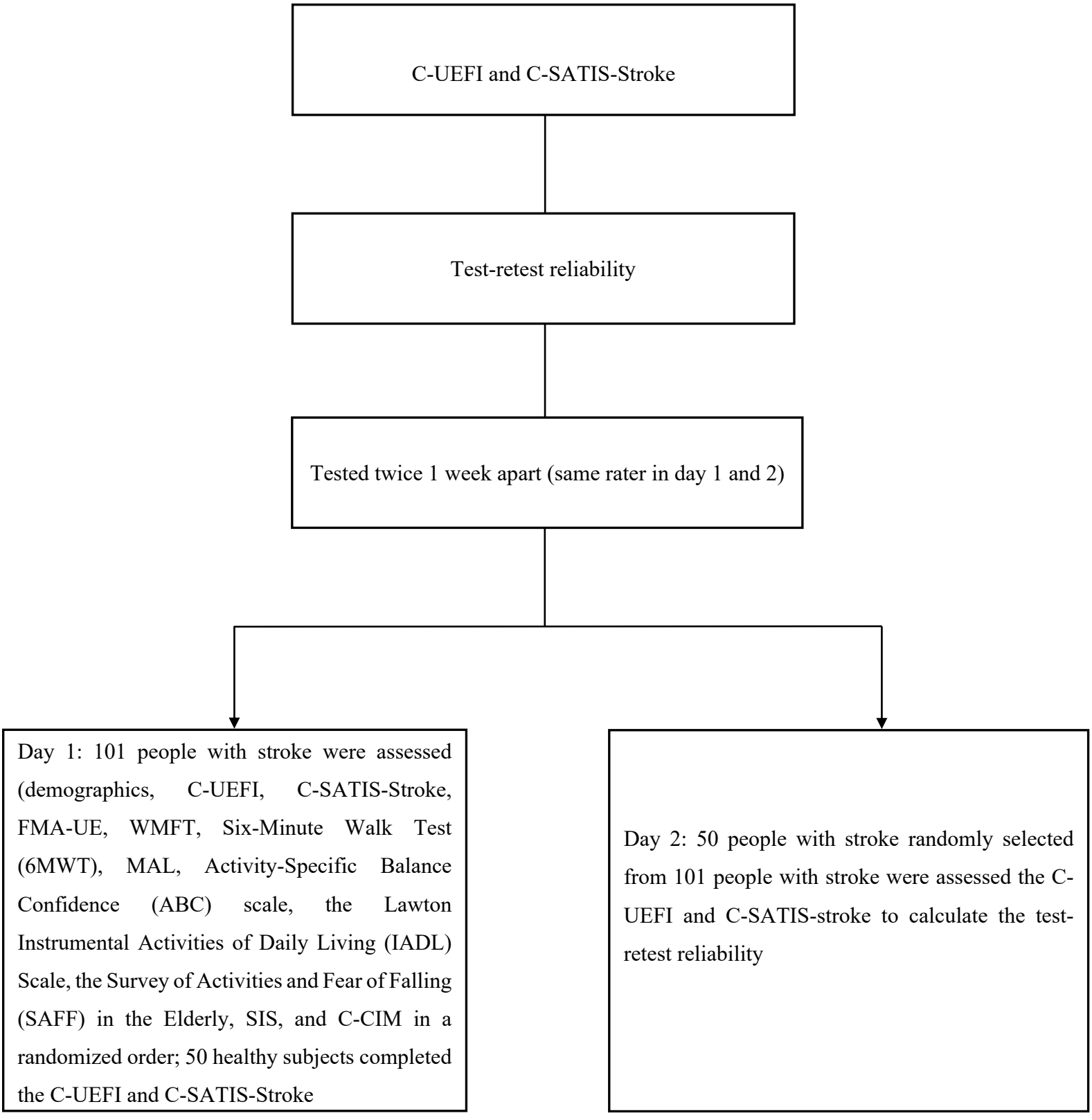


Figure 5.2 Structure of data collection and analysis for the C-UEFI and C-SATIS-Stroke

5.3.3 Sample size estimation and statistical analysis

To achieve an ICC value of 0.9 for the C-UEFI, more than 46 stroke survivors were needed to achieve 80% power. To establish the differences in the C-UEFI score between people with stroke and healthy subjects, more than 50 people with stroke and more than 50 healthy subjects were determined to be required to achieve a CA_0 value of 0.3 and CA_1 value of 0.7 (Bujang et al., 2018). To conduct factor analysis estimation (Arafat et al., 2016), a sample size of more than 100 stroke survivors were needed.

To validate the C-SATIS-Stroke, the formula for testing and estimating Cronbach's α (Bonett, 2003) was used to calculate the required sample size using the below parameters: α value = 0.05; β value = 0.1; k value (number of item) = 36; Cronbach's α (CA_0) value = 0.0; expected Cronbach's alpha (CA_1) value = 0.7; and power value = 0.9. Accordingly, a minimum of 30 people with chronic stroke were found to be required for this study. However, a minimum of 50 participants were needed for the questionnaire test–retest analysis according to the guideline (Pereira et al., 2021; Terwee et al., 2007). Meanwhile, to determine the difference in the C-SATIS-Stroke scores between people with stroke and healthy subjects, a minimum of 50 people with stroke and 50 healthy subjects were needed to achieve an CA_0 value of 0.3 and CA_1 value of 0.7 (Bujang et al., 2018). To ensure a sufficient sample size for the convergence validity analysis of the questionnaire in people with neurological disorders (Hobart et al., 2012; Pereira et al., 2021), more than 100 stroke survivors were needed (Arafat et al., 2016).

Furthermore, to ensure a sufficient sample size for the convergence validity analysis of both the C-UEFI and C-SATIS-Stroke questionnaires in people with neurological disorders (Hobart

et al., 2012; Pereira et al., 2021), more than 100 stroke survivors were needed (Arafat et al., 2016).

All data analyses were conducted using SPSS software (version 26.0). Test–retest reliability was assessed using $ICC_{3,1}$ (Koo & Li, 2016). Internal consistency was evaluated using Cronbach's α coefficient (Pereira et al., 2019).

The standard error of measurement relative to the total score was calculated using the following formula (PW, 2004):

$$\text{Standard error of measurement} = \text{standard deviation} \times \sqrt{1 - r}\,,$$

The minimal detectable change was calculated using the following formula (Haley & Fragala-Pinkham, 2006):

$$\text{Minimal detectable change} = \text{standard deviation} \times 1.96 \times \sqrt{2(1 - r)},$$

where standard deviation indicates the standard deviation of the baseline total C-UEFI and C-SATIS-Stroke scores, and *r* denotes the test–retest reliability coefficient.

The receiver operating characteristic curve was used to quantify the accuracy of the C-UEFI and C-SATIS-Stroke for discriminating upper extremity activity limitations and the level of satisfaction with social participation, respectively, between stroke survivors and healthy subjects. The area under the curve values were considered to indicate no discrimination (< 0.5),

poor discrimination (0.5–0.7), acceptable discrimination (0.7–0.8), excellent discrimination (0.8–0.9), or outstanding discrimination (> 0.9) (Liu, 2019).

The Pearson correlation coefficients were used to establish the convergent validity of the C-UEFI and C-SATIS-Stroke with other outcome measures used in people with stroke. The known-group validity was used to indicate the ability of the C-UEFI and C-SATIS-Stroke scores to distinguish between people with stroke and healthy people.

To establish the optimal factor structure for the C-UEFI, both exploratory factor analysis and confirmatory factor analysis were used, followed by the principal component analysis and a scree plot to determine the optimal number for factor extraction and promax rotation to enhance the interpretability of the factors.

The ceiling and floor effects of the C-SATIS-Stroke were calculated in people with stroke based on the percentage of participants who had the highest (ceiling) and lowest (floor) scores. The ceiling and floor effects for each item are considered to exist according to the criterion that at least 15% of the participants attain the maximum or minimum scores, respectively (Terwee et al., 2007).

5.4 Results

5.4.1 Psychometric Properties of the C-UEFI

Total 101 people with stroke and 50 healthy subjects were included in this cross-sectional study. The demographic characteristics of the people with stroke and healthy controls are presented in Table 5.1.

Table 5.1 Demographics of the people with stroke and the healthy people

Characteristics	Stroke group (n = 101)	Healthy group (n = 50)	Test value	p
Age, years	63.82(6.4)	61.58(7.56)	t (-1.906)	0.06
Sex, Male/Female, n	58/43	14/36	χ^2 (11.61)	0.001
Body mass index(kg/m^2)	23.56(3.95)	21.78(4.38)	Z (3.23)	0.001
Years since stroke	6.74±4.42			
Stroke-affected side, n				
Left	46(46%)			
Right	55(54%)			
Stroke type, n				
Ischemic	69(68%)			
Haemorrhagic	32(32%)			
Mobility status, n				
Unaided	29(28.71%)			
Stick	55(54.46%)			
Small base quadripod	10(9.9%)			
Large base quadripod	5(4.95%)			
Others	2(1.98%)			
Characteristics	Stroke group (n = 50)	Healthy group (n = 50)	Test value	p
Age, years	63.23 (6.18)	61.58(7.56)	t (1.286)	0.201
Sex, M/F, n	22/28	14/36	χ^2 (2.778)	0.096
Body mass index (kg/m^2)	22.20 (2.32)	21.78 (4.38)	Z (0.052)	0.96
Years since stroke	4.95 ± 1.77			
Stroke-affected side, n				
Left	26 (52%)			
Right	24 (48%)			

Stroke type, *n*	
Ischemic	29 (58%)
Haemorrhagic	21 (42%)
Mobility status, *n*	
Stick	13 (26%)
Small base quadripod	17 (34%)
Large base quadripod	13 (26%)
Others	7 (14%)

Abbreviation: Data were presented as mean and standard deviation of parametric data, median and interquartile range for nonparametric data, and absolute values and percentage of total sample for categorical variables, respectively.

The re-assessment was conducted after a 1-week interval to quantify the test–retest reliability of the C-UEFI. The test–retest reliability of the C-UEFI in 50 randomly selected stroke survivors is presented in Table 5.2. The total C-UEFI score had good test–retest reliability after a week, as reflected by an $ICC_{3,1}$ of 0.872 (95% confidence interval [CI]: 0.798–0.92, $P < 0.001$), in stroke survivors. The test–retest reliability of individual items ranged from 0.22 to 0.771. The standard error of measurement and minimal detectable change were 3.6 and 9.98, respectively.

Table 5.2 Test-retest reliability of C-UEFI in people with stroke ($n = 50$)

Item	$ICC_{3,1}$	Lower	Upper	*p*-value
1.	0.543	0.346	0.694	$P < 0.001$
2.	0.385	0.158	0.574	$P = 0.001$
3.	0.581	0.394	0.722	$P < 0.001$
4.	0.684	0.529	0.794	$P < 0.001$
5.	0.541	0.344	0.692	$P < 0.001$

6.	0.653	0.487	0.773	$P < 0.001$
7.	0.733	0.597	0.828	$P < 0.001$
8.	0.771	0.651	0.854	$P < 0.001$
9.	0.736	0.600	0.830	$P < 0.001$
10.	0.539	0.342	0.691	$P < 0.001$
11.	0.220	-0.023	0.439	$P = 0.038$
12.	0.734	0.597	0.829	$P < 0.001$
13.	0.682	0.527	0.793	$P < 0.001$
14.	0.604	0.423	0.738	$P < 0.001$
15.	0.644	0.476	0.767	$P < 0.001$
Total score	0.872	0.798	0.920	$P < 0.001$

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index; ICC: Intraclass correlation coefficient.

The internal consistency of the C-UEFI in 50 randomly selected among 101 people with stroke is presented in Table 5.3, which was excellent with a Cronbach's α of 0.922. The item–total correlation was moderate to strong, with *r* values ranging from 0.51 to 0.80. Although five of the item–total correlations had an $r < 0.6$ (item 3, 4, 5,10, and 15), the deletion of none of these items improved the overall Cronbach's α.

Table 5.3 Internal consistency of C-UEFI in people with stroke ($n = 50$)

Item	Corrected Item-Total Correlation	Alpha if Item Deleted
1.	0.680	0.916
2.	0.631	0.918
3.	0.485	0.923
4.	0.476	0.922
5.	0.558	0.920
6.	0.658	0.917
7.	0.797	0.913
8.	0.780	0.912
9.	0.707	0.915
10.	0.510	0.921
11.	0.615	0.919
12.	0.794	0.913
13.	0.780	0.912

14.	0.683	0.916
15.	0.586	0.921

Cronbach's α coefficient for the entire Chinese Version of UEFI is 0.922

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index.

The known-group validity of the C-UEFI in 50 randomly selected stroke survivors compared with healthy controls is presented in Table 5.4. The results demonstrated that the healthy controls had higher levels of upper extremity functional activity than people with stroke.

Table 5.4 Known-group validity of C-UEFI in people with stroke (n = 50)

Group	Stroke (n=50)		Healthy (n=50)				
Items	Median (IR)	Mean Rank	Median (IR)	Mean Rank	Mann-Whitney U	Z	P-value
1	3.0(2.0)	61.18	4.0(0.0)	105.94	1028.00	-6.372	<0.001
2	3.0(2.0)	68.56	4.0(0.0)	91.02	1774.00	-3.55	<0.001
3	3.0(2.0)	64.05	4.0(1.0)	100.13	1318.50	-5.089	<0.001
4	4.0(0.5)	71.15	4.0(0.0)	85.80	2035.00	-2.863	<0.001
5	4.0(1.0)	70.48	4.0(0.0)	87.16	1967.00	-2.882	0.004
6	3.0(2.0)	61.43	4.0(0.0)	105.43	1053.50	-6.395	<0.001
7	4.0(1.0)	67.18	4.0(0.0)	93.82	1634.00	-4.514	<0.001
8	3.0(2.0)	64.55	4.0(0.0)	99.12	1369.00	-5.199	<0.001
9	3.0(1.5)	51.88	4.0(0.0)	124.72	89.00	-10.048	<0.001
10	3.0(1.0)	64.51	4.0(2.0)	99.21	1364.50	-5.334	<0.001
11	4.0(0.0)	70.52	4.0(0.0)	87.06	1972.00	-3.385	0.001
12	4.0(1.0)	65.01	4.0(0.0)	98.19	1415.50	-5.180	<0.001
13	3.0(2.0)	63.60	4.0(0.0)	101.04	1273.00	-5.655	<0.001
14	3.0(2.0)	66.41	4.0(0.0)	95.37	1556.50	-4.230	<0.001
15	3.0(2.0)	58.18	4.0(0.0)	112.00	725.00	-7.499	<0.001
Total score	48(15.50)	54.95	60(1.0)	118.52	399.00	-8.447	<0.001

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index; IR: interquartile range.

The convergent validity of the C-UEFI with stroke-specific impairment outcome measures in 101 people with stroke is presented in Table 5.5. The overall C-UEFI mean score showed significant positive correlations with the FMA-UE, Fugl-Meyer Assessment of Lower Extremity (FMA-LE), BBS, ABC scale, WMFT, MAL (Amount of Use), MAL (Quality of Movement), Lawton IADL scale, SIS, and C-CIM mean scores (r = 0.217–0.759, $P < 0.05$) and with the mean distance covered in the 6MWT (r = 0.519, $P < 0.001$). The overall C- UEFI mean score also showed significant negative moderate correlations with the mean TUGT completion time (r = -0.58, $P < 0.001$) and SAFFE mean score (r = -0.551, $P < 0.001$).

Table 5.5 Correlations of performance between C-UEFI and stroke-specific impairments in people with stroke (n = 101)

	C-UEFI scores	
	Correlation Coefficient	*p*-value
Fugl-Meyer Assessment of Upper Extremity (FMA-UE) scores	0.423*	<0.001
Fugl-Meyer Assessment of Lower Extremity (FMA-LE) scores	0.430*	<0.001
Timed Up and Go Test (TUGT) scores	-0.580*	<0.001
Six-Minute Walking Test (6MWT) scores	0.519*	<0.001
Berg Balance Test (BBS) scores	0.444*	<0.001
The Activity-Specific Balance Confidence (ABC) scale scores	0.633*	<0.001
The Survey of Activities and Fear of Falling in the Elderly (SAFFE) scores	-0.551*	<0.001
Wolf Motor Function Test (Affected Side) scores	0.42*	<0.001
Motor Activity Log (MAL)-Amount of Movement (Affected Side) scores	0.536*	<0.001
Motor Activity Log (MAL)-Quality of Movement (Affected Side) scores	0.519*	<0.001
The Lawton instrumental activities of daily living (IADL) scale scores	0.711*	<0.001
Stroke Impact Scale (SIS) scores		
Strength	0.337*	0.001
Hand function	0.534*	<0.001
Mobility	0.569*	<0.001
ADLs	0.759*	<0.001
Memory	0.165	0.099
Communication	0.217*	0.029
Emotion	0.262*	0.008
Participation	0.589*	<0.001
Stroke recovery	0.696*	<0.001

Chinese version of Community Integration Measure (C-CIM) scores	0.333*	0.001

*The level of confidence for significance was set as α = 0.05. all correlations are Spearman's rho coefficients.

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index; FMA-UE: Fugl-Meyer Assessment of Upper Extremity; FMA-LE: Fugl-Meyer Assessment of Lower Extremity; TUGT: Timed Up and Go Test; 6 MWT: Six-Minute Walking Test; BBS: Berg Balance Test; ABC: Activity-Specific Balance Confidence; SAFFE: Survey of Activities and Fear of Falling in the Elderly; WMFT: Wolf Motor Function Test; IADL: Instrumental Activities of Daily Living; SIS: Stroke Impact Scale; C- CIM: Chinese version of Community Integration Measure.

The rotated factor matrix of the exploratory factor analysis of the C-UEFI with two factor models in 101 people with stroke is presented in Table 5.6. The confirmatory factor analysis of the C-UEFI with two factors of upper extremity functional activity in 101 stroke survivors is presented in Table 5.7 and Figure 5.3. The exploratory factor analysis suggested a two-factor structure, accounting for 58.4% of the total variance with two factors with eigenvalues of approximately 7.3 and 1.4, respectively. The Kaiser–Meyer–Olkin value was 0.886, which indicated sampling adequacy (Kaiser, 1974). Bartlett's test of sphericity was significant ($P < 0.001$), which indicated that the factor analysis was appropriate and satisfactory (Field, 2009). The confirmatory factor analysis showed that an acceptable fit model was achieved, with a robust χ^2/df of 2.27 ($P < 0.001$), a robust comparative fit index of 0.872, a robust Tucker–Lewis index of 0.849, and a robust root mean square error approximation of 0.113. According to the difficulty of bilateral upper extremity functional activities in daily life living, one factor was labelled as "Basic Daily Activity" and another as "Advanced Functional Activity."

Table 5.6 The Rotated factor matrix of exploratory factor analysis of the C-UEFI: two factor model (n = 101)

	Factors	
Item	Basic daily activity （One）	Advanced functional activity (Two)
13	0.900	
6	0.786	
8	0.767	
14	0.758	
15	0.735	
7	0.705	
12	0.698	
1	0.549	
5	0.507	
2		0.753
3		0.746
10		0.700
11		0.576
4		0.543
9		0.516
Eigenvalues	7.394	1.371
Variance explained (%)	58.434	

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index.

Table 5.7 Confirmatory factor analysis and item statistics of the C-UEFI (n = 101)

Items description	Model
Basic Daily Activity (One)	
13. 洗衣（例如清洗，熨衫，摺疊）	0.88
6. 預備食材（例如去皮，且東西）	0.76
8. 吸塵，掃地或打掃露台	0.89
14. 開瓶	0.71
15.以患肢提著小型行李	0.60
7.在商鋪內使用購物車選購商品	0.83
12. 清潔	0.86
1.您的任何日常活動，家務或學校活動	0.69
5.以手撐起自己（例如從浴缸或椅子）	0.60
Advanced Functional Activity (Two)	
2.提起一袋日用品至腰間位置	0.72
3.從高於頭部的置物架放置或取出物件	0.56
10.使用工具或電器	0.66
11.開門	0.63
9. 扣鈕	0.44
4. 洗頭	0.67
Robust $\chi 2$/degree of freedom	2.27 ($P < 0.001$)
Robust Comparative Fit Index	0.872
Robust Tucker–Lewis index	0.849
Robust Root mean square error of approximation	0.113
Inter-factor correlation	0.78
Cronbach α value for two subscales	0.922 (One) /0.774 (Two)
Cronbach α value for total score	0.921

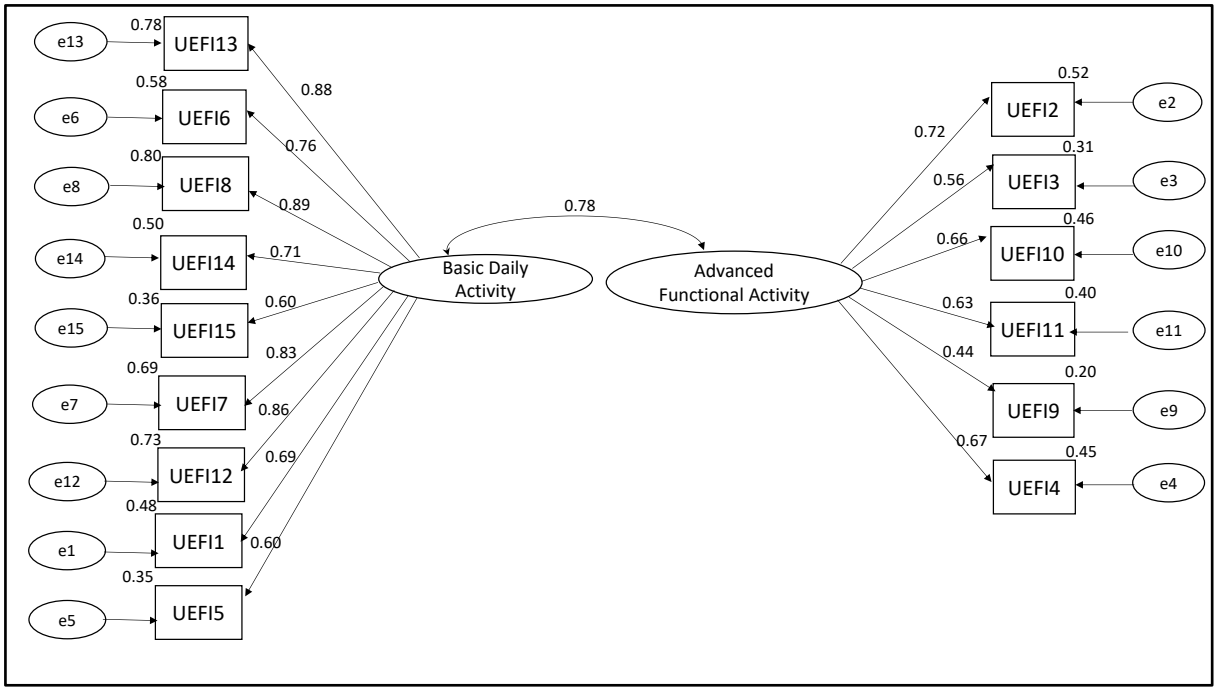


Figure 5.3 Confirmatory factor analysis of the C-UEFI: two factor model (*n* = 101)

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index; UEFI: Upper Extremity Functional Index.

The receiver operating characteristic curve, sensitivity, and specificity of the optimal cut-off scores of the C-UEFI in 101 people with chronic stroke are presented in Table 5.8 and Figure 5.4. The optimal cut-off score of the C-UEFI was calculated to be 57.5 (sensitivity, 89.1% [0.83–0.95]; specificity, 84% [0.74–0.94]; positive predictive value, 0.918 [0.86–0.97]; negative predictive value, 0.792 [0.68–0.9]; Youden index J = 1.72; area under the curve = 0.921; $P < 0.001$).

Table 5.8 Value of area under the receiver operating characteristic curve, sensitivity, and specificity for the optimal cut-offs of C-UEFI (*n* = 101)

	Area under the curve	Sensitivity %	Specificity %	Cutoff point	*p*-value
C-UEFI	0.921	88.1	84	57.5	$p < 0.001$

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index.

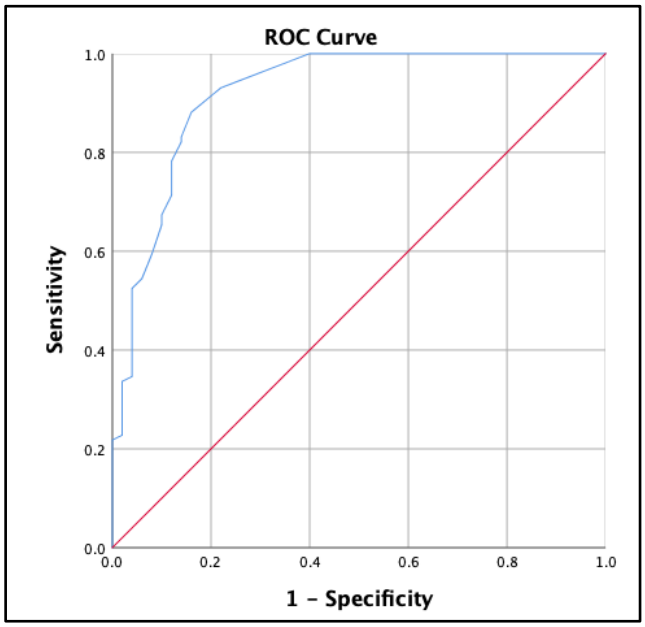


Figure 5.4 Receiver operator characteristics of the C-UEFI to distinguish people with stroke (n = 101) from healthy people (n = 50)

Abbreviation: C-UEFI: Chinese Upper Extremity Functional Index.

5.4.2 Psychometric Properties of the C-SATIS-Stroke

Total 101 people with stroke and 50 healthy subjects were included in this cross-sectional study. The demographic characteristics of the participants with stroke and healthy controls are presented in Table 5.9.

Table 5.9 Demographics of the people with stroke and the healthy people

Characteristics	Stroke group (n = 101)	Healthy group (n = 50)	Test value	p
Age, years	63.82(6.4)	61.58(7.56)	t (-1.906)	0.06
Sex, Male/Female, n	58/43	14/36	χ^2 (11.61)	0.001
Body mass index(kg/m^2)	23.56(3.95)	21.78(4.38)	Z (3.23)	0.001
Years since stroke	6.74±4.42			
Stroke-affected side, n				
Left	46(46%)			
Right	54(54%)			
Stroke type, n				
Ischemic	69(68%)			
Haemorrhagic	32(32%)			
Mobility status, n				
Unaided	29(28.71%)			
Stick	55(54.46%)			
Small base quadripod	10(9.9%)			
Large base quadripod	5(4.95%)			
Others	2(1.98%)			
Characteristics	Stroke group (n = 50)	Healthy group (n = 50)	Test value	p
Age, years	63.23 (6.18)	61.58(7.56)	t (1.286)	0.201
Sex, M/F, n	22/28	14/36	χ^2 (2.778)	0.096
Body mass index (kg/m^2)	22.20 (2.32)	21.78 (4.38)	Z (0.052)	0.96
Years since stroke	4.95 ± 1.77			
Stroke-affected side, n				
Left	26 (52%)			
Right	24 (48%)			
Stroke type, n				
Ischemic	29 (58%)			

Haemorrhagic	21 (42%)
Mobility status, *n*	
Stick	13 (26%)
Small base quadripod	17 (34%)
Large base quadripod	13 (26%)
Others	7 (14%)

Abbreviation: Data were presented as mean and standard deviation of parametric data, median and interquartile range for nonparametric data, and absolute values and percentage of total sample for categorical variables, respectively.

The re-assessment was conducted after a 1-week interval to quantify the test–retest reliability of the C-SATIS-Stroke. The test–retest reliability of the C-SATIS-Stroke in 50 randomly selected people with stroke is presented in Table 5.10. The total C-SATIS-Stroke score had excellent test–retest reliability after a week, as reflected by an $ICC_{3,1}$ of 0.913 (95% CI: 0.861–0.946, $P < 0.001$) in stroke survivors. The test–retest reliability of individual items ranged from 0.217 to 0.662. The standard error of measurement and minimal detectable change were 63(0.36 in logits) and 78 (1.0 in logits), respectively.

Table 5.10 Test-retest reliability of C-SATIS-Stroke (n = 50)

Item	$ICC_{3,1}$	Lower	Upper	*p*-value
1.	0.842	0.833	0.850	*P*<0.001
2.	0.844	0.835	0.852	*P*<0.001
3.	0.840	0.830	0.848	*P*<0.001
4.	0.837	0.828	0.846	*P*<0.001
5.	0.838	0.829	0.847	*P*<0.001

6.	0.837	0.828	0.846	*P*<0.001
7.	0.839	0.829	0.847	*P*<0.001
8.	0.848	0.840	0.857	*P*<0.001
9.	0.841	0.832	0.849	*P*<0.001
10.	0.837	0.828	0.846	*P*<0.001
11.	0.836	0.827	0.845	*P*<0.001
12.	0.836	0.826	0.845	*P*<0.001
13.	0.839	0.830	0.848	*P*<0.001
14.	0.838	0.829	0.847	*P*<0.001
15.	0.838	0.828	0.847	*P*<0.001
16.	0.840	0.830	0.848	*P*<0.001
17.	0.847	0.839	0.856	*P*<0.001
18.	0.837	0.828	0.846	*P*<0.001
19.	0.837	0.828	0.846	*P*<0.001
20.	0.838	0.829	0.847	*P*<0.001
21.	0.841	0.831	0.849	*P*<0.001
22.	0.836	0.827	0.845	*P*<0.001
23.	0.839	0.830	0.848	*P*<0.001
24.	0.842	0.833	0.851	*P*<0.001
25.	0.837	0.827	0.846	*P*<0.001
26.	0.837	0.827	0.845	*P*<0.001
27.	0.840	0.831	0.849	*P*<0.001
28.	0.838	0.829	0.847	*P*<0.001
29.	0.841	0.832	0.850	*P*<0.001
30.	0.839	0.829	0.847	*P*<0.001
31.	0.840	0.831	0.849	*P*<0.001
32.	0.840	0.831	0.849	*P*<0.001
33.	0.840	0.831	0.849	*P*<0.001
34.	0.844	0.835	0.852	*P*<0.001
35.	0.841	0.831	0.849	*P*<0.001
36.	0.854	0.845	0.862	*P*<0.001
Total score	**0.913**	**0.861**	**0.946**	***P* <0.001**

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke.

This form of C-SATIS-Stroke is the first one in 10 random orders in English. The internal consistency of the C-SATIS-Stroke in 50 randomly selected people with stroke is presented in Table 5.11, which was excellent with a Cronbach's α of 0.959. The item–total correlation was fair to strong, with *r* values ranging from 0.31 to 0.85. Although four of the item–total correlations had an $r < 0.5$ (item 2 [using knife, fork and spoon in all circumstances], $r = 0.31$; item 8 [participating in arts and culture, such as cinema and theatre], $r = 0.48$; item 17 [participating in spousal relationships], $r = 0.43$; item 36 [having a sexual relationship with another], $r = 0.37$), the deletion of none of these items improved the overall Cronbach's α.

Table 5.11 Internal consistency of C-SATIS-Stroke ($n = 50$)

Item	Corrected Item-Total Correlation	Alpha if Item Deleted
1.	0.505	0.959
2.	0.306	0.960
3.	0.677	0.958
4.	0.542	0.958
5.	0.628	0.958
6.	0.645	0.958
7.	0.606	0.958
8.	0.475	0.961
9.	0.569	0.958
10.	0.628	0.958
11.	0.776	0.957
12.	0.789	0.957
13.	0.696	0.958
14.	0.803	0.957
15.	0.774	0.957
16.	0. 773	0.957
17.	0.434	0.961

18.	0.803	0.957
19.	0.759	0.958
20.	0.672	0.958
21.	0.584	0.958
22.	0.850	0.957
23.	0.752	0.957
24.	0.581	0.958
25.	0.763	0.957
26.	0.757	0.957
27.	0.738	0.957
28.	0.729	0.957
29.	0.689	0.958
30.	0.722	0.958
31.	0.588	0.958
32.	0.679	0.958
33.	0.532	0.959
34.	0.563	0.959
35.	0.715	0.957
36.	0.366	0.961
Cronbach's α coefficient for the entire C-SATIS-Stroke is 0.959		

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke.

This form of C-SATIS-Stroke is the first one in 10 random orders in English.

The ceiling and floor effects of the C-SATIS-Stroke in 50 randomly selected people with stroke is presented in Table 5.12. The results demonstrated that the C-SATIS-Stroke had ceiling but not floor effects. The possible reason may be that the included people with chronic stroke had stable physical conditions and favourable functional recovery, which may have promoted adaptation to daily life and social activities and thus yielded high satisfaction scores.

Table 5.12 Ceiling and floor effects for C-SATIS-Stroke items (n = 50)

Items	Ceiling effect (%)	Floor effect (%)	NA option obtained (%)
1.	15.8	-	3.96
2.	9.17	3.96	-
3.	18.81	0.99	-
4.	25.45	-	0.99
5.	29.70	0.99	-
6.	28.71	0.99	-
7.	23.76	0.99	-
8.	13.86	-	30.69
9.	14.85	0.99	2.97
10.	20.79	2.97	-
11.	30.69	0.99	0.99
12.	34.65	-	-
13.	20.79	2.97	2.97
14.	26.73	-	1.98
15.	27.72	0.99	-
16.	22.77	0.99	-
17.	21.81	1.98	20.79
18.	27.72	-	0.99
19.	25.74	0.99	-
20.	24.75	-	0.99
21.	15.84	1.98	3.96
22.	32.67	-	-
23.	21.78	1.98	-
24.	15.84	1.98	3.96
25.	29.70	0.99	-
26.	29.70	-	-
27.	19.80	-	-
28.	24.75	-	-
29.	14.54	-	-
30.	20.79	-	-

31.	14.85	0.99	0.99
32.	19.8	0.99	3.96
33.	20.79	-	5.94
34.	15.84	-	4.95
35.	17.82	1.98	0.99
36.	6.93	4.95	26.73
Total score	1.98	-	-

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke. NA: not applicable (Activity and living situations not performed in the previous 30 days).

This form of C-SATIS-Stroke is the first one in 10 random orders in English.

The known-group validity of the C-SATIS-Stroke in 50 randomly selected people with stroke in Table 5.13. The results demonstrated that the healthy controls had higher levels of satisfaction with daily life and social participation activities than people with stroke. However, the known-group validity of item 36 (participating in spousal relationships) for discriminating between people with stroke and healthy subjects was not significant.

Table 5.13 Known-group validity of C-SATIS-Stroke (*n* = 50)

Group	Stroke (*n* = 50)		Healthy (*n* = 50)				
Items	Median (IR)	Mean Rank	Median (IR)	Mean Rank	Mann-Whitney U	Z	P-value
1	-3.81(0.00)	67.84	-3.46(0.35)	92..48	1701.00	-3.74	<0.001
2	-3.81(0.00)	61.15	-3.46(0.35)	105.99	1025.50	-6.67	<0.001
3	-3.81(0.00)	64.75	-3.46(0.35)	98.73	1388.50	-5.06	<0.001
4	-3.81(0.35)	64.62	-3.46(0.09)	98.98	1376.00	-5.174	<0.001
5	-3.81(0.35)	65.60	-3.46(0.35)	97.00	1475.00	-4.66	<0.001
6	-3.81(0.35)	64.23	-3.46(0.09)	99.77	1336.50	-5.34	<0.001
7	-3.81(0.00)	63.93	-3.46(0.35)	100.39	1305.50	-5.40	<0.001

8	-3.81(1002.0)	70.41	-3.46(1002.81)	87.30	1960.00	-2.36	0.02
9	-3.81(0.00)	65.72	-3.46(0.35)	96.76	1487.00	-4.65	<0.001
10	-3.81(0.00)	67.10	-3.46(0.35)	93.98	1626.00	-3.89	<0.001
11	-3.81(0.35)	68.91	-3.46(0.35)	90.32	1809.00	-3.23	0.001
12	-3.81(0.35)	66.28	-3.46(0.35)	95.63	1543.50	-4.429	<0.001
13	-3.81(0.00)	65.80	-3.46(0.35)	96.60	1495.00	-4.58	<0.001
14	-3.81(0.35)	64.08	-3.46(0.09)	100.08	1321.00	-5.35	<0.001
15	-3.81(0.35)	65.12	-3.46(0.35)	97.98	1426.00	-4.89	<0.001
16	-3.81(0.00)	66.27	-3.46(0.35)	95.66	1542.00	-4.39	<0.001
17	-3.81(0.35)	72.64	-3.46(0.35)	82.79	2185.50	-1.44	0.15
18	-3.81(0.35)	64.90	-3.46(0.35)	98.43	1403.50	-5.03	<0.001
19	-3.81(0.35)	64.86	-3.46(0.35)	98.51	1399.50	-5.08	<0.001
20	-3.81(0.35)	64.96	-3.46(0.35)	98.30	1410.00	-4.90	<0.001
21	-3.81(0.26)	68.39	-3.81(0.35)	91.38	1756.00	-3.34	0.001
22	-3.81(0.35)	67.33	-3.46(0.35)	93.51	1649.50	-3.97	<0.001
23	-3.81(0.00)	65.49	-3.46(0.35)	97.24	1463.00	-4.72	<0.001
24	-3.81(0.00)	63.64	-3.46(0.35)	100.97	1276.50	-5.33	<0.001
25	-3.81(0.35)	66.72	-3.46(0.35)	94.74	1588.00	-4.21	<0.001
26	-3.81(0.35)	65.85	-3.46(0.35)	96.50	1500.00	-4.61	<0.001
27	-3.81(0.00)	66.47	-3.46(0.35)	95.25	1562.50	-4.24	<0.001
28	-3.81(0.18)	65.75	-3.46(0.35)	96.71	1489.50	-4.67	<0.001
29	-3.81(0.00)	66.63	-3.46(0.35)	94.92	1579.00	-4.26	<0.001
30	-3.81(0.00)	65.28	-3.46(0.35)	97.66	1442.00	-4.92	<0.001
31	-3.81(0.00)	68.50	-3.81(0.35)	91.15	1767.50	-3.50	<0.001
32	-3.81(0.00)	67.06	-3.46(0.35)	94.06	1622.00	-4.12	<0.001
33	-3.81(0.35)	69.73	-3.46(0.35)	88.66	1892.00	-2.84	0.005
34	-3.81(0.35)	67.53	-3.64(0.35)	93.11	1669.50	-3.75	<0.001
35	-3.81(0.00)	67.91	-3.64(0.35)	92.35	1707.50	-3.71	<0.001
36	-3.81(1003.07)	71.01	-3.46(1004.11)	86.08	2021.00	-2.09	0.037
Total score	0.694(0.63)	62.08	2.497(3.351)	104.11	1119.50	-5.56	<0.001

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke. IR: interquartile range.

This form of C-SATIS-Stroke is the first one in 10 random orders in English.

The convergent validity of the C-SATIS-Stroke with stroke-specific impairment outcome measures in 101 people with stroke is presented in Table 5.14. The overall C-SATIS-Stroke mean score showed significant positive correlations with the ABC scale, SIS, and C-CIM mean scores (r = 0.329–0.55, $P < 0.05$). The overall C-SATIS-Stroke mean score also showed a significant negative moderate correlation with the SAFFE mean score (r = -0.519, $P < 0.001$).

Table 5.14 Correlations of performance between C-SATIS-Stroke and stroke-specific impairments in people with stroke (n = 101)

Outcome Measures	C-SATIS-Stroke	
	Correlation Coefficient	*p*-value
Fugl-Meyer Assessment of Upper Extremity (FMA-UE) scores	0.051	0.61
Fugl-Meyer Assessment of Lower Extremity (FMA-LE) scores	0.089	0.38
Fugl-Meyer Assessment (FMA) -total scores	0.063	0.53
Five Times sit-to-stand (FTSTS) test scores	-0.177	0.08
Timed Up and Go Test (TUGT) scores	-0.082	0.42
Six-minute walking test (6MWT) scores	0.134	0.19
Wolf Motor Function Test (WMFT) scores	-0.041	0.69
Berg Balance Scale (BBS) scores	0.106	0.29
The Activity -Specific Balance Confidence (ABC) scale scores	0.55*	< 0.001
The Survey of Activities and Fear of Falling in the Elderly (SAFFE) scores	-0.519*	< 0.001
Stroke Impact Scale (SIS) scores		
Strength	0.329*	0.001
Hand function	0.268*	0.007
Mobility	0.484*	< 0.001
ADLs	0.42*	< 0.001

Memory	0.358*	< 0.001
Communication	0.463*	< 0.001
Emotion	0.464*	< 0.001
Participation	0.528*	< 0.001
Stroke recovery	0.427*	< 0.001
Chinese version of Community Integration Measure (C-CIM) scores	0.525*	< 0.001

*The level of confidence for significance was set as α = 0.05. all correlations are Spearman's rho coefficients.

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke; FMA-UE: Fugl-Meyer Assessment of Upper Extremity; FMA-LE: Fugl-Meyer Assessment of Lower Extremity; FAM: Fugl-Meyer Assessment; FTSTS: Five Times Sit-to-Stand; TUGT: Timed Up and Go Test; 6MWT: Six-Minute Walking Test; WMFT: Wolf Motor Function Test; BBS: Berg Balance Scale; ABC: Activity-Specific Balance Confidence; SAFFE: Survey of Activities and Fear of Falling in the Elderly; SIS: Stroke Impact Scale; C-CIM: Chinese version of Community Integration Measure.

The receiver operator characteristics, sensitivity, and specificity of the optimal cut-off scores of the C-SATIS-Stroke in 101 people with chronic stroke are presented in Table 5.15 and Figure 5.5. The optimal cut-off score was calculated to be 1.035 in logits (raw scores: 79–80) (sensitivity, 77%; specificity, 72%; AUC = 0.779; $P < 0.001$).

Table 5.15 Value of area under the receiver operating characteristic curve, sensitivity, and specificity for the optimal cut-offs of C-SATIS-Stroke (n = 101)

	Area under the curve	Sensitivity %	Specificity %	Cutoff point (logits)	*p*-value
C-SATIS-Stroke	0.779	77	72	1.035	$p < 0.001$

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke.

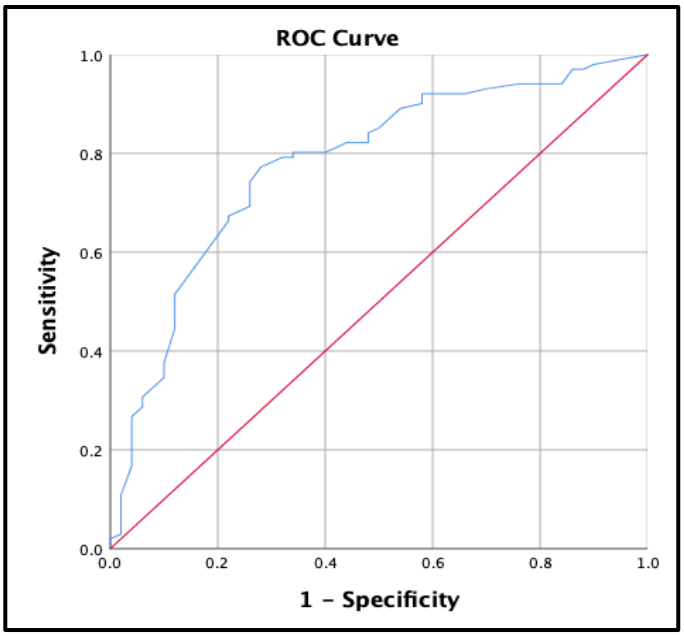


Figure 5.5 Receiver operator characteristics of the C-SATIS-Stroke to distinguish people with stroke (n = 101) from healthy people (n = 50)

Abbreviation: C-SATIS-Stroke: Chinese SATIS-Stroke.

5.5 Discussion

5.5.1 Psychometric Properties of the C-UEFI

5.5.1.1 Reliability and measurement error (standard error of measurement and minimal detectable change)

Our results demonstrated when sufficient and standard training was provided for the raters, the standardized experimental protocol contributed to good test–retest reliability, which is consistent with previous studies in people who had undergone breast cancer surgery and had upper extremity activity limitations (ICC = 0.87) (Chesworth et al., 2014) and in people with shoulder impingement syndrome (ICC = 0.8) (Hamilton & Chesworth, 2013).

Good correlations among all individual items of C-UEFI contributed to excellent internal consistency, indicating that each item measured the same domain. This finding is consistent with previous studies on people with shoulder impingement syndrome (Aytar et al., 2015), in people with Chronic Obstructive Pulmonary Disease (Alnahdi, 2021). Future study is warranted to investigate whether redundancy contributed to the high internal consistency in the C-UEFI.

The standard error of measurement in the final score was 3.6 out of 20, indicating that the measurement error of the C-UEFI was only a small portion of the total scale range. This is consistent with the standard error of measurements reported in previous studies (Alnahdi, 2021; Aljathlani et al., 2022). The minimal detectable change in the final score was approximately 9.98 out of 33.1, indicating that a C-UEFI score of at least 9.98 is required to indicate a true change in the upper extremity function activity in people with stroke. This is consistent with the minimal detectable changes reported in previous studies: 11.32 in people with Chronic Obstructive Pulmonary Disease (Alnahdi & Albarrati, 2021) and in people with upper extremity musculoskeletal disorders (Aljathlani et al., 2022).

5.5.1.2 Known-group validity

The known-group validity results demonstrated that the upper extremity functional activity performance in people with stroke was significantly worse than that in healthy subjects for all individual items of the C-UEFI. This finding may be due to the fact that chronic stroke survivors exhibit physical deterioration, e.g., motor disabilities and sensory deficits (Ng et al., 2022), which worsens their ability to perform specific upper extremity movements compared with age-matched healthy older adults.

5.5.1.3 Correlations with other outcome measures

The concurrent validity results demonstrated that the FMA-UE, WMFT, MAL (Amount of Use), and MAL (Quality of Movement) mean scores had significant positive fair to moderate correlations with the C-UEFI mean score in people with stroke. The FMA-UE evaluates upper extremity gross gripping with neural motor control (Lundquist, 2017), the WMFT evaluates upper extremity motor ability with upper extremity dexterity and strength (Edwards et al., 2012), and the MAL evaluates upper extremity functional tasks (Uswatte et al., 2006), all of which are essential components required to perform upper extremity daily functional activity.

The concurrent validity results demonstrated that the FMA-LE, BBS, ABC scale, and Lawton IADL scale mean scores and the mean distance covered in the 6MWT had significant positive moderate to excellent correlations with the C-UEFI mean score in people with chronic stroke. Furthermore, the mean TUGT completion time and SAFFE mean score had significant negative moderate correlations with the C-UEFI score. The reasons for explaining these significant

correlations are multifactorial. The FAM-LE assesses lower extremity motor control (Kwong & Ng, 2019). The BBS assesses functional balance (Au-Yeung et al., 2003). The TUGT assesses functional mobility (Mathias et al., 1986). The 6MWT assesses the aerobic capacity or walking endurance during a 6-minute walk (Macchiavelli et al., 2021). The ABC scale assesses the subjective balance confidence to conduct daily activities without fear of losing balance (Mak et al., 2007). The Lawton IADL assesses a person's ability to perform ADLs (Graf, 2008). The SAFFE assesses the avoidance behaviour due to fear of falling (Chou et al., 2005). The motor control of upper and lower extremities, walking endurance, performance of functional balance, the ability to avoid falling, and the ability to engage in ADLs are essential components required to coordinate and incorporate the bilateral upper extremity into various daily life tasks assessed in the C-UEFI.

The concurrent validity results demonstrated that the SIS and CIM mean scores had significant positive fair to excellent correlations with the C-UEFI mean score, which may be because an increase in engagement in upper extremity functional activity lead more participation in activity of daily living tasks in people with stroke. Finally, people with stroke may have more confidence and satisfaction about the health-related quality of life and community integration.

5.5.1.4 Factor analysis

This is the first study to explore the components of the C-UEFI in people with stroke using a factor structure analysis. The hypothesized two-factor structure based on the self-perceived difficulty in performing upper extremity functional activity in daily life was identified in 101 people with stroke. The first factor (items 13, 6, 8, 14, 15, 7, 12, 1, and 5) mainly involved basic ADLs, which required a little assistance and strength. The second factor (items 2, 3, 10,

11, 4, and 9) mainly involved advanced functional activity or dexterity in ADLs. Although an acceptable model fit was achieved for the factor model, further analyses are warranted, such as a robust parallel analysis to determine the structural validity (Alnahdi et al., 2024) of the C-UEFI in stroke survivors.

5.5.1.5 Optimal cut-off score

This is the first study to estimate the optimal cut-off score of the C-UEFI for distinguishing the self-perceived difficulty in upper extremity functional activity between people with stroke and age-matched healthy older adults. The optimal cut-off score of 57.5 was found to best discriminate between these groups. The area under the curve was 0.921, which indicates that the C-UEFI score can offer greater than 92% accuracy in discriminating the performance of upper extremity functional activity level of stroke survivors from age-matched healthy older adults.

5.5.2 Psychometric Properties of the C-SATIS-Stroke

5.5.2.1 Reliability and measurement error (standard error of measurement and minimal detectable change)

Consistent with previous studies in stroke survivors (Pereira et al., 2021; Pereira et al., 2019), our results showed that our study found that, when sufficient and standard training was provided for the raters, the standardized experimental protocol yielded good test–retest reliability results for the C-SATIS-Stroke.

Good correlations among all individual items of C-SATIS-Stroke contributed to excellent internal consistency, indicating that each item of the questionnaire measures the same domain. Future studies are warranted to examine whether redundancy contributed to the high internal consistency of the C-SATIS-Stroke in the evaluation of people with stroke.

The standard error of measurement in the C-SATIS-Stroke score was 0.36 in logits (raw score: 63), which represents 7.1% of the C-SATIS-Stroke score range, indicating that the measurement error was only a small portion of the total scale range. This is consistent with the findings reported by Pereira et al. (62 [0.29–0.31 in logits]) (Pereira et al., 2021). The minimal detectable change in the C-SATIS-Stroke score was approximately 1.0 in logits (raw score: 78), representing 19.69% of the total score range, similar to that reported in a previous study (88 [1.49–1.54 in logits]) (Pereira et al., 2021). At least 1.0 in logits of the C-SATIS-Stroke of is required to indicate a real change at the level of satisfaction daily life and social activities in stroke survivors.

5.5.2.2 Known-group validity

The known-group validity results demonstrated that the level of satisfaction with daily life and social activities in stroke survivors was significantly worse than that in healthy older adults for all individual items of the C-SATIS-Stroke (except item 36: participating in spousal relationships). This may be due to the fact that people with chronic stroke survivors exhibit stroke-specific impairments e.g., motor disabilities and sensory deficits (Ng et al., 2022), which worsens their ability to execute movements, perform ADLs, and participate in social activities compared with age-matched healthy older adults. However, a spousal relationship is also a type of social participation, and a marriage is a long-term social relationship that is very stable which

may not be easily affected by stroke. This may explain why no significant difference was noted in the scores for item 17 of the C-SATIS-Stroke between the two groups.

5.5.2.3 Correlations with other outcome measures

The concurrent validity results demonstrated that the ABC Scale, SIS, CIM mean scores had significant positive moderate correlations with the C-SATIS-Stroke mean score in people with chronic stroke. Furthermore, the SAFFE mean score had a significant negative moderate correlation with the C-SATIS-Stroke mean score. The ABC scale is used to assess confidence in performing daily activities without the fear of losing balance (Mak et al., 2007), and the SAFFE is used to assess avoidance behaviour due to fear of falling (Chou et al., 2005). Our result indicates that the ability to maintain functional balance using strategies to avoid falling could improve the subjective feeling of satisfaction with daily life and social activities. The SIS is used to assess disability and health-related quality of life in people with stroke (Guidetti et al., 2014), and the CIM is used to assess community integration (Liu et al., 2014). The result indicates that the subjective feeling of improved health-related quality of life and community integration may improve the level of satisfaction with daily life and social activities in people with stroke. The possible reason may be that more participation in daily life tasks and social community would increase the subjective satisfaction feeling about the life in people with stroke.

5.5.2.4 Optimal cut-off scores

This is the first study to calculate the optimal cut-off score of the C-SATIS-Stroke to distinguish the level of satisfaction with daily life and social activities between people with

stroke and age-matched healthy old people. The optimal cut-off score of 1.035 in logits (raw score: 79–80) was found to best discriminate between the groups. The area under the curve was 0.779, which indicates that the C-SATIS-Stroke can have 77.9% accuracy in discriminating the level of satisfaction with daily life and social activities between people with stroke and healthy old people.

5.5.2.5 Ceiling and floor effects

Consistent with a previous study (Pereira et al., 2019), our results demonstrated that the total C-SATIS-Stroke score had no ceiling or floor effects. However, the ceiling effects were beyond acceptable standards for several individual items (e.g., item 11, 12, 22), while no floor effects were observed for any item. One probable reason for the possible ceiling effect is that people with chronic stroke with maximum functional recovery may be better adapted to daily life and social activities, leading to higher satisfaction scores in this study.

5.6 Limitations

This cross-sectional study has several limitations. First, people with chronic stroke in this study were recruited from a local self-help group and displayed a relatively high level of motor activity function recovery, which reduces the generalizability of the results to people with chronic stroke having lower levels of motor functions. Second, the body mass index and sex ratio was significantly different ($P < 0.05$) between people with stroke and age-matched healthy subjects; these biases should be eliminated in future studies. Third, the people with stroke included in the correlation analysis were only matched by age. Future studies are needed to determine whether upper extremity functional activity recovery assessed using the C-UEFI and

the subjective level of satisfaction with activities and social participation assessed using the C-SATIS-Stroke are affected by other parameters, such as gender or body mass index. Fourth, as the incidence of stroke is associated with age and doubles each decade after 55 years (Ng et al., 2022), only participants aged > 50 years were included in this study. Fourth, as the incidence of stroke is associated with age and doubles each decade after 55 years (Ng et al., 2022), only participants aged > 50 years were included in this study Further investigations should explore and confirm the applicability of the C-UEFI and C- SATIS-Stroke in wider range of people with stroke. Fifth, only 50 healthy older adults and 101 people with chronic stroke participated in the reliability, validity, and correlation analyses. The limited sample size hindered our ability to conduct advanced analyses, such as factor analysis for the C-SATIS-Stroke. Hence, studies with a larger sample size are needed to draw more robust conclusions regarding the psychometric properties of the C-SATIS-Stroke. Sixth, the psychometric study of C-UEFI and C-SATIS-Stroke focused solely on the people with chronic stroke, which reduces the generalizability of the results to people with acute or sub-acute stroke. Future research should specifically validate C-UEFI and C-SATIS-Stroke for acute or sub-acute stroke.

5.7 Conclusion

This cross-sectional study showed that the final versions of the C-UEFI and C-SATIS-Stroke exhibited satisfactory semantic, idiomatic, cultural, and conceptual equivalence to the corresponding original English versions. The C-UEFI and C-SATIS-Stroke exhibited excellent reliability and validity and could differentiate between people with stroke and healthy controls in terms of functional recovery of upper extremity activity and the level of satisfaction with activity and social participation, respectively. Both the scales are reliable, valid, and sensitive for evaluating upper extremity functional activity level in daily life and the level of satisfaction

with daily life and social activities, respectively, in Chinese people with chronic stroke. Both of these outcome measures are suitable for use in our main studies to evaluate the effects of MT + Bi-TENS and Sham-MT + Bi-TENS on people with sub-acute stroke (Chapter 6) and people with chronic stroke (Chapter 7).

CHAPTER SIX

Randomized controlled trial of upper extremity training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper extremity functions in people with sub-acute stroke

6.1 Abstract

Mirror therapy (MT) and transcutaneous electrical nerve stimulation (TENS) has shown to have beneficial effects in improving the recovery of paretic upper extremity motor function in people with stroke, respectively. In this study, we evaluated whether the addition of MT to bilateral transcutaneous electrical nerve stimulation (Bi-TENS) and conventional therapy could improve the recovery of upper extremity motor function and health-related outcome measures when compared with Sham-MT combined with Bi-TENS and conventional therapy in people with sub-acute stroke.

Total 30 people with sub-acute stroke were randomly allocated into two groups: MT + Bi-TENS + conventional therapy or Sham-MT + Bi-TENS + conventional therapy. Two groups received total 3-hour intervention session with 2 sessions per week within 8 weeks. The primary outcome measures were Fugl-Meyer Assessment of Upper Extremity (FMA-UE) and Wolf Motor Function Test (WMFT) scores. The secondary outcome measures included maximum paretic grip strength, Jacket Test, Chinese version of Upper Extremity Functional Index (C-UEFI), Motor Activity Log (MAL), Stroke Impact Scale (SIS), Chinese version of Community Integration Measures (C-CIM), Chinese version of SATIS-Stroke (C-SATIS-Stroke) scores. Total 4 time-points were used to assess all outcome measures: baseline (A_0), after 8 sessions (A_1), after 16 sessions (A_2), and 1-month follow-up (A_{FU}).

MT + Bi-TENS + conventional therapy group showed significantly greater improvement in FMA-UE scores at A_1 (Mean Difference (MD) = 5.7, $P < 0.001$) and A_2 (MD = 11.8, $P < 0.001$), maximum paretic grip strength at A_1 (MD = 2.9, $P < 0.001$) and A_2 (MD = 4.6, $P < 0.001$), and C-CIM scores at A_2 (MD = 3.9, $P = 0.002$) in 30 people with sub-acute stroke

compared with Sham-MT + Bi-TENS + conventional therapy. The within-group effects demonstrated that both MT + Bi-TENS + conventional therapy and Sham-MT + Bi-TENS + conventional therapy groups demonstrated significant improvements in FMA-UE (Experimental Group (EG), MD = 10.7-22.0, $P < 0.001$; Control Group (CG), MD = 5.0-10.2, $P < 0.001$), WMFT (EG, MD = 11-21.5, $P < 0.001$; CG, MD = 6.7-12.9, $P < 0.001$), MAL (Amount of Use) (EG, MD = 22.8 - 36.3, $P < 0.001$; CG, MD = 9.9 -19.8, $P = 0.001$ and $P < 0.001$, respectively), and MAL (Quality of Movement) (EG, MD = 19.1-31.2, $P < 0.001$; CG, MD = 9.2 -17.3, $P < 0.001$) scores at both A_1 and A_2. Those carryover effects persisted until A_{FU}.

The within-group effects demonstrated that MT + Bi-TENS + conventional therapy group showed significant improvement in maximum paretic grip strength (3.9-6.4, $P < 0.001$) and SIS (MD = 8.5-14.5, $P < 0.001$) scores at both A_1 and A_2 while Sham-MT + Bi-TENS + conventional therapy group only showed significant improvement in paretic grip strength (MD = 1.9, $P = 0.001$) and SIS (MD = 6.8, $P = 0.001$) scores at A_2. The within-group effects demonstrated that only MT + Bi-TENS + conventional therapy group showed significant within-group improvement in C-CIM (MD = 3.4-5.2, $P < 0.001$), Jacket Test (MD = 6.3-8.2, $P < 0.001$), and C-UEFI (MD = 6.8-11.7, $P < 0.001$) scores at both A_1 and A_2. Those carryover effects persisted until A_{FU}. Both MT + Bi-TENS + conventional therapy and Sham-MT + Bi-TENS + conventional therapy showed no significant within-group improvement in C-SATIS-Stroke score at both A_1 and A_2.

To conclude, MT + Bi-TENS + conventional therapy is superior to Sham-MT + Bi-TENS + conventional therapy in improving upper extremity motor impairment, paretic upper extremity grip strength, and community integration in sub-acute stroke survivors. MT is an effective

complementary therapy to Bi-TENS and conventional therapy in terms of improving upper extremity impairment and health-related outcome measures in people with sub-acute stroke.

6.2 Introduction

The first six months of stroke recovery witness the most significant motor function improvement due to fast spontaneous recovery (Grefkes & Fink, 2020). One longitudinal study (Duncan et al., 1992) showed that the 30-day FMA-UE score could explain almost 86% of the variance in motor recovery after 6 months in people with stroke, which indicated that the sub-acute phase is associated with the most dramatic recovery of motor function. A possible reason may be the occurrence of greater neuroplastic changes, e.g., functional cortical reorganization and neurogenesis (generation of new neurons), which induce the most rapid recovery of motor function within the first 6 months of stroke rehabilitation recovery (Sartor et al., 2021). During the sub-acute stroke period, lasting less than 6 months post-stroke, people with stroke are encouraged to begin rehabilitation strategies once their vital signs, such as blood pressure, have been stabilized (Buma et al., 2013; Kwakkel et al., 2004). Hence, studies are needed to identify effective and safe stroke rehabilitation protocols that could maximize the benefits for people with sub-acute stroke.

Bi-TENS has been used to improve motor recovery in stroke survivors recently (Chen et al., 2022; Kwong et al., 2018). The results showed that Bi-TENS can induce significantly greater improvement of upper extremity (Chen et al., 2022) and lower extremity (Kwong et al., 2018) motor function in stroke survivors compared with Uni-TENS. One study (Kwong et al., 2018) found that 20 sessions of Bi-TENS + task-oriented training could induce greater and earlier benefits than Uni-TENS + task-oriented training in improving the paretic ankle dorsiflexion

strength (15.9 ± 7.3 vs. 13.9 ± 6.8, $P = 0.03$) and completion time for the Timed Up and Go Test (14.5 ± 6.4 vs. 17.5 ± 7.3, $P = 0.004$) in 80 people with chronic stroke. Another recent randomized controlled trial (Chen et al., 2022) found that 20 sessions of Bi-TENS + task-oriented training could induce greater and earlier benefits than Uni-TENS + task-oriented training in improving FMA-UE scores (3.39 vs. 1.26, $P < 0.001$) in 120 chronic stroke survivors.

Neurophysiological study working on the mechanisms of Bi-TENS on motor recovery after stroke is lacking. Previous studies demonstrated that Bi-TENS combined with bilateral upper extremity exercises could significantly improve the recovery of upper extremity (Chen et al., 2022) and lower extremity (Kwong et al., 2018) motor function in people with stroke. Possible mechanisms of Bi-TENS in improving the motor functions in stroke survivors were proposed by Chen et al (2022) and Kwong et al. (2018). It has been proposed that Bi-TENS can provide additional sensory input to improve recovery of motor function in people with stroke on the basis of bilateral exercises, including by the recruitment of neural networks of the contralesionally hemisphere (Chen et al., 2024), and by increasing the excitability of transcallosal projections from the ipsilesionally to the contralesionally primary motor cortex by rebalancing interhemispheric inhibition (Cunningham et al., 2019).

MT is used to improve recovery of motor function after stroke by creating a visual illusion of an affected extremity with the mirror-image reflection of the non-affected extremity (Gygax et al., 2011). Total twenty-five sessions of treatment by MT combined with occupational therapy demonstrated significantly better improvement than Sham-MT combined with occupational therapy in FMA-UE scores (12.06 ± 5.84 vs. 6.46 ± 3.92, $P = 0.005$) in 30 people with sub-acute stroke with post-stroke duration less than 6 months (Madhoun et al., 2020). MT can

provide extra visual stimulation to improve recovery of upper extremity motor function in stroke survivors, which can activate parts of the mirror neuron system (e.g., inferior parietal lobule) to improve perceptual–motor control (Zhang et al., 2024), increase the interhemispheric functional connectivity between motor cortex, and increase the attention processing of the affected extremity (Wasaka & Kakigi, 2012) in people with stroke.

As motor recovery is greatest within the first 6 months post-stroke and the synergistic effects of MT combined with ES (functional electrical stimulation, electromyographic biofeedback electrical stimulation, and mesh glove afferent stimulation) for improving upper extremity motor function had been demonstrated in Chapter 3, the potential effectiveness of the addition of MT to Bi-TENS for improving recovery of upper extremity motor function in people with sub-acute stroke has not yet been investigated. As MT and Bi-TENS recruit different neural pathways, it is logical to propose that MT combined with Bi-TENS can exert a synergistic effect to improve the recovery of upper extremity motor function in people with sub-acute stroke.

6.3 Method

The study was conducted from January 2021 to April 2024 in the Physiotherapy Department in the Geriatric Day Hospital at Shatin Hospital, Hong Kong, SAR. The written informed consents were obtained from all people with sub-acute stroke before any study-related procedures in the Physiotherapy Department in the Geriatric Day Hospital at Shatin Hospital, Hong Kong, SAR (Appendix 6.1).

6.3.1 Inclusion and exclusion criteria

People with sub-acute were recruited if they: (1) were between 50 and 85 years of age, (2) have been diagnosed by magnetic resonance imaging or computed tomography as having unilateral ischemic brain injury, or intracerebral hemorrhage within 3 weeks-6 months after the first onset of stroke, (3) have volitional control of their intact arm, (4) have at least minimal antigravity movement in the shoulder of the paretic arm, and at least 5º paretic wrist extension in the antigravity position, (5) obtained a score ≥ 6 out of 10 on the Abbreviated Mental Test (Lam et al., 2010), (6) had no unilateral neglect, hemianopia, or apraxia, (7) were the people with sub-acute stroke admitted to the Geriatric Day Hospital of Shatin Hospital.

Potential people with sub-acute stroke were excluded if they: (1) had any additional medical, cardiovascular, or orthopaedic conditions (e.g., arthritis, pain, or other neurological disorders) that would hinder proper treatment or assessment, (2) had a cardiac pacemaker which preclude the application of Bi-TENS, (3) had receptive dysphasia, (4) had significant upper extremity peripheral neuropathy (e.g., diabetic polyneuropathy), (5) were involved in drug studies or other clinical trials, (6) had severe shoulder, elbow, wrist, of finger contractures that would preclude passive range of arm motions, (7) had a skin allergy that would prevent the application of Bi-TENS, (8) had visual deficits that may hinder them from benefiting from visual mirror feedback.

6.3.2 Study design

This study was a randomized, sham-controlled clinical trial. The ethical approvals were obtained from Joint Chinese University of Hong Kong-New Territories East Cluster Clinical

Research Ethics Committee (Reference Number: 2019.665-T) (Appendix 6.2). This study was prospectively registered on ClinicalTrials.gov (identifier: NCT03631628).

6.3.3 Study procedures

The flowchart of study and data collection plan is demonstrated in Figure 6.1. The training program included 8 weeks of twice per week of the treatment. All people with sub-acute stroke at Shatin Hospital were assessed at A_0(baseline), A_1(after 8 sessions), A_2(after 16 sessions), and A_{FU}(1-month follow-up). The people with sub-acute stroke received total 16 sessions training.

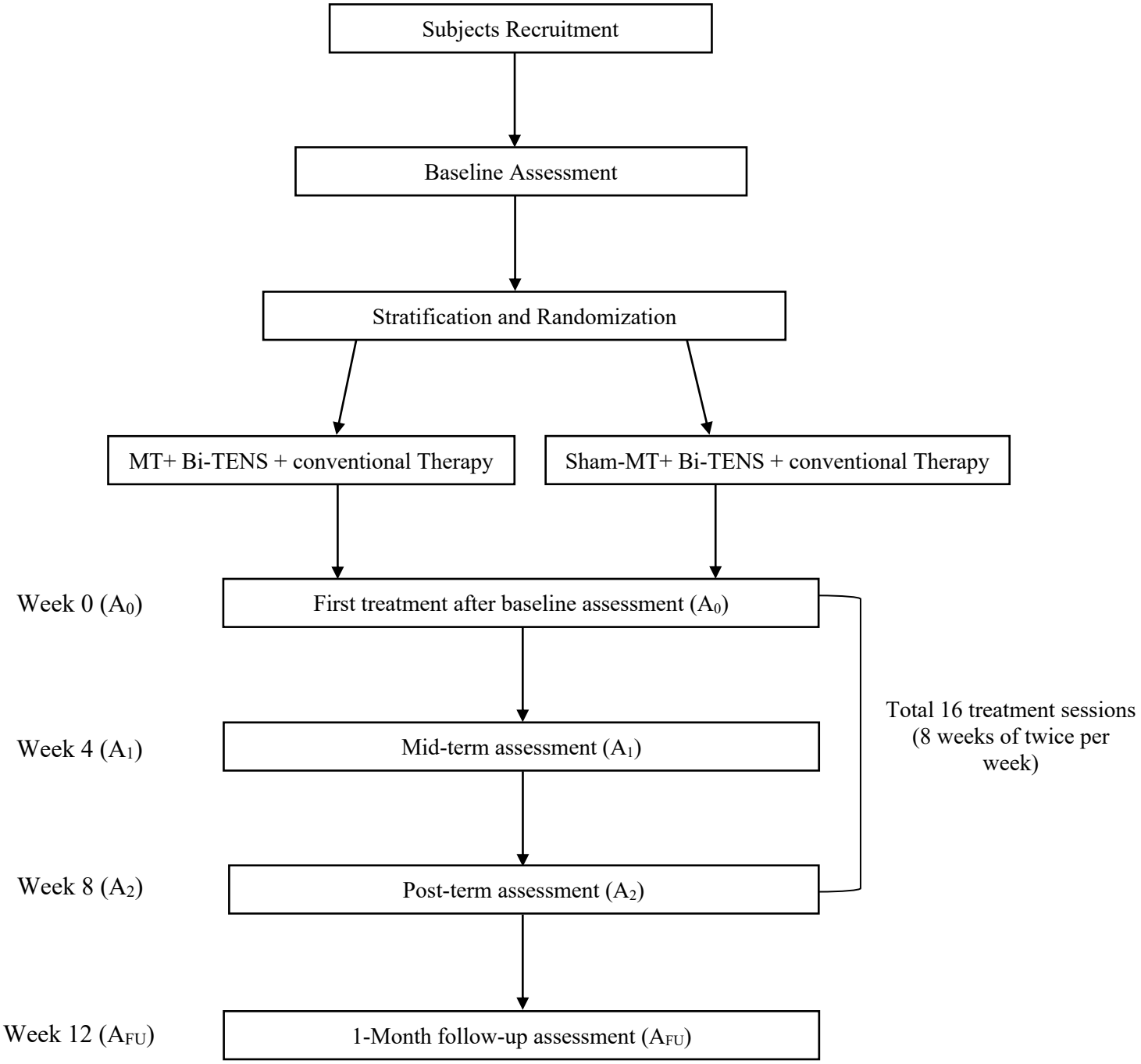


Figure 6.1 Flowchart of the study procedure

6.3.4 Stratification and randomization

The stratification and randomization were conducted by one Minimize computer software (Jensen, 1991). Previous evidence have shown that the age (Roy-O'Reilly & McCullough, 2018), gender (Gibson, 2013), type of stroke (Andersen et al., 2009), side of hemiplegia (Rajashekaran et al., 2013), and the baseline motor impairment (Zarahn et al., 2011) have significant impacts on recovery of upper extremity motor function in people with stroke. In order to minimize the potential bias due to the imbalanced distribution of the major demographic characteristics between two groups, the stratification was conducted based on the age (50-60, 60-70, or 70-85), sex (male or female), the type of stroke (ischemia or haemorrhage), the side of hemiplegia (left or right), and the baseline FMA-UE score (0-22, 23-47, 48-56, or 57-66) (Hoonhorst et al., 2015) before the randomization among 2 groups (Jensen, 1991). In order to ensure effective concealed randomization, the people with sub-acute stroke were informed with the results of the group allocation (only the group number but not the details of interventions).

6.3.5 Sample size calculation

The sample size was calculated using G*Power version 3.1.0 with an alpha level of 0.05, study power of 80%, number of primary outcome measures of 2, correlation among measurements of 0.5, and nonsphericity correlation of 1 (Faul et al., 2007). As no previous study has compared the effects of MT + TENS with those of Sham-MT + TENS on recovery of upper extremity motor function in people with sub-acute stroke, the estimation was based on a recent systematic review and meta-analysis (Zeng et al., 2018). Using pooled data from 11 randomized controlled trials, this meta-analysis calculated a medium effect size (Cohen's d = 0.51, 95% CI = 0.29–0.73, $P < 0.001$) for MT combined with conventional therapy on the improvement of upper extremity motor function, assessed by the FMA-UE, in people with stroke compared with

conventional therapy alone (Zeng et al., 2018). According to this meta-analysis, the addition of MT could result in a medium effect size on improvement of recovery of upper extremity motor function in people with sub-acute stroke. A more conservative effect size of 0.35 was selected in our model, so the total sample size was estimated to be 20 subjects (10 per group) to detect significant between-group differences in people with sub-acute stroke. Due to the pandemic, to be more conservative, we planned to recruit an additional 10 sub-acute stroke survivors to account for dropouts. Hence, we planned a sample size of 30, with 15 subjects for each group.

6.3.6 Intervention protocol

The intervention protocols of two groups in people with sub-acute stroke in the Physiotherapy Department in the Geriatric Day Hospital at Shatin Hospital is summarized in Table 6.1. All people with sub-acute stroke underwent 16 sessions of the intervention protocol, twice per week for total 8 weeks. The people with sub-acute stroke received with concurrent MT and Bi-TENS stimulation practising bilateral upper extremity exercises in the Physiotherapy Department in the Geriatric Day Hospital at Shatin Hospital, Hong Kong, SAR.

Apart from the MT + Bi-TENS and Sham-MT + Bi-TENS for upper extremity, the people with sub-acute stroke participated total 2.5 hours training of standardized occupational therapy, speech therapy, and health education in the Physiotherapy Department in the Geriatric Day Hospital at Shatin Hospital provided by the occupational therapists, speech therapists, and nurses, respectively, whom were blinded for the randomization and allocation. The people with sub-acute stroke took 30 minutes MT + Bi-TENS or Sham-MT + Bi-TENS and 2.5 hours for convention therapy at Geriatric Day Hospital of Shatin Hospital.

Table 6.1 The arrangement of intervention protocols in two groups in people with sub-acute stroke at Shatin Hospital

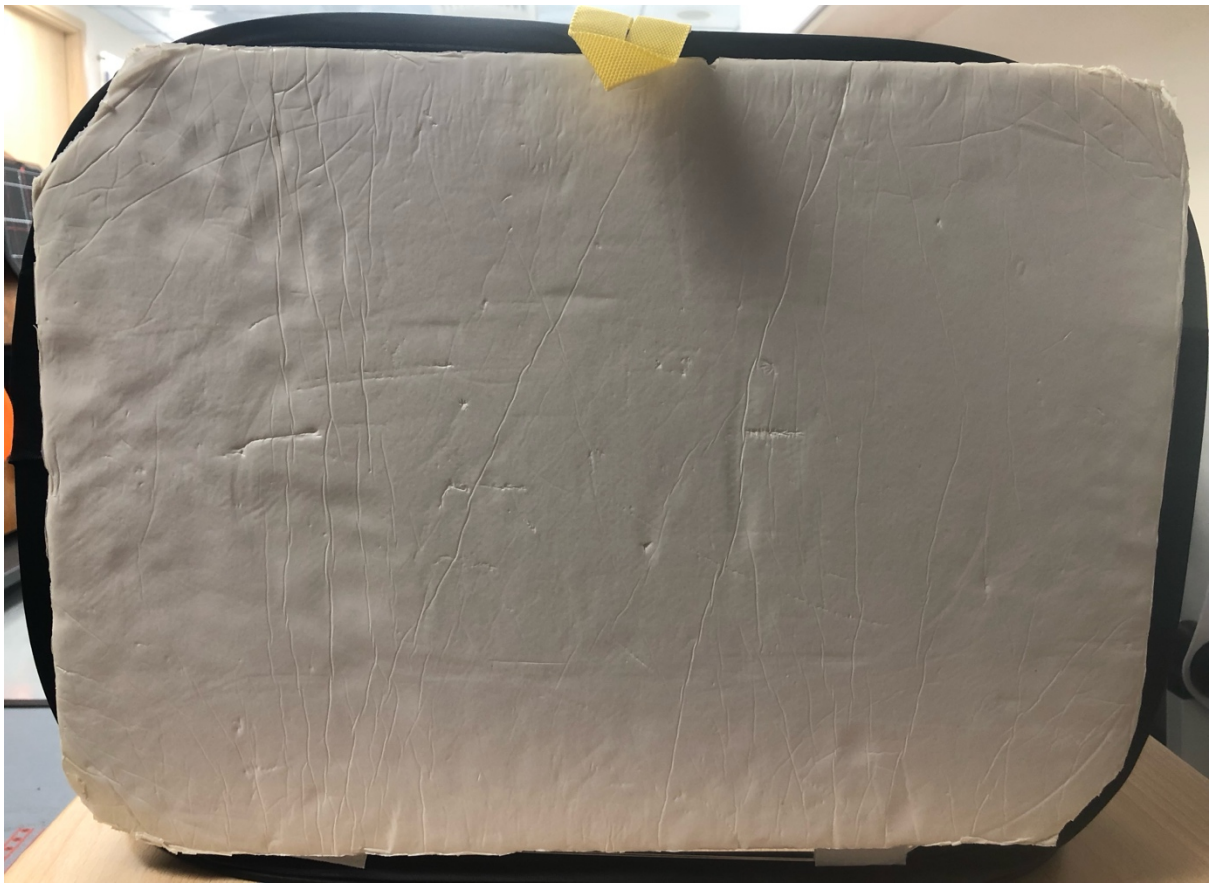
Training Time	Groups	
Duration (3 hours)	MT + Bi-TENS Group	Sham-MT + Bi-TENS Group
Experimental intervention (30 minutes)	MT (with bilateral upper extremity exercise) + Bi-TENS	Sham-MT (with bilateral upper extremity exercise) + Bi-TENS
Convention Therapy provided at the Geriatric Day Hospital of Shatin Hospital (2.5 hours)	Convention Therapy (Standardized occupational therapy + Speech therapy+ Health education)	

6.3.6.1 Mirror therapy protocol

MT and Sham-MT are presented in Figure 5.2 and 5.3, respectively. An angle-adjustable frame with a mirror box (60 × 40 cm) was used for MT. For experimental group, the paretic arm was positioned behind the mirror, with the non-paretic arm facing the reflective surface. For the control group, the mirror box was covered by a paper. The experimental set-up and protocol was the same as the experimental group. In the Sham-MT group, the people with sub-acute stroke were reminded to focus on the bilateral upper extremity exercises.

Figure 6.2 Mirror Box for Experimental Group

Figure 6.3 Sham-Mirror Box for Control Group



6.3.6.2 Bilateral TENS protocol

Two pairs of TENS electrodes applied over median (pronator quadratus and flexor digitorum superficialis) and radial (extensor pollicis longus and extensor digitorum communis) nerve are presented in Figure 6.4 and 6.5, respectively. The TENS parameters were applied according to previous studies (Chen et al., 2022; Kwong et al., 2018; Ng, 2007). Previous studies demonstrated that sensory stimulation of TENS with similar parameters could induce beneficial effects for improving upper (Chen et al., 2022) and lower extremities (Kwong et al., 2018; Ng, 2007) recovery of motor function in stroke survivors. The sensory stimulation intensity was set below the motor threshold without the muscle twitching in this study according to previous studies (Chen et al., 2022; Kwong et al., 2018; Ng, 2007).

Figure 6.4 TENS applied over the median nerve

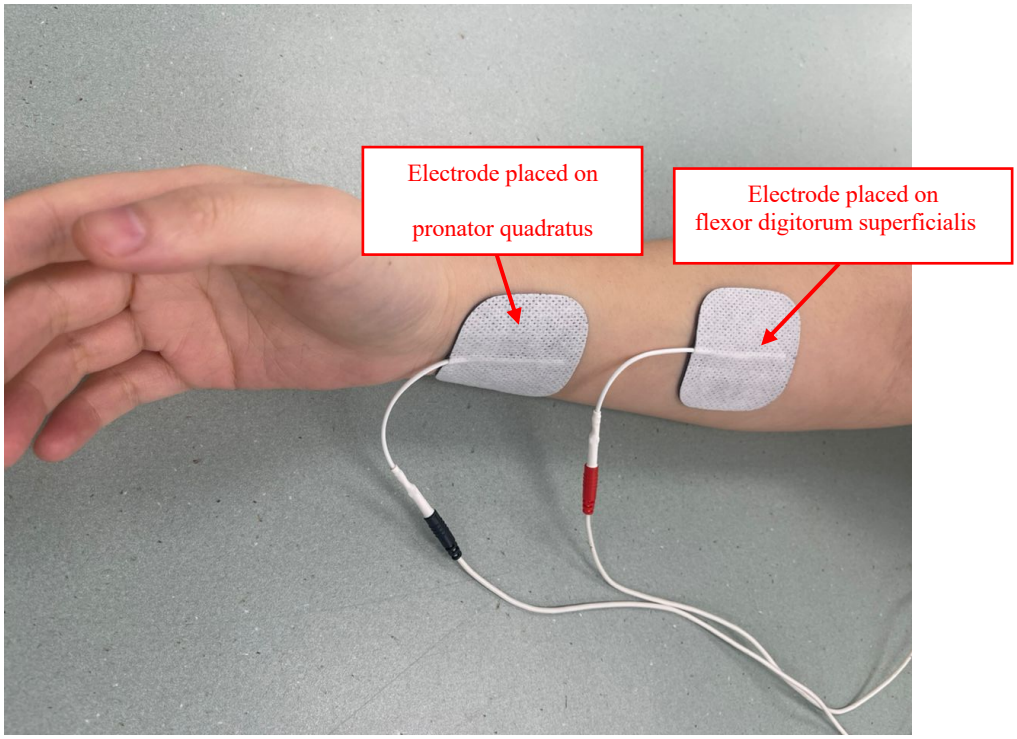
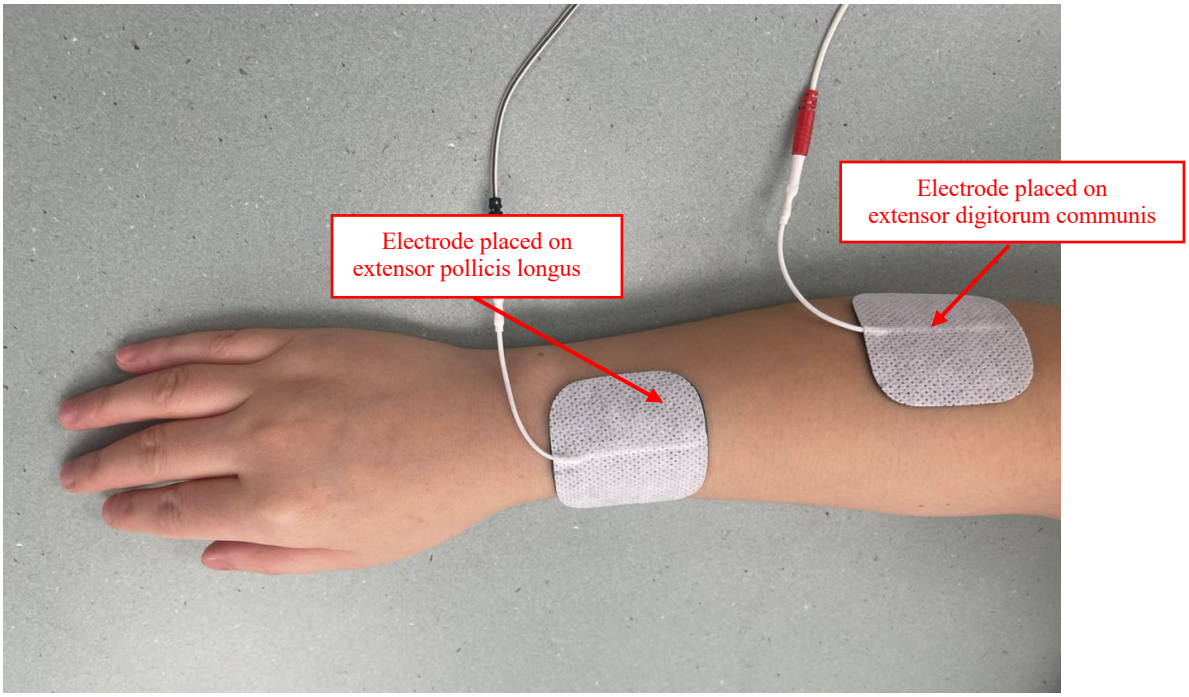


Figure 6.5 TENS applied over the radial nerve



6.3.6.3 Bilateral upper extremity exercises

Concurrent with MT or Sham-MT with electrical stimulation, the people with sub-acute stroke were required to complete 30 minutes training comprising six 5-minute upper extremity exercises. During the exercises, the non-paretic arm was placed in front of mirror and paretic arm was placed behind the mirror. The people with sub-acute stroke were required to flex and extend all joints (elbow, wrist, and fingers) in full available range in sitting position to improve the active control of elbow, wrist, and fingers joint, respectively. The people with sub-acute stroke were encouraged to focus on the image of non-paretic arm when performing bilateral upper extremity exercises. If people with sub-acute stroke felt tired, 1-minute rest interval was provided during the training. The people with sub-acute stroke were required to complete as many repetitions as possible within each 5 minutes. The detailed protocol for each upper extremity exercise were provided in Table 6.2. The demonstration for each upper extremity exercises could be found in Appendix 6.3.

Table 6.2 The details of summarized protocol of the bilateral upper extremity exercises

Items	Exercise	Duration	Exercise protocol	Progression
1	Elbow flexion and extension	5 minutes	Both the paretic and non-paretic placed on neutral position and the subjects were asked to perform elbow flexion and extension alternately as much as until reaching the end of active range of motion.	The subjects were required to complete as many repetitions as possible during each 5 minutes. According to improvements, the subjects were encouraged to increase the range of motion and speed of movement for each exercise.
2	Forearm supination and pronation	5 minutes	Both the paretic and non-paretic placed on neutral position and the subjects were asked to perform forearm supination and pronation alternately as much as until reaching the end of active range of motion.	
3	Wrist flexion and extension	5 minutes	Both the paretic and non-paretic placed on neutral position and the subjects were asked to perform wrist flexion and	

			extension alternately as much as until reaching the end of active range of motion.	
4	Wrist radial and ulnar deviation	5 minutes	Both the paretic and non-paretic placed on neutral position and the subjects were asked to perform wrist radial and ulnar deviation alternately as much as until reaching the end of active range of motion.	
5	Finger opposition	5 minutes	Both the paretic and non-paretic placed on neutral position and the subjects were asked to perform finger opposition from Thumb to Pinky alternately until fully opposition.	
6	Gripping	5 minutes	Both the paretic and non-paretic placed on neutral position and the subjects were asked to perform hand gripping with fingers flexion and extension alternately until reaching the end of active range of motion.	

6.3.7 Outcome measures

Those outcome measures were selected according to the framework of International Classification of Functioning, Disability and Health (W, 1959).The outcome measures of FMA-UE and Paretic Maximum Grip Strength belong to body function domain. The outcome measures of WMFT, the Jacket Test, C-UEFI, and MAL belong to activity domain. The outcome measures of SIS, C-CIM, and C-SATIS-Stroke belong to participation domain.

6.3.7.1 Primary outcomes

6.3.7.1.1 Fugl-Meyer Assessment of Upper Extremity (FMA-UE)

The FMA-UE was used to assesses the upper extremity motor impairment and motor control in people with stroke (Fugl-Meyer et al., 1975). Details of FMA-UE has been reported in Chapter 5, Section 5.3.2.3. The detailed protocol of FMA-UE was provided in Appendix 6.4.

6.3.7.1.2 Wolf Motor Function Test (WMFT)

The WMFT is a quantitative outcome measure to assess the upper extremity motor ability in people with stroke (Wolf et al., 2005). Details of WMFT has been reported in Chapter 5, Section 5.3.2.4. The detailed protocol of WMFT was provided in Appendix 6.5.

6.3.7.2 Secondary Outcomes

6.3.7.2.1 Paretic Maximum Grip Strength

The paretic maximum grip strength is an appropriate measurement to quantify upper extremity weakness and recovery in older adults (Abizanda et al., 2012) and stroke survivors (Bertrand et al., 2015). As people with sub-acute stroke had low exercises endurance (Potempa et al., 1995), only the paretic maximum grip strength for once was assessed in this study. The maximum grip strength was evaluated using dynamometer with standardised sitting position (Abizanda et al., 2012). The maximal grip strength assessment has previously demonstrated excellent test-retest reliability (ICC = 0.91-0.99) for the paretic hand in stroke survivors (Bertrand et al., 2015; Boissy et al., 1999).

6.3.7.2.2 The Jacket Test

The Jacket Test was used to assess the upper extremity proficiency in wearing the jacket in stroke survivors (Chen et al., 2017). The time it took to complete the task was recorded. The Jack Test has demonstrated good to excellent test-retest reliability (ICC = 0.78-1.00) in stroke survivors (Chen et al., 2017). The detailed protocol of Jacket Test was provide in the Appendix 6.6.

6.3.7.2.3 Chinese version of Upper Extremity Functional Index (C-UEFI)

The C-UEFI was used to assess the self-perceived upper extremity functional recovery in daily life activity in stroke survivors (Pan et al., 2023). Details of C-UEFI has been reported in Chapter 5, Section 5.3.2.1. The detailed protocol of Jacket Test was provide in the Appendix 6.7.

6.3.7.2.4 Motor Activity Log (MAL)

The MAL was used to assess the amount of use and quality of movement of the paretic upper extremity function during the daily living activities in people with stroke as indicated in semi-structured interview (van der Lee et al., 2004). Details of MAL has been reported in Chapter 5, Section 5.3.2.9. The detailed protocol of the MAL was provided in Appendix 6.8.

6.3.7.2.5 Stroke Impact Scale (SIS)

The SIS was used to assess the subjective level of disability and health-related quality of life as a self-reported questionnaire in people with stroke (MacIsaac et al., 2016). Details of SIS has been reported in Chapter 5, Section 5.3.2.13. The detailed protocol of the SIS was provided in Appendix 6.9.

6.3.7.2.6 Chinese version of Community Integration Measures (C-CIM)

The C-CIM was used to assess the integration in community people with stroke (Liu et al., 2014). Details of C-CIM has been reported in Chapter 5, Section 5.3.2.14. The detailed protocol of the C-CIM was provided in Appendix 6.10.

6.3.7.2.7 Chinese version of SATIS-Stroke (C-SATIS-Stroke)

The C- SATIS-Stroke was used to assess the subjective satisfaction feeling in terms of social participation among people with stroke (Pan et al., 2024). Details of C- SATIS-Stroke has been

reported in Chapter 5, Section 5.3.2.2. The detailed protocol of the C-SATIS-Stroke was provided in Appendix 6.11.

6.3.8 Statistical analysis

The IBM SPSS version 28 (IBM Corp, Armonk, NY,USA) was used to conduct the statistical analyses. The Shapiro-Wilk statistic method was applied for data normality checking. Independent t-test and Mann-Whitney U test were used to compare the between-group difference for the parametric and non-parametric data in demographics, respectively. Parametric data were presented as mean and standard deviation while nonparametric data were presented as median and interquartile range. The categorical variables were presented as frequency and percentages The Chi-squared test was used to calculate the statistically significant differences in categorical variables. As nine outcome measures were tested on the same participants, the threshold of statistical significance was set at alpha of 0.006 (0.05/9) (2-sided) with the Bonferroni correction to decrease the risk of a type I error.

The linear mixed-effect model could automatically handle the missing data without using the last observation carried forward method. Moreover, to deal with issues of repeated measures, and the criterion of normality was not met of ordinal variables, the linear mixed-effect model analysis was used to evaluate the treatment effects over time between MT + Bi-TENS + conventional therapy and Sham-MT + Bi-TENS + conventional therapy in this study.

The treatment effects from A_0 to A_2 was first analysed. Another linear mixed-effect model was then quantified any carryover effect from A_2 to A_{FU} evaluation. In case when any significant time-by-group interaction effect (between group effects) was found in total effects from A_0 to

A_2, post-hoc comparison tests with another Bonferroni correction (0.006/2) = 0.003, with 2 comparison time points of A_0 vs. A_1 and A_0 vs. A_2) were conducted by using the linear mixed-effect model to analysis the between group and time effects, respectively.

6.3.9 Safety consideration

The safety consideration and precautions were taken to measure the blood pressure and heart rate before, during, and after the training at Shatin hospital, Hong Kong, according to the American Heart Association recommendation (Fletcher et al., 2013) (120 beats per minute (peak rate), and systolic blood pressure of 200mmHg or a diastolic blood pressure of 110mmH). If blood pressure or heart rate exceed this limits, all training would be terminated.

6.4 Results

6.4.1 The recruitment of people with sub-acute stroke

Forty-three potential people with sub-acute stroke were screened between January 2021 and April 2024, of whom 30 eligible people with sub-acute stroke were enrolled and randomized into two groups (See Figure 6.6). Intention-to-treat analysis was used to evaluate the participants according to the groups to which they were originally assigned.

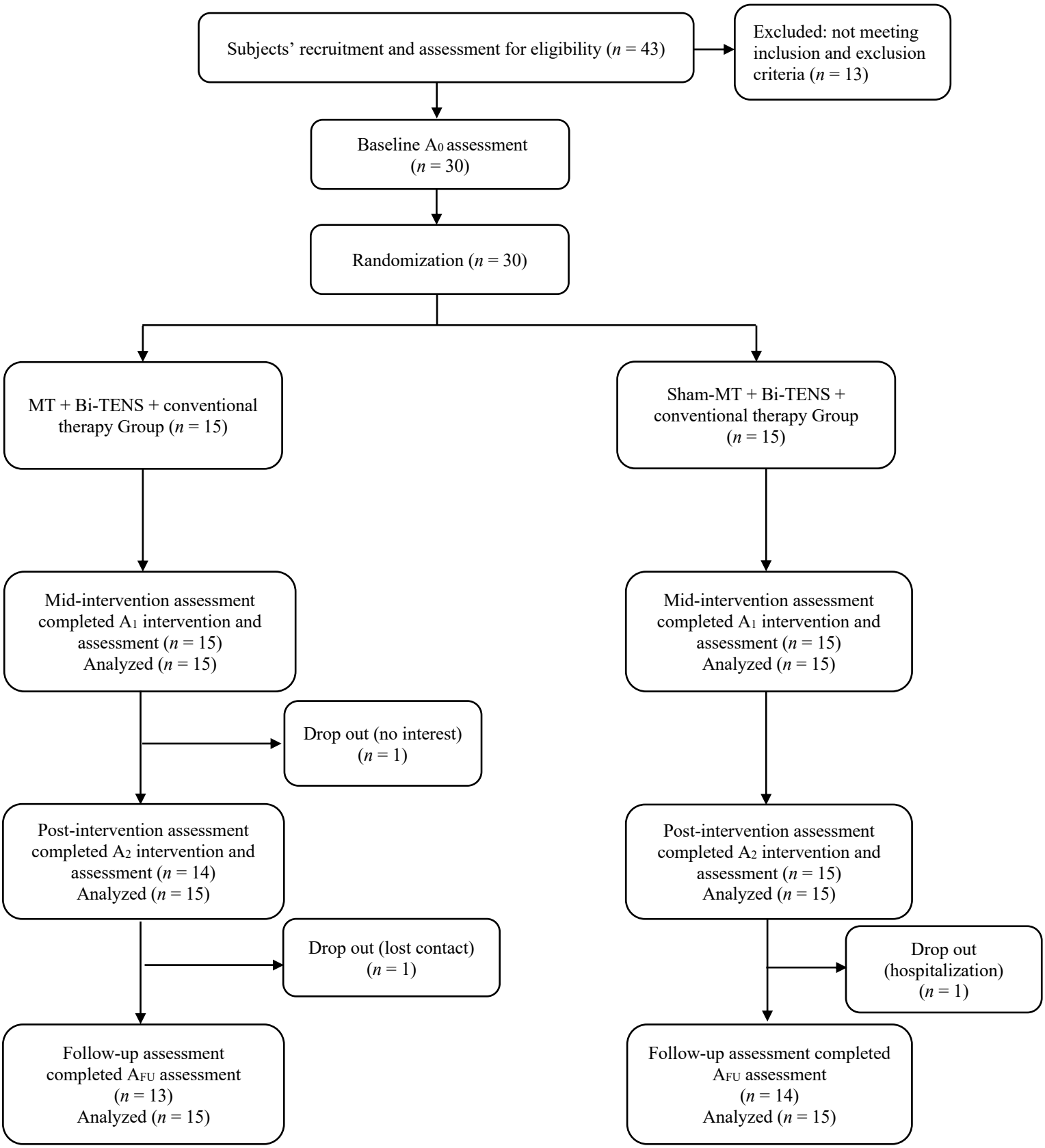


Figure 6.6 Flow diagram of the study

6.4.2 Demographic information

All demographic parameters showed no significant differences at A_0 (Table 6.1). One participant in the MT + Bi-TENS + conventional therapy group dropped out at A_2 (not interested in this study). Two participants in the MT + Bi-TENS + conventional therapy and Sham-MT + Bi-TENS + conventional therapy group, respectively, dropped out at A_{FU} (i.e., lost contact after being discharged from Shatin Hospital and hospitalization, respectively). In total, 29 subjects (97%) completed the intervention and assessment at A_2, and 27 subjects (90%) completed the assessment at A_{FU} (See Figure 6.1). No adverse effects occurred during the study in Shatin Hospital, Hong Kong.

Table 6.3 The Baseline Characteristics of People with Sub-acute Stroke (n = 30)

	MT + Bi-TENS (n = 15)	Sham-MT + Bi-TENS (n = 15)	Between-groups Comparison
Variables	Number (Frequency, %)		χ^2 Test, P-value
Gender (Male/ Female)	10(67)/5(33)	7(47)/8(53)	0.269
Side of Hemiplegia (Left/Right)	8(53)/7(47)	7(47)/8(53)	0.715
Type of Stroke (Ischemia/Haemorrhage)	13(87)/2(13)	12(80)/3(20)	0.624
Living Arrangement (Live alone/Live with family)	14(93)/1(7)	14(93)/1(7)	1.000
Education Level (Primary or below/Secondary/College or above)	7(47)/7(47)/1(6)	6(40)/8(54)/1(6)	0.931
Variables	Mean ± SD		Independent t Test, P-value
Age (Year)	61.4±7.8	62.9±7.7	0.593
Time since stroke (Month)	2.5±0.9	2.2±0.7	0.358
Body Mass Index, kg/m^2	24.3±2.9	25.5±2.9	0.259
Variables	Median (IR)		Mann-Whitney U Test, P-value
Abbreviated Mental Test (Total score)	10.0(10-10)	10.0(10-10)	1.000
FMA-UE (Paretic side) (Total score)	33.0(30-34)	31.0(25-36)	0.250

WMFT (Paretic side) (Total score)	38.0(37-41)	39.0(23-44)	1.000
Grip Strength (Paretic side) (kg)	7.5(5-10.7)	5.3(3.2-7.5)	0.116
Jacket Test (Second)	22.0(18.2-23.5)	19.4(18.1-29.1)	0.775
C-UEFI (Total score)	21.0(15-44.5)	29.0(17-35)	0.893
MAL(Amount of Use) (Total score)	26.0(16.5-32)	25.0(12-38)	0.744
MAL(Quality of Movement) (Total score)	23.0(15.5-33)	26.0(8-31)	0.624
SIS (Total Score)	59.9(52.5-71.6)	66.9(45.3-69.9)	0.683
C-CIM (Total score)	39.0(38-45)	42.0(38-45)	0.624
C-SATIS-Stroke (Total score)	0.3(0.1-0.5)	0.3(-0.2-0.6)	0.501

Note: n, number; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; SD, standard deviation; IR, interquartile range; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure. C-SATIS-Stroke, Chinese SATIS-Stroke.

6.4.3 The effects of MT + Bi-TENS + conventional therapy versus Sham-MT + Bi-TENS + conventional therapy

The results from A_0 to A_2 were showed in Table 6.4, Table 6.5, and Table 6.6.The results for the carryover effects from the A_2 to A_{FU} were showed table 6.7.

6.4.3.1 Primary outcome measures

A significant time-by-group interaction effect (MD = 5.9; $P < 0.001$, Table 6.4) was observed, with the MT + Bi-TENS group demonstrating a greater improvement in FMA-UE score than Sham-MT + Bi-TENS at A_1 (MD = 5.7; $P < 0.001$, Table 6.5) and A_2 (MD = 11.8; $P < 0.001$, Table 6.5). A significant time-by-group interaction effect (MD = 4.3; $P < 0.001$, Table 6.4) was observed, with the MT + Bi-TENS group demonstrating no significantly improvement in WMFT scores than Sham-MT + Bi-TENS at A_1 and A_2 of post-hoc analysis (Table 6.5).

The within-group effect demonstrated that both MT + Bi-TENS and Sham-MT + Bi-TENS groups demonstrated significant improvement in FMA-UE (EG, MD = 10.7- 22.0, $P < 0.001$; CG, MD = 5.0-10.2, $P < 0.001$; Table 6.6) and WMFT (EG, MD = 11- 21.5, $P < 0.001$; CG, MD = 6.7-12.9, $P < 0.001$; Table 6.6) scores at both A_1 and A_2. No significant between-group differences between two groups from A_2 to A_{FU} (Table 6.7). No significant results in FAM-UE and WMFT scores from A_2 to A_{FU}, indicating the improvement in FMA-UE and WMFT scores in two groups were maintained at A_{FU} (Table 6.7).

6.4.3.2 Secondary outcome measures

Significant time-by-group interaction effects were observed for paretic maximum grip strength (MD = 2.1; $P < 0.001$), MAL (Quality of Movement) (MD = 6.7; $P = 0.005$), C-CIM (MD = 1.5; $P < 0.001$) scores (Table 6.4). The post-hoc analysis of between-group effects shown that MT + Bi-TENS group demonstrated a greater improvement in paretic maximum grip strength at A_1 (MD = 2.9; $P < 0.001$, (Table 6.5)) and A_2 (MD = 4.6; $P < 0.001$, (Table 6.5)), improvement in C-CIM scores at A_2 (MD = 3.9; $P = 0.002$, (Table 6.5)), and no improvement in MAL (Quality of Movement) scores at A_1 and A_2 than Sham-MT + Bi-TENS (Table 6.5). The post-hoc analysis of within-group effects demonstrated that both MT + Bi-TENS and Sham-MT + Bi-TENS groups showed significant improvement in MAL (Quality of Movement) (EG, MD = 19.1-31.2, $P < 0.001$; CG, MD = 9.2 -17.3, $P < 0.001$) scores at A_1 and A_2 (Table 6.6). The post-hoc analysis of within-group effects demonstrated that experimental group showed significant improvement in paretic grip strength (MD = 3.9-6.4, $P < 0.001$) at both A_1 and A_2 while control group only showed significant improvement in paretic grip strength at A_2 (MD = 1.9, $P = 0.001$) (Table 6.6). The post-hoc analysis of within-group effects demonstrated that only control group showed significant improvement in C-CIM (MD = 3.4-5.2, $P < 0.001$) scores at both A_1 and A_2 (Table 6.6).

No significant time-by-group interaction effects were observed for MAL (Amount of Use) and SIS mean scores between MT + Bi-TENS and Sham-MT + Bi-TENS groups (Table 6.4). The post-hoc analysis of within-group effects demonstrated that both MT + Bi-TENS and Sham-MT + Bi-TENS groups showed significant improvement in MAL (Amount of Use) (EG, MD = 22.8-36.3, $P < 0.001$; CG, MD = 9.9 -19.8, $P = 0.001$ and $P < 0.001$, respectively) scores at both A_1 and A_2 (Table 6.6). The results also demonstrated that the experimental group showed earlier improvement in SIS scores of within-group analysis (MD = 8.5, $P < 0.001$) at A_1, while

the control group only showed significant improvement SIS scores of within-group analysis (MD = 6.8, $P = 0.001$) at A_2 (Table 6.6).

No significant time-by-group interaction effects were observed for Jacket Test, C-UEFI, C-SATIS-Stroke mean scores between MT + Bi-TENS and Sham-MT + Bi-TENS groups (Table 6.4). The results also demonstrated that only experimental group showed significant improvement in Jacket Test (MD = 6.3 - 8.2, $P < 0.001$) and C-UEFI (MD = 6.8-11.7, $P < 0.001$) scores at both A_1 and A_2 of within-group analysis (Table 6.6), while both MT + Bi-TENS and Sham-MT + Bi-TENS showed no significant within-group improvement in C-SATIS-Stroke score at both A_1 and A_2 (Table 6.6).

The Linear Mixed Model analysis showed that the experimental group showed no significant results in paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, C-CIM, and C-SATIS-Stroke scores to Sham-MT + Bi-TENS between A_2 and A_{FU} (Table 6.7). The Linear Mixed Model analysis demonstrated that two groups showed no significant results in paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, C-CIM, and C-SATIS-Stroke scores between A_2 and A_{FU} of within-group analysis, indicating that the improvement of those outcome measure scores in both two groups were maintained at A_{FU} (Table 6.7).

Table 6.4 The Results of Linear Mixed Models of the Outcome Measures Across A_0, A_1, and A_2 in People with Sub-acute Stroke (n = 30)

Outcome Measures	Group	Baseline (A_0)	1 Month (A_1)	2 Month (A_2)	Time effect (MD (95%CI)), P Value	Group effect (MD (95%CI)), P Value	Interaction effect (MD (95%CI)), P Value
			Primary Outcomes				
FMA (Total score) (range) (0 to 66, higher better)	MT + Bi-TENS	33(30-34)	42(39-47)	54(50-59)	10.9 (9.5, 12.3), $P < 0.001^*$	18.8 (11.4, 26.3), $P < 0.001$	5.9 (3.9, 7.9), $P < 0.001^*$
	Sham-MT + Bi-TENS	29(25-36)	35(28-43)	42(30-49)	5.1 (3.6, 6.5), $P < 0.001^*$		
WMFT (Total score) (range) (0 to 75, higher better)	MT + Bi-TENS	39(37-41)	50(43-52)	59(52-66)	10.8 (9.0, 12.6), $P < 0.001^*$	14.8 (5.6, 24.0), $P = 0.002$	4.3 (1.8, 6.8), $P < 0.001^*$
	Sham-MT + Bi-TENS	36(23-44)	40(28-49)	50(35-60)	6.5 (4.8, 8.2), $P < 0.001^*$		
			Secondary Outcomes				
Grip Strength (Kg) (range) (Higher better)	MT + Bi-TENS	7.5(5-11)	12(7-16)	12(10-19)	3.1 (2.6, 3.5), $P < 0.001^*$	8.3 (4.7, 11.9), $P < 0.001$	2.1 (1.5, 2.8), $P < 0.001^*$
	Sham-MT + Bi-TENS	5(3-8)	6(4-9)	6(5-9)	0.9 (0.5, 1.3), $P < 0.001^*$		

Jacket Test (Second)(range) (Lesser better)	MT + Bi-TENS	21(18-24)	16(13-19)	14(13-18)	-3.1 (-3.9, -2.2), $P < 0.001^*$	-8.9 (-4.7, -13.0), $P < 0.001$	-1.5 (-2.7, -0.4), $P = 0.010$
	Sham-MT + Bi-TENS	23(18-29)	22(17-28)	21(17-26)	-1.5 (-2.3, -0.7), $P < 0.001^*$		
C-UEFI (Total score) (range) (0 to 59, higher better)	MT + Bi-TENS	21(15/45)	32(24/49)	36(26/52)	5.8 (3.2, 8.4), $P < 0.001^*$	10 (1.4, 21.5), $P = 0.083$	2.9 (-1.0, 6.8), $P = 0.139$
	Sham-MT + Bi-TENS	29(17/35)	33(19/35)	34(20/45)	2.9 (0.0, 5.8), $P = 0.051$		
MAL(Amount of Use) (Total score) (range) (Higher better)	MT + Bi-TENS	29(17-32)	49(35-55)	58(49-70)	16.7 (13.1, 20.3), $P < 0.001^*$	25.8 (10.9, 40.7), $P < 0.001$	6.8 (1.8, 12.0), $P = 0.009$
	Sham-MT + Bi-TENS	25(12-38)	42(22-46)	50(27-56)	9.9 (6.3, 13.5), $P < 0.001^*$		
MAL(Quality of Movement) (Total score) (range)	MT + Bi-TENS	27(16-33)	42(33-55)	52(46-63)	15.2 (12.1, 18.4), $P < 0.001^*$	25.6 (12.4, 38.8), $P < 0.001$	6.7 (2.1, 11.2), $P = 0.005^*$
	Sham-MT + Bi-TENS	26(8-31)	27(19-44)	33(27-54)	8.6 (5.4, 11.8), $P < 0.001^*$		

(Higher better)							
SIS (Total score) (range) (Higher better)	MT + Bi-TENS	61(52-72)	70(61-75)	76(68-84)	7.3 (5.4, 9.2), $P < 0.001$*	15.5 (7.1, 24), $P < 0.001$	3.9 (1.2, 6.6), $P = 0.007$
	Sham-MT + Bi-TENS	63(45-70)	63(47-73)	65(49-73)	3.4 (1.5, 5.3), $P = 0.001$*		
C-CIM (Total score) (range) (0 to 100, higher better)	MT + Bi-TENS	40(38-45)	43(40-49)	46(40-50)	2.1 (0.6, 2.7), $P < 0.001$*	4.6 (0.90, 8.36), $P = 0.017$	1.5 (0.8, 2.3), $P < 0.001$*
	Sham-MT + Bi-TENS	41(38-45)	41(39-45)	43(40-46)	0.6 (0.0, 1.1), $P = 0.037$		
C-SATIS-Stroke (Total score) (range) (0 to 1.03, higher better)	MT + Bi-TENS	0.3(0.1-0.5)	0.4(0.2-0.7)	0.6(0.3-1.1)	0.2 (0.1, 0.3), $P = 0.003$*	0.6 (0.0, 1.1), $P = 0.057$	0.1 (-0.1, 0.3), $P = 0.374$
	Sham-MT + Bi-TENS	0.3 (-0.2-0.6)	0.4(-0.1-0.7)	0.3(-0.1-0.7)	0.1(0.0, 0.2), $P = 0.109$		

*indicated significant difference ($P < 0.006$)

Note: CI, confidence interval; MD, mean difference; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

Table 6.5 Between-group Effects of MT + Bi-TENS and Sham-MT + Bi-TENS in People with Sub-acute Stroke (n = 30) (Post-Hoc Analysis)

Outcome Measures	1 Month (A_1) VS. Baseline (A_0)		2 Month (A_2) VS. Baseline(A_0)	
	Estimate (Standard Error)	P Value (95% CI)	Estimate (Standard Error)	P Value (95% CI)
Primary Outcomes				
FMA-UE (Total score): 0 to 66, higher better	5.7 (1.2)	$P < 0.001$ (3.2, 8.3) *	11.8 (2.0)	$P < 0.001$ (7.6, 16.0) *
WMFT (Total score) :0 to 75, higher better	4.3 (1.7)	$P = 0.014$ (0.9, 7.7)	8.6 (3.0)	$P = 0.007$ (2.6, 14.6)
Secondary Outcomes				
Grip Strength (Kg): higher better	2.9 (0.8)	$P < 0.001$ (1.4, 4.5) *	4.6 (0.7)	$P < 0.001$ (3.1, 6.1) *
Jacket Test (Second): lesser better	-5.3 (1.3)	$P < 0.001$ (-7.9, -2.6)	-5.5 (1.4)	$P < 0.001$ (-8.3, -2.7)
C-UEFI (Total score): 0 to 59, higher better	4.4 (2.3)	$P = 0.069$ (-0.4, 9.2)	6.0 (3.8)	$P = 0.126$ (-1.8, 13.8)

MAL(Amount of Use) (Total score): higher better	12.9 (3.9)	*P* = 0.002 (4.9, 20.8)	16.5 (5.7)	*P* = 0.006 (4.9, 28.0)
MAL(Quality of Movement) (Total score): higher better	9.9 (6.2)	*P* = 0.005 (3.3, 16.5)	13.9 (4.5)	*P* = 0.004 (4.8, 23.1)
SIS (Total score): higher better	4.8 (2.0)	*P* = 0.024 (0.7, 8.9)	7.7 (2.7)	*P* = 0.007 (2.3, 13.2)
C-CIM (Total score): 0 to 100, higher better	2.6 (1.2)	*P* = 0.038 (0.1,5.1)	3.9 (1.1)	*P* = 0.002 (1.6, 6.2) *
C-SATIS-Stroke (Total score): 0 to 1.03, higher better	0.1 (0.1)	*P* = 0.386 (-0.2,0.4)	0.2 (0.2)	*P* = 0.369 (-0.2, 0.5)

*indicated significant difference ($P < 0.003$)

Note: CI, confidence interval; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

Table 6.6 Within-group Effects of MT + Bi-TENS and Sham-MT + Bi-TENS in People with Sub-acute Stroke (n = 30) (Post-Hoc Analysis)

Groups	1 Month (A_1) VS. Baseline(A_0)		2 Month (A_2) VS. Baseline(A_0)	
	Estimate (Standard Error)	*P* Value (95% CI)	Estimate (Standard Error)	*P* Value (95% CI)
		Primary Outcomes		
		FMA-UE (Total score): 0 to 66, higher better		
MT + Bi-TENS	10.7 (0.9)	$P < 0.001$ (8.9, 12.5) *	22.0 (1.4)	$P < 0.001$ (19.0, 24.9) *
Sham-MT + Bi-TENS	5.0 (0.9)	$P < 0.001$ (3.2, 6.8) *	10.2 (1.4)	$P < 0.001$ (7.2, 13.1) *
		WMFT (Total score):0 to 75, higher better		
MT + Bi-TENS	11.0 (1.2)	$P < 0.001$ (8.6, 13.4) *	21.5 (2.1)	$P < 0.001$ (17.3, 25.8) *
Sham-MT + Bi-TENS	6.7 (1.2)	$P < 0.001$ (4.3, 9.1) *	12.9 (2.1)	$P < 0.001$ (8.7, 17.2) *
		Secondary Outcomes		
		Grip Strength (kg): higher better		
MT + Bi-TENS	3.9 (0.5)	$P < 0.001$ (2.8, 5.0)*	6.4 (0.5)	$P < 0.001$ (5.4, 7.5) *
Sham-MT + Bi-TENS	0.9 (0.5)	$P = 0.090$ (-0.2, 2.0)	1.9 (0.5)	$P = 0.001$ (0.8, 2.9)*
		Jacket Test (Second): lesser better		
MT + Bi-TENS	-6.3 (0.9)	$P < 0.001$ (-8.1, -4.4)*	-8.2 (1.0)	$P < 0.001$ (-10.2, -6.2)*
Sham-MT + Bi-TENS	-1.0 (1.0)	$P = 0.278$ (-2.9, 0.85)	-2.7 (1.0)	$P = 0.010$ (-4.7, -0.7)
		C-UEFI (Total score): higher better		
MT + Bi-TENS	6.8 (1.5)	$P < 0.001$ (3.6, 10.0)*	11.7 (2.5)	$P < 0.001$ (6.5, 16.9)*
Sham-MT + Bi-TENS	2.4 (1.7)	$P = 0.187$ (-1.2, 6.0)	5.7 (2.8)	$P = 0.054$ (-0.1, 11.6)
		MAL(Amount of Use) (Total score): higher better		
MT + Bi-TENS	22.8 (2.8)	$P < 0.001$ (17.1, 28.4)*	36.3 (4.0)	$P < 0.001$ (28.1, 44.4)*
Sham-MT + Bi-TENS	9.9 (2.8)	$P = 0.001$ (4.3, 15.5)*	19.8 (4.1)	$P < 0.001$ (11.7, 27.9)*
		MAL(Quality of Movement) (Total score): higher better		
MT + Bi-TENS	19.1 (2.3)	$P < 0.001$ (14.4, 23.8)*	31.2 (3.2)	$P < 0.001$ (24.8, 37.7)*
Sham-MT + Bi-TENS	9.2 (2.3)	$P < 0.001$ (4.5, 13.9)*	17.3 (3.2)	$P < 0.001$ (10.9, 23.7)*
		SIS (Total score): higher better		
MT + Bi-TENS	8.5 (1.4)	$P < 0.001$ (5.6, 11.4)*	14.5 (1.9)	$P < 0.001$ (10.6, 18.4)*

Sham-MT + Bi-TENS	3.7 (1.4)	$P = 0.013$ (0.8, 6.6)	6.8 (1.9)	$P = 0.001$ (2.9, 10.6)*
C-CIM (Total score): 0 to 100, higher better				
MT + Bi-TENS	3.4 (0.8)	$P < 0.001$ (1.7, 5.1)*	5.2 (0.8)	$P < 0.001$ (3.6, 6.8)*
Sham-MT + Bi-TENS	0.8 (0.8)	$P = 0.354$ (-0.9, 2.5)	1.3 (0.8)	$P = 0.104$ (-0.3, 3.0)
C-SATIS-Stroke (Total score): 0 to 1.03, higher better				
MT + Bi-TENS	0.2 (0.1)	$P = 0.021$ (0.0, 0.4)	0.4 (0.1)	$P = 0.004$ (0.1,0.6)
Sham-MT + Bi-TENS	0.1 (0.1)	$P = 0.326$ (-0.1, 0.3)	0.2 (0.1)	$P = 0.115$ (-0.1, 0.5)

*indicated significant difference ($P < 0.003$)

Note: CI, confidence interval; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

Table 6.7 The Carryover Effects of the Linear Mixed Models of Outcome Measures Across A_2 and A_{FU} in People with Sub-acute Stroke (n = 30)

Outcome Measures	Group	2 Month (A_2)	1 Month Follow-Up (A_{FU})	Time effect (MD (95%CI)), *P* Value	Group effect (MD (95%CI)), *P* Value	Interaction effect (MD (95%CI)), *P* Value
FMA-UE	MT + Bi-TENS	54(50-59)	54(50-60)	0.3 (-0.7, 1.3), $P = 0.506$	10.3 (3.1, 17.6), $P = 0.007$	-1.4 (-2.8, 0.0), $P = 0.055$
(Total score) (range) (0 to 66, higher better)	Sham-MT + Bi-TENS	42(30-49)	42(32-52)	1.7 (0.7, 2.7), $P = 0.001^*$		
WMFT	MT + Bi-TENS	59(52-66)	59(52-66)	1.0 (0.3, 1.7), $P = 0.006$	11.7 (3.5, 19.8), $P = 0.007$	0.6 (-0.4, 1.6), $P = 0.228$
(Total score) (range) (0 to 75, higher better)	Sham-MT + Bi-TENS	50(35-60)	50(38-60)	0.4 (-0.3, 1.1), $P = 0.255$		
Grip Strength	MT + Bi-TENS	12.4(9.8-18.7)	13.1(10.2-20.4)	1.15 (-0.8, 3.1), $P = 0.23$	6.8 (2.5, 11.3), $P = 0.003$	0.37 (-2.3, 3.06), $P = 0.780$
(kg) (range) (higher better)	Sham-MT + Bi-TENS	5.9(4.8-9.1)	7(5-12.2)	0.78 (-1.1, 2.9), $P = 0.42$		

Jacket Test (Second)(range) (lesser better)	MT + Bi-TENS	14(13-18)	14(9-17)	-1.0 (-2.3, 0.3), *P* = 0.102	-5.9 (-10.0, -1.9), *P* = 0.007	0.7 (-1.1, 2.5), *P* = 0.394
	Sham-MT + Bi-TENS	21(17-26)	19(15-24)	-1.7 (-2.9,-0.4), *P* = 0.014		
C-UEFI (Total score) (range) (higher better)	MT + Bi-TENS	36(26-52)	36(27-54)	2.2 (0.5, 4.0), *P* = 0.015	10.2 (-1.8, 22.2), *P* = 0.093	1.7 (-1.0, 4.3), *P* = 0.202
	Sham-MT + Bi-TENS	34(20-45)	34(20-46)	0.5 (-1.4, 2.5), *P* = 0.572		
MAL(Amount of Use) (Total score) (range) (higher better)	MT + Bi-TENS	58(49-70)	58(49-70)	0.5 (-3.6, 2.7), *P* = 0.763	8.2 (-8.9, 25.2), *P* =0.336	-3.8 (-8.2, 0.6), *P* = 0.092
	Sham-MT + Bi-TENS	50(27-56)	51(27-66)	4.3 (1.1, 7.4), *P* =0.010		
MAL(Quality of Movement) (Total score) (range)	MT + Bi-TENS	52(46-63)	52(46-63)	0.5 (-1.3, 2.3), *P* = 0.576	11.1 (-3.6, 25.8), *P* = 0.133	-2.6 (-5.2, -0.1), *P* = 0.043
	Sham-MT + Bi-TENS	33(27-54)	35(27-57)	3.1 (1.3, 4.9), *P* = 0.001*		

(higher better)						
SIS (Total score) (range) (higher better)	MT + Bi-TENS Sham-MT + Bi-TENS	76(68-84) 65(49-73)	76(68-86) 67(51-73)	1.2 (-3.1, 5.5), *P* = 0.573 1.0 (-3.3, 5.3), *P* = 0.634	11.4 (1.95, 20.87), *P* = 0.020	0.18 (-5.88, 6.26), *P* = 0.951
C-CIM (Total score) (range) (0 to 100, higher better)	MT + Bi-TENS Sham-MT + Bi-TENS	46(40-50) 43(40-46)	46(40-50) 43(40-46)	0.3 (0.0, 0.6), *P* = 0.081 0.1 (-0.2, 0.4), *P* = 0.655	3.5 (-0.4, 7.4), *P* = 0.079	0.2 (-0.2, 0.6), *P* = 0.346
C-SATIS-Stroke (Total score) (range) (0 to 1.03, higher better)	MT + Bi-TENS Sham-MT + Bi-TENS	0.4(0.3-1.1) 0.3(-0.1-0.7)	0.4(0.3-1.7) 0.4(-0.1-0.7)	0.1 (-0.1, 0.3), *P* = 0.205 0.0 (-0.2, 0.2), *P* = 0.886	0.7 (-0.1, 1.5), *P* = 0.087	0.1 (-0.2, 0.4), *P* = 0.457

*indicated significant difference ($P < 0.003$)

Note: CI, confidence interval; MD, mean difference; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

6.5 Discussion

This was the first study to investigate the combined effects of MT with Bi-TENS and conventional therapy on the recovery of upper extremity motor function in people with sub-acute stroke compared with combined Sham-MT with Bi-TENS and conventional therapy. This study yielded promising results in improving the recovery of upper extremity motor function and health-related outcomes in sub-acute stroke survivors. Several key findings are as follows. First, compared with those in the Sham-MT + Bi-TENS + conventional therapy group, people with sub-acute stroke had significantly greater improvements in FMA-UE scores and paretic maximum grip strength at both A_1 and A_2 in the MT + Bi-TENS + conventional therapy group. These effects persisted at A_{FU}. Second, compared with the Sham-MT + Bi-TENS + conventional therapy group, people with sub-acute stroke had significantly greater improvements in C-CIM scores at A_2 in the MT + Bi-TENS + conventional therapy group. These effects persisted at A_{FU}. Third, compared with A_0, there were significant within-group improvements in FMA-UE, WMFT, paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, and C-CIM scores for people with sub-acute stroke in the MT + Bi-TENS + conventional therapy group. These effects persisted at A_{FU}. Fourth, compared with A_0, there were significant within-group improvements in FMA-UE, WMFT, MAL (Amount of Use), and MAL (Quality of Movement) scores at both A_1 and A_2, and paretic maximum grip strength and SIS scores at A_2, for people with sub-acute stroke in the Sham-MT + Bi-TENS + conventional therapy group. These effects persisted at A_{FU}.

6.5.1 The effects of MT + Bi-TENS + conventional therapy in people with sub-acute stroke

The results of previous systematic reviews and meta-analyses have demonstrated that Uni-TENS applied on the paretic extremity significantly improves the recovery of paretic upper extremity (Yang et al., 2019) and lower extremity (Kwong et al., 2018) motor function in stroke survivors. Yang et al. (2019) concluded that Uni-TENS was superior to Sham-TENS in improving upper extremity motor function immediately, with an effect size of 0.67, by pooling data from 23 trials (95% confidence interval: 0.51–0.84, $P < 0.001$) and at one-month follow-up, with an effect size of 0.66, by pooling data from 12 trials (95% confidence interval: 0.35–0.97, $P < 0.001$) in stroke survivors. Kwong et al. (2018) demonstrated that TENS was superior to Sham-TENS in improving walking capacity, assessed by the Timed Up and Go Test, with an effect size of 0.392 (95% confidence interval: 0.178–0.606, $P < 0.001$) by pooling data from 9 trials in people with stroke. The mechanisms underlying these beneficial effects of Uni-TENS over the paretic extremity for improving recovery of motor function include decreasing the hyperexcitability of alpha motor neurons (Levin & Hui-Chan, 1992) by activating the A alpha–beta range, reducing the short-interval intra-cortical inhibition (Celink et al., 2007) with decreased MEPs, increasing corticospinal excitability (Khaslavskaia et al., 2002), and increased corticomuscular coherence (Lai et al., 2016) in people with stroke.

The results of recent placebo-controlled clinical trials demonstrated that Bi-TENS was superior to Uni-TENS in improving the paretic upper extremity (Chen et al., 2022) and lower extremity (Kwong et al., 2018) motor function in stroke survivors. Chen et al. (2022) found that Bi-TENS + task-oriented training could induce greater benefits than Uni-TENS + task-oriented training in improving FMA-UE scores (3.39 vs. 1.26, $P < 0.001$) in 120 chronic stroke survivors. Kwong et al. (2018) found that Bi-TENS + task-oriented training could induce greater benefits than Uni-TENS + task-oriented training in improving the dorsiflexion strength of paretic ankle (15.9 ± 7.3 vs. 13.9 ± 6.8, $P = 0.03$) in 80 chronic stroke survivors. The mechanisms underlying

these beneficial effects of Bi-TENS on the recovery of motor function include recruiting the neural networks of the contralesionally hemisphere (Chen et al., 2024) and increasing the excitability of transcallosal projections from the ipsilesionally to contralesionally primary motor cortex by rebalancing interhemispheric inhibition (Cunningham et al., 2019).

As hypothesized, MT and Bi-TENS were found to exert synergistic effects, as MT combined with Bi-TENS showed significantly greater improvements in FMA-UE and maximum paretic grip strength at both A_1 and A_2, and CIM scores at A_2, compared with the Sham-MT + Bi-TENS group in people with sub-acute stroke. There were significant within-group improvements in FMA-UE, WMFT, paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, and C-CIM scores in the MT + Bi-TENS group. These effects persisted at A_{FU}. Three possible underlying mechanisms of the combined effect of MT and Bi-TENS with bilateral exercises could explain the improvement of paretic upper extremity motor function in 30 sub-acute stroke survivors in experimental group compared with control group.

First, MT could increase activations of parts of mirror neuron system to involve in the action observation and execution in people with stroke. The human mirror neuron system is crucial for action observation and execution, involved in imitation learning and motor memory formation (Aizu et al., 2023). Zhang et al. (2024) demonstrated that compared with the baseline, significant activation was observed in the ipsilesionally inferior frontal gyrus and contralesionally superior temporal gyrus of the mirror neuron system, and the activation of the contralesionally superior temporal gyrus was significantly associated with FMA-UE scores in people with stroke after MT intervention (r = 0.44, P = 0.008). Zhang et al. (2024) also demonstrated that compared with no MT intervention, significant activation was observed in

the ipsilesionally inferior frontal gyrus and ipsilesionally superior temporal gyrus in people with stroke, and the activation of those two regions had significant correlations with FMA-UE scores in the MT group in people with stroke (r = 0.49, P = 0.003 and r = 0.34, P = 0.04, respectively).

Second, MT could increase the activations of both ipsilesionally and contralesionally primary motor cortex and re-establish the functional connectivity between ipsilesionally and contralesionally primary motor cortex in people with stroke. Zhang et al. (2024) demonstrated that total 3-week total 20 sessions of MT combined with conventional therapy of upper extremity significantly induced the activations of ipsilesionally and contralesionally primary motor cortex, and the interhemispheric functional connectivity between ipsilesionally and contralesionally primary motor cortex the in 16 people with stroke compared with conventional therapy group (Zhang et al., 2024). Such increase in the interhemispheric functional connectivity between ipsilesionally and contralesionally primary motor cortex after training significantly correlated with FMA-UE improvement (r = 0.7, P = 0.005) (Zhang et al., 2024).

Third, MT could increase the spatial attention processing of paretic upper extremity in people with stroke. During MT training, people with stroke are required to look into a mirror and imagine the non-paretic-side movements are paretic-side movements while they perform bilateral exercises (Deconinck et al., 2015). Previous studies (Michielsen et al., 2011; Zhang et al., 2024) demonstrated that MT could induce significant activation in the precuneus, which is associated with attention network interaction (Luo et al., 2020). Zhang et al. (2024) showed that both ipsilesionally and contralesionally precuneus could be significantly activated after 3 weeks (20 sessions) of MT combined with conventional therapy of the upper extremity, compared with the conventional therapy group, in 35 people with stroke. The results also

demonstrated that the fractional amplitude of low-frequency fluctuation changes of the ipsilesionally and contralesionally precuneus from pre- to post-intervention had a significant correlation with FMA-UE scores (r = 0.439, P = 0.008) in the mirror condition in 35 people with stroke (Zhang et al., 2024).

The observed improvement in the MT + Bi-TENS + conventional therapy group had clinical significance. The change in FMA-UE scores (11.8) at A_2 exceeded the estimated minimal clinically important difference (10) (Arya & R K Garg, 2011). This improvement in FMA-UE scores, representing the level of motor recovery in stroke survivors, probably explained the improvement in other outcome measures of motor functions, including maximum paretic grip strength and Jacket Test, MAL (Amount of Use), MAL (Quality of Movement), and SIS scores after 8-week treatment of MT + Bi-TENS + conventional therapy. Indeed, improved motor functions of paretic extremity are expected to allow stroke survivors actively involving in daily life tasks, e.g., objective manipulation, the use of the arm for gross motor activities of transferring, which probably led to higher level of community integration as well as better health-related of life in sub-acute stroke survivors demonstrated in this study.

6.5.2 The effects of Sham-MT + Bi-TENS + conventional therapy in people with sub-acute stroke

In our study, the control group showed significant improvements in FMA-UE, WMFT, MAL (Amount of Use), and MAL (Quality of Movement) scores at both A_1 and A_2, and paretic maximum grip strength and SIS scores at A_2 of within-group analysis. The Sham-MT + Bi-TENS group received Bi-TENS while practicing bilateral upper extremity training but did not receive any MT (e.g., experiencing a visual illusion of enhanced function over the paretic

extremity). Thus, the above-mentioned within-group improvements in the Sham-MT + Bi-TENS group are probably attributable to Bi-TENS with bilateral upper extremity training. As mentioned in Section 6.5.1, the mechanisms underlying these beneficial effects of Bi-TENS on the recovery of motor function include recruiting the neural networks of the contralesionally hemisphere (Chen et al., 2024) and increasing the excitability of transcallosal projections from the ipsilesionally to the contralesionally primary motor cortex by rebalancing interhemispheric inhibition (Cunningham et al., 2019).

To date, no study has investigated the "pure" effect of Sham-MT. Whether Sham-MT can provide any therapeutic benefits for the recovery of upper extremity motor function in sub-acute stroke survivors is unclear. Future studies to investigate the neurophysiological, behavioral, and psychological responses to Sham-MT intervention are warranted.

6.5.3 Limitations

This study started on September 1, 2020, and finished on April 30, 2024. During the study period, many great challenges were encountered. The main challenges included the closure of the university campus and laboratories of The Hong Kong Polytechnic University because of social unrest in 2019–2020. Due to COVID-19 pandemic surges, there were several periods of suspension of services at the Geriatric Day Hospital of Shatin Hospital. The ongoing clinical study was temporarily suspended several times. In addition, stringent infection control was enforced in the Geriatric Day Hospital of Shatin Hospital as well as all PolyU laboratories from 2021 to 2023. The progression of our study was seriously affected. Given the above-mentioned adverse social and research environments, our study had limitations.

First, the follow-up period was limited to one month after the intervention training ended because of limitations in research resources under conditions of social unrest and pandemic. Hence, a longer-term carryover effect should be examined in future studies. Second, the neurophysiological mechanisms that mediate the effects of MT, Sham-MT, and Bi-TENS were not examined in this study. Further study in this area is warranted. Third, the results can only be applied to people with sub-acute stroke fulfilling our inclusion/exclusion criteria. Hence, our results have limited generalizability to all sub-acute stroke survivors. Fourth, the optimal dosage of the experimental protocol (e.g., TENS parameters, duration of the intervention) could not be determined in this study. Hence, future studies should be conducted to explore the optimal dosage of MT + Bi-TENS for improving the recovery of upper extremity motor function. Fifth, all participants with sub-acute stroke received 2.5-hour conventional therapy, including occupational therapy, speech therapy, and health education, in both experimental and control groups. However, the 'pure' effects of conventional therapy on within-group improvement or on experimental intervention needs further investigation. Sixth, compliance with MT and Sham-MT treatment was not recorded systematically. In addition, the actual treatment dosage, such as the number of repetitions performed during each treatment session, might have affected the overall effectiveness of the interventions. Thus, future studies should record compliance with treatment.

6.6 Conclusion

Compared with Sham-MT + Bi-TENS + conventional Therapy treatment, MT + Bi-TENS + conventional Therapy treatment induced greater increases in FMA-UE at both A_1 and A_2, and paretic maximum grip strength, C-CIM scores at A_2 after 16 treatment sessions, in the people with sub-acute stroke. These treatment effects were maintained at A_{FU}, 4 weeks after treatment had ended. Both MT + Bi-TENS + conventional therapy and Sham-MT + Bi-TENS +

conventional therapy induced significant within-group improvements in the majority of the outcome measures after 8 and 16 sessions of treatment at A_1 and A_2, respectively in people with sub-acute stroke. These training effects were maintained at A_{FU}, 4 weeks after treatment had ended.

CHAPTER SEVEN

Randomized controlled trial of upper extremity training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper extremity functions in people with chronic stroke

7.1 Abstract

The recovery of upper extremity motor function in people with chronic stroke often plateaus compared with people with subacute stroke (3 weeks to 6 months). However, previous evidence showed that therapy-based rehabilitation can induce significant improvement of motor function in people more than 6 months after stroke. The findings from Chapter 6 showed combining MT with Bi-TENS and conventional therapy significant effects in subacute stroke survivors. In this Chapter, we further investigate the potential effects of combining MT with Bi-TENS to improve the recovery of upper extremity motor function in chronic stroke survivors.

Total 60 people with chronic stroke were randomly allocated into two groups. Two groups received total 30-minute intervention sessions with 2 sessions per week within 8 weeks. The primary outcome measures were Fugl-Meyer Assessment of Upper Extremity (FMA-UE) and Wolf Motor Function Test (WMFT) scores. The secondary outcome measures included maximum paretic grip strength, Jacket Test, Chinese version of Upper Extremity Functional Index (C-UEFI), Motor Activity Log (MAL), Stroke Impact Scale (SIS), Chinese version of Community Integration Measures (C-CIM), Chinese version of SATIS-Stroke (C-SATIS-Stroke) scores.

Experimental group showed significantly improvement in FMA-UE (Mean Difference (MD) = 5.2, $P < 0.001$) and WMFT (MD = 3.7, $P = 0.001$) scores at A_2 in 60 people with chronic stroke compared with control group. The post-hoc analysis of within-group effects demonstrated that both MT + Bi-TENS and Sham-MT + Bi-TENS groups demonstrated significant improvements in FMA-UE (Experimental Group (EG), MD = 5.6 -12.4, $P < 0.001$; Control Group (CG), MD = 3.8 -7.2, $P < 0.001$), WMFT (EG, MD = 3.8 - 8.4, $P < 0.001$; CG,

MD = 2.2 - 4.7, $P < 0.001$), C-UEFI (EG, MD = 3.2 - 6.1, $P < 0.001$; CG, MD = 4.5 - 5.4, $P < 0.001$), MAL (Quality of Movement) (EG, MD = 9.8 -20.0, $P < 0.001$; CG, MD = 6.9 -11.4, $P = 0.002$ and $P < 0.001$, respectively), and SIS (EG, MD = 4.2 -7.0, $P < 0.001$;CG, MD = 4.4 - 7.2, $P < 0.001$) scores at both A_1 and A_2. Those carryover effects persisted until A_{FU}.

Experimental group showed earlier within-group improvement in paretic maximum grip strength (MD = 2.7, $P < 0.001$), Jacket Test (MD = -4.3, $P < 0.001$), and MAL (Amount of Use) (MD = 13.0, $P < 0.001$) at A_1, while the control group only showed significant within-group improvement in paretic maximum grip strength (MD = 2.4, $P < 0.001$), Jacket Test (MD = -2.9, $P < 0.001$), and MAL (Amount of Use) (MD = 15.7, $P < 0.001$) at A_2. Only experimental group showed significant within-group improvement in C-CIM (MD = 1.9 - 3.5, $P < 0.001$) at both A_1 and A_2, and only experimental group showed significant within-group effects in C-SATIS-Stroke (MD = 0.3, $P = 0.002$) at A_2. Those carryover effects persisted until A_{FU}.

To conclude, experimental group is superior to control group in improving upper extremity motor impairment, motor ability in chronic stroke survivors. MT is an effective complementary therapy to Bi-TENS in improving the recovery of upper extremity motor function and health-related outcome measures in people with chronic stroke.

7.2 Introduction

Globally, according to the World Stroke Organization, more than 12 million people have a new stroke each year (World Health Organization, 2022). Currently, there are over 80 million stroke survivors globally, and more than 50 million live with permanent disabilities (World Stroke Organization, 2024). Stroke is the third leading cause of disability across the globe and the

number of cases is anticipated to increase in the coming decades (World Economic Forum, 2023). The high incidence and rate of disability highlight the necessity for comprehensive rehabilitation strategies for people with stroke.

After a stroke, the recovery of motor function follows a nonlinear, logarithmic pattern (Hatem et al., 2016). The fastest recovery of motor function happens during the first month following the stroke, with improvement of motor function ranging from 30% to 68% and improvement of functional activity from 26% to 58% (Lee et al., 2015). Motor function showed small to moderate recovery between 3 to 6 months after stroke, ranging from 4% to 9%, according to one study (Lee et al., 2015). The recovery of motor function may often reach a plateau at 6 months post-stroke, with less significant improvement subsequently (Grefkes, 2020).

However, previous studies (Ferrarello et al., 2011; Teasell et al., 2012) have consistently shown that appropriate therapy-based rehabilitation interventions can significantly reduce the risk of further functional deterioration and can induce significant improvement of motor functions in community-dwelling individuals more than 6 months post-stroke. The results of a meta-analysis demonstrated that therapy-based rehabilitation interventions had a favorable pooled effect size (0.29) on all included outcome measures for people with stroke more than 6 months post-stroke (95% confidence interval = 0.14–0.45, $P < 0.001$) with no heterogeneity, compared with no intervention (Ferrarello et al., 2011). As stated in Chapter 1, improvements in paretic upper extremity motor function may be induced by both Bi-TENS and MT. As MT and Bi-TENS recruit different neural pathways, it is reasonable to hypothesize that MT could augment the effectiveness of Bi-TENS and exert synergistic effects to improve the recovery of upper extremity motor function in chronic stroke survivors.

7.3 Method

The study was conducted at Neurorehabilitation Laboratory of The Hong Kong Polytechnic University from April 2023 to April 2024. The written informed consents were obtained from all people with chronic stroke before any study-related procedures (Appendix 7.1).

7.3.1 Inclusion and exclusion criteria

Chronic stroke survivors were recruited through local self-help organization. The people with chronic stroke were recruited if they have been diagnosed by magnetic imaging or computed tomography as having unilateral ischemic brain injury, or intracerebral haemorrhage from 6 months to 10 years after the first onset of stroke. Other inclusion and exclusion criteria at The Hong Kong Polytechnic University was the same as the people with subacute stroke at the Shatin Hospital.

7.3.2 Study design

This study was a randomized, sham-controlled clinical trial. The ethical approvals were obtained from The Hong Kong Polytechnic University (Reference Number: HSEARS20180221001-04) (Appendix 7.2). This study was prospectively registered on ClinicalTrials.gov (identifier: NCT03631628).

7.3.3 Study procedures

The procedure of this study is demonstrated in Figure 7.1. The training program included 8 weeks of twice per week of the treatment. The assessment procedure of all people with chronic stroke was the as the people with subacute stroke at the Shatin Hospital.

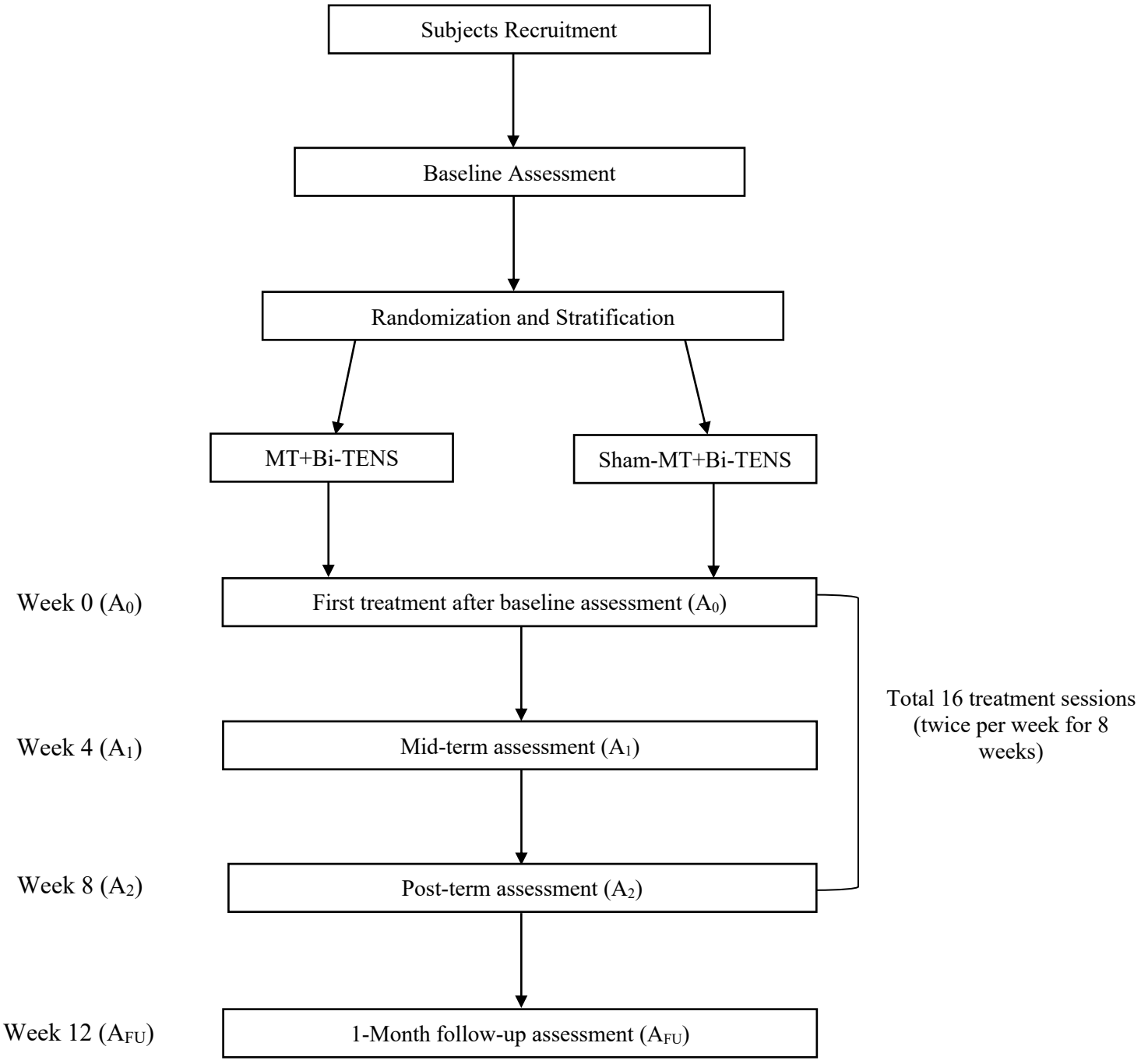


Figure 7.1 Flowchart of the study procedure

7.3.4 Stratification and randomization

The procedures were conducted by another Minimize computer software (Jensen, 1991). For the details of stratification and randomization, please refer to chapter 6.3.4.

7.3.5 Sample size calculation

The G*Power was used to calculate the sample size with an alpha level of 0.05, study power of 80%, number of primary outcome measures of 2, correlation among measurements with 0.5, and nonsphericity correlation of 1 (Faul et al., 2007). The estimation is based on a recent systematic review and meta-analysis (Pan et al., 2024). Using pooled data from 7 randomized controlled trials, this meta-analysis calculated a medium effect size (Cohen's d = 0.42, 95% confidence interval: 0.04-0.89, $P = 0.03$) for the MT combined with conventional therapy on the improvement of recovery of upper extremity motor function assessed by FMA-UE in people with stroke compared with conventional therapy alone (Pan et al., 2024). A more conservative effect size of 0.2 was selected, so total 50 subjects were needed to detect significant differences between two groups. According to dropout rates in previous studies (Chen et al., 2022; Kwong et al., 2018), we recruited an additional 10 people with chronic stroke survivors for the dropouts. Hence, we plan the sample size is 60, with 30 subjects for each group.

7.3.6 Intervention protocol

The intervention protocols of two groups in people with chronic stroke is summarized in Table 7.1. The people with chronic stroke underwent 16 sessions of the intervention protocol, twice per week for total 8 weeks. The people with chronic stroke received with concurrent MT and Bi-TENS stimulation while practising bilateral upper extremity exercises.

Table 7.1 The intervention protocol in two experimental groups of people with chronic stroke

Training Time	Groups	
Duration (30 minutes)	MT + Bi-TENS Group	Sham-MT + Bi-TENS Group
Experimental intervention (30 minutes)	MT (with bilateral upper extremity exercise) + Bi-TENS	Sham-MT (with bilateral upper extremity exercise) + Bi-TENS

7.3.6.1 Mirror therapy protocol

The mirror therapy protocol in chronic stroke survivors at The Hong Kong Polytechnic University was the same as the subacute stroke survivors at the Shatin Hospital. Please refer to 6.3.6.1 for the details of mirror therapy protocol.

7.3.6.2 Bilateral TENS protocol

The bilateral TENS protocol in chronic stroke survivors at The Hong Kong Polytechnic University was the same as the subacute stroke survivors at the Shatin Hospital. Please refer to 6.3.6.2 for the details of bilateral TENS protocol.

7.3.6.3 Bilateral upper extremity exercises

The bilateral upper extremity exercises in chronic stroke survivors at The Hong Kong Polytechnic University was the same as the people with subacute stroke at Shatin Hospital. Please refer to 6.3.6.3 for the details of bilateral upper extremity exercises. For the demonstration for each upper extremity exercises, please refer to Appendix 6.3.

7.3.7 Outcome measures

The selected outcome measures in this Chapter were the same as the Chapter 6.

7.3.7.1 Primary outcomes

7.3.7.1.1 Fugl-Meyer Assessment of Upper Extremity (FMA-UE)

The FMA-UE was used to assesses the upper extremity motor impairment and motor control in people with stroke (Fugl-Meyer et al., 1975). Details of FMA-UE has been reported in Chapter 5, Section 5.3.2.3. The detailed protocol of the FAM-UE was provided in Appendix 6.4.

7.3.7.1.2 Wolf Motor Function Test (WMFT)

The WMFT is a quantitative outcome measure to assess the upper extremity motor ability in people with stroke (Wolf et al., 2005). Details of WMFT has been reported in Chapter 5, Section 5.3.2.4. The detailed protocol of the WMFT was provided in Appendix 6.5.

7.3.7.2 Secondary outcomes

7.3.7.2.1 Paretic Maximum Grip Strength

The paretic maximum grip strength is an appropriate measurement to quantify upper extremity weakness and recovery in older adults (Abizanda et al., 2012) and stroke survivors (Bertrand et al., 2015). Details of paretic maximum grip strength has been reported in Chapter 6, Section 6.3.7.2.1.

7.3.7.2.2 The Jacket Test

The Jacket Test was used to assess the upper extremity proficiency in wearing the jacket in stroke survivors (Chen et al., 2017). Details of Jacket Test has been reported in Chapter 6, Section 6.3.7.2.2. The detailed protocol of the Jacket Test was provided in Appendix 6.6.

7.3.7.2.3 Chinese version of Upper Extremity Functional Index (C-UEFI)

The C-UEFI was used to assess the self-perceived upper extremity functional recovery in daily life activity in stroke survivors (Pan et al., 2023). Details of C-UEFI has been reported in Chapter 5, Section 5.3.2.1. The detailed protocol of the C-UEFI was provided in Appendix 6.7.

7.3.7.2.4 Motor Activity Log (MAL)

The MAL was used to assess the amount of use and quality of movement of the paretic upper extremity function during the daily living activities in people with stroke as indicated in semi-structured interview (van der Lee et al., 2004). Details of MAL has been reported in Chapter 5, Section 5.3.2.9. The detailed protocol of the MAL was provided in Appendix 6.8.

7.3.7.2.5 Stroke Impact Scale (SIS)

The SIS was used to assess the subjective level of disability and health-related quality of life as a self-reported questionnaire in people with stroke (MacIsaac et al., 2016). Details of SIS has been reported in Chapter 5, Section 5.3.2.13. The detailed protocol of the SIS was provided in Appendix 6.9.

7.3.7.2.6 Chinese version of Community Integration Measures (C-CIM)

The C-CIM was used to assess the integration in community people with stroke (Liu et al., 2014). Details of C-CIM has been reported in Chapter 5, Section 5.3.2.14. The detailed protocol of the C-CIM was provided in Appendix 6.10.

7.3.7.2.7 Chinese version of SATIS-Stroke (C-SATIS-Stroke)

The C-SATIS-Stroke was used to assess the subjective satisfaction feeling in terms of social participation among people with stroke (Pan et al., 2024). Details of C- SATIS-Stroke has been reported in Chapter 5, Section 5.3.2.2. The detailed protocol of the C-SATIS-Stroke was provided in Appendix 6.11.

7.3.8 Statistical analysis

The same method of statistical analysis was applied in the studies on patients with sub-acute stroke (Chapter 6) and on patients with chronic stroke (Chapter 7), respectively. Please refer to Chapter 6, Section 6.3.8 for the details of statistical analysis.

7.3.9 Safety consideration

The safety consideration and precautions in this Chapter were the same as in Chapter 6 in Shatin Hospital.

7.4 Results

7.4.1 Participants

Ninety-seven potential people with chronic stroke were screened between April 2023 and April 2024, of whom 60 eligible people with chronic stroke were enrolled and randomized into two groups (See Figure 7.2). Intention-to-treat analysis was used to evaluate the participants according to the groups to which they were originally assigned.

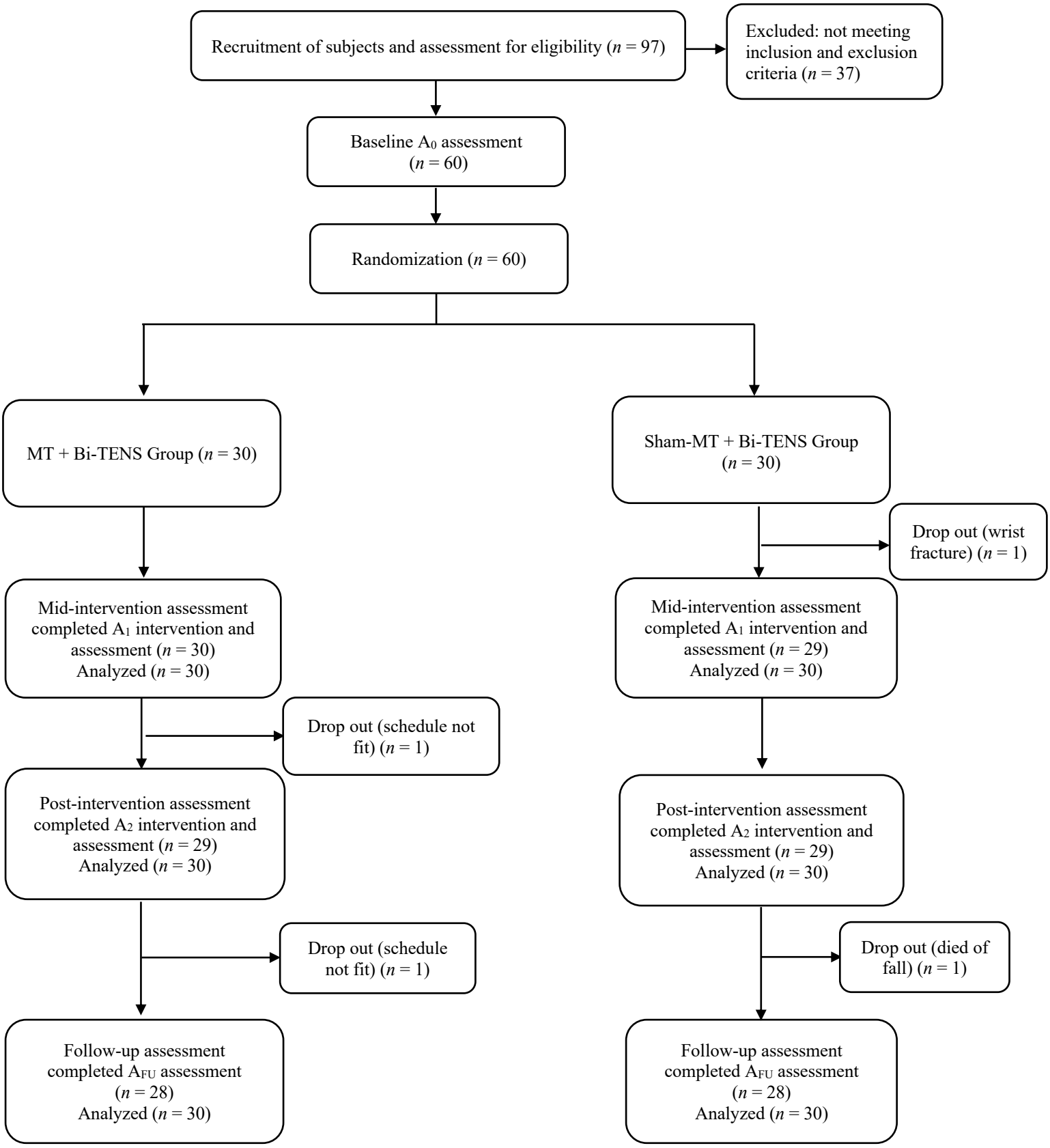

Recruitment of subjects and assessment for eligibility (n = 97)
Excluded: not meeting inclusion and exclusion criteria (n = 37)
Baseline A0 assessment (n = 60)
Randomization (n = 60)
MT + Bi-TENS Group (n = 30)
Sham-MT + Bi-TENS Group (n = 30)
Drop out (wrist fracture) (n = 1)
Mid-intervention assessment completed A1 intervention and assessment (n = 30) Analyzed (n = 30)
Mid-intervention assessment completed A1 intervention and assessment (n = 29) Analyzed (n = 30)
Drop out (schedule not fit) (n = 1)
Post-intervention assessment completed A2 intervention and assessment (n = 29) Analyzed (n = 30)
Post-intervention assessment completed A2 intervention and assessment (n = 29) Analyzed (n = 30)
Drop out (schedule not fit) (n = 1)
Drop out (died of fall) (n = 1)
Follow-up assessment completed AFU assessment (n = 28) Analyzed (n = 30)
Follow-up assessment completed AFU assessment (n = 28) Analyzed (n = 30)

Figure 7.2 Flow diagram of the study

7.4.2 Demographic information

All demographic parameters showed no significant differences at A_0 (Table 7.2). One participant in the Sham-MT + Bi-TENS group dropped out at A_1 (i.e., having wrist fracture). One participant in the MT + Bi-TENS group dropped out at A_2 (i.e., schedule not fit). Two participants in the MT + Bi-TENS and Sham-MT + Bi-TENS group, respectively, dropped out at A_{FU} (i.e., schedule not fit and died of fall, respectively). In total, 58 subjects (97%) completed the intervention and assessment at A_2, and 56 subjects (93%) completed the assessment at A_{FU} (Figure 7.2). No adverse effects occurred during the study.

Table 7.2 The Baseline Characteristics of People with Chronic Stroke (n = 60)

	MT + Bi-TENS (n = 30)	Sham-MT + Bi-TENS (n = 30)	Between-groups Comparison
Variables	Number (Frequency, %)		χ^2 Test, P-value
Gender (Male/ Female)	16(53)/14 (47)	14 (47)/16(53)	0.606
Side of Hemiplegia (Left/Right)	15(50)/15(50)	15(50)/15(50)	1.000
Type of Stroke (Ischemia/Haemorrhage)	11(37)/19(63)	11(37)/19(63)	1.000
Living Arrangement (Live alone/Live with family)	4(13)/26(87)	1(3)/29(27)	0.161
Education Level (Primary or below/Secondary/College or above)	4(13)/22(74)/4(13)	7(23)/19(64)/4(13)	0.595
Variables	Mean ± SD		Independent t Test, P-value
Age (Year)	61.1±7.2	60.1±7.5	0.576
Variables	Median (IR)		Mann-Whitney U Test, P-value
Time since stroke (Month)	70.4(26.1-101.2)	63.5(45.4-100.2)	0.882
Body Mass Index, kg/m^2	23.9(22-27.4)	24.7(22.1-28.4)	0.451
Abbreviated Mental Test (Total score)	10.0 (10.0-10.0)	10.0(10.0-10.0)	1.000
FMA-UE (Paretic side) (Total score)	24.5(15-34)	25.0(13.8-34.3)	0.935
WMFT (Paretic side) (Total score)	31.0(18.8-50)	32.0(17.8-39.5)	0.779

Grip Strength (Paretic side) (kg)	6.3(2.8-14.5)	5.4(3.0-9.0)	0.745
Jacket Test (Second)	22.0(16.7-32.4)	21.5(18.7-30.4)	0.701
C-UEFI (Total score)	40.5(29-46.3)	38.0(31.8-43.5)	0.842
MAL(Amount of Use) (Total score)	10.5(7-28.5)	14.8(8-42.6)	0.386
MAL(Quality of Movement) (Total score)	11.0(5-27.3)	12.5(4.8-39.5)	0.518
SIS(Total Score)	62.8(58.6-67.4)	63.0(55.7-67.6)	0.859
C-CIM (Total score)	40.0(36.8-46.5)	43.0(34.8-45.3)	0.756
C-SATIS-Stroke (Total score)	0.5(0.3-0.7)	0.5(0.3-0.8)	0.739

Note: n, number; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; SD, standard deviation; IR, interquartile range; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

7.4.3 The effects of MT + Bi-TENS versus Sham-MT + Bi-TENS

The results from A_0 to A_2 were showed in Table 7.3, Table 7.4, and Table 7.5. The results for the carryover effects from the A_2 to A_{FU} were showed Table 7.6.

7.4.3.1 Primary outcome measures

Significant time-by-group interaction effects (MD = 2.5, $P < 0.001$; MD = 1.7 ; $P < 0.001$, Table 7.3) were observed, with the experimental group demonstrating a greater improvement in FMA-UE and WMFT scores than control group at A_2 (MD = 5.2, $P < 0.001$; MD = 3.7, $P = 0.001$; Table 7.4), respectively. The post-hoc analysis demonstrated that both MT + Bi-TENS and Sham-MT + Bi-TENS groups demonstrated significant improvements of within-group effects in FMA-UE scores (EG, MD = 5.6 -12.4, $P < 0.001$; CG, MD = 3.8 -7.2, $P < 0.001$) (Table 7.5)), and WMFT scores (EG, MD = 3.8 - 8.4, $P < 0.001$; CG, MD = 2.2 - 4.7, $P < 0.001$) (Table 7.5)) at both A_1 and A_2, respectively.

No significant results in two groups from A_2 to A_{FU} (Table 7.6). Both two groups showed no within group differences in FMA-UE and WMFT scores from A_2 to A_{FU}, indicating the improvement in FMA-UE and WMFT scores in two groups were maintained at A_{FU} (Table 7.6).

7.4.3.2 Secondary outcome measures

A significant time-by-group interaction effect was observed for MAL (Quality of Movement) (MD = 5.1; $P < 0.001$) mean score between two groups (Table 7.3), with the experimental group demonstrating no significantly improvement in MAL (Quality of Movement) scores than

control group at A_1 and A_2 of post-hoc analysis (Table 7.4). Both two groups demonstrated significant improvements of within-group effects in MAL (Quality of Movement) scores (EG, MD = 9.8 -20.0, $P < 0.001$; CG, MD = 6.9 -11.4, $P = 0.002$ and $P < 0.001$, respectively) at both A_1 and A_2 (Table 7.5).

No significant time-by-group interaction effects were observed in C-UEFI and SIS mean scores between two groups (Table 7.3). Both two groups showed significant improvements of within-group effects in C-UEFI (EG, MD = 3.2 - 6.1, $P < 0.001$; CG, MD = 4.5 - 5.4, $P < 0.001$), and SIS (EG, MD = 4.2 -7.0, $P < 0.001$;CG, MD = 4.4 -7.2, $P < 0.001$) scores at both A_1 and A_2 (Table 7.5).

No significant time-by-group interaction effects were observed in paretic maximum grip strength, Jacket Test, and MAL (Amount of Use) mean scores between two groups (Table 7.3). The experimental group showed earlier within-group improvement in paretic maximum grip strength (MD = 2.7, $P < 0.001$), Jacket Test (MD = -4.3, $P < 0.001$), and MAL (Amount of Use) (MD = 13.0, $P < 0.001$) at A_1, while the control group only showed significant within-group improvement in paretic maximum grip strength (MD = 2.4, $P < 0.001$), Jacket Test (MD = -2.9, $P < 0.001$), and MAL (Amount of Use) (MD = 15.7, $P < 0.001$) at A_2 (Table 7.5). No significant time-by-group interaction effects were observed in C-CIM and C-SATIS-Stroke mean scores between two groups (Table 7.3). Only experimental group showed significant within-group improvement in C-CIM (MD = 1.9 - 3.5, $P < 0.001$) at both A_1 and A_2 and C-SATIS-Stroke (MD = 0.3, $P = 0.002$) scores at A_2 (Table 7.5).

The experimental group showed no significant between-group results in paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, C-

CIM, and C-SATIS-Stroke scores to control group from A_2 to A_{FU} (Table 7.6). Both two groups showed no significant within-group results in paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, C-CIM, and C-SATIS-Stroke scores from A_2 to A_{FU} (Table 7.6), indicating the improvement in those outcome measures in two groups were maintained at A_{FU}.

Table 7.3 The Results of Linear Mixed Models of the Outcome Measures Across A_0, A_1, and A_2 in People with Chronic Stroke (n = 60)

Outcome Measures	Group	Baseline(A_0)	1 Month(A_1)	2 Month(A_2)	Time effect (MD (95%CI)), *P* Value	Group effect (MD (95%CI)), *P* Value	Interaction effect (MD (95%CI)), *P* Value
				Primary Outcomes			
FMA	MT + Bi-TENS	25(15-34)	32(20-41)	39(26-49)	6.1 (5.4, 6.9), $P < 0.001^*$	7.5 (-0.3, 15.4), $P = 0.060$	2.5 (1.4, 3.5), $P < 0.001^*$
(Total score) (range)	Sham-MT + Bi-TENS	24(14-34)	27(18-39)	31(20-43)	3.6 (2.9, 4.4), $P < 0.001^*$		
0 to 66, higher better							
WMFT	MT + Bi-TENS	32(19-50)	36(22-52)	42(28-58)	4.0 (3.3, 4.7), $P < 0.001^*$	5.7 (-3.4, 14.8), $P = 0.213$	1.7 (0.7, 2.8), $P = 0.001^*$
(Total score) (range)	Sham-MT + Bi-TENS	32(18-40)	34(19-41)	36(22-42)	2.3 (1.5, 3.0), $P < 0.001^*$		
0 to 75, higher better							
				Secondary Outcomes			
Grip Strength	MT + Bi-TENS	6.6(2.8-14.5)	8.2(4.3-18)	9.6(5.0-19)	2.0 (1.5, 2.5), $P < 0.001^*$	4.5 (0.4, 8.6), $P = 0.034$	0.8 (0.1, 1.6), $P = 0.033$
(kg)(range) Higher better	Sham-MT + Bi-TENS	5.3(3.0-9.0)	7.4(5.0-10.0)	7.9(6.0-11)	1.2 (0.6, 1.7), $P < 0.001^*$		

Jacket Test (Second)(range) lesser better	MT + Bi-TENS	21.9(17-32)	17.4(15-25)	16(14-22)	-1.5 (-2.1, -1.0), $P < 0.001^*$	-2.7 (-6.7, -1.2), $P = 0.176$	-0.2 (-1.0, 0.6), $P = 0.553$
	Sham-MT + Bi-TENS	21.6(19-30)	21(18-29)	19(15-28)	-1.3 (-1.9, -0.7), $P < 0.001^*$		
C-UEFI (Total score) (range) 0 to 59, higher better	MT + Bi-TENS	41(29-46)	43(35-48)	46(39-50)	2.9 (1.9, 3.8), $P < 0.001^*$	2.0 (-2.8, 6.7), $P = 0.406$	1.4 (0.0, 2.7), $P = 0.048$
	Sham-MT + Bi-TENS	38(32-44)	43(38-47)	44(39-50)	1.5 (0.6, 2.5), $P = 0.002^*$		
MAL(Amount of Use) (Total score) (range) Higher better	MT + Bi-TENS	11(7-29)	23(12-46)	31(15-65)	10.2 (8.2, 12.2), $P < 0.001^*$	3.3 (-14.2, 20.9), $P = 0.702$	1.7 (1.2, 4.5), $P = 0.250$
	Sham-MT + Bi-TENS	12(8-43)	19(10/51)	33(15-66)	8.5 (6.5, 10.5), $P < 0.001^*$		
MAL(Quality of Movement)	MT + Bi-TENS	14(5-27)	20(7-42)	28(13-59)	10.1 (8.3, 11.9), $P < 0.001^*$	7.5 (-8.0, 23.1), $P = 0.334$	5.1 (2.6, 7.6), $P < 0.001^*$
	Sham-MT + Bi-TENS	12(5-40)	23(9-48)	30(12-51)	5.0 (3.2, 6.8), $P < 0.001^*$		

(Total score)(range) Higher better							
SIS (Total score) (range) Higher better	MT + Bi-TENS	63(59-67)	67(62-70)	69(65-75)	3.2 (2.4, 3.9), $P < 0.001$*	0.3 (-4.7, 5.3), $P = 0.909$	0.0 (-1.1, 1.1), $P = 0.993$
	Sham-MT + Bi-TENS	63(56-68)	69(61-74)	70(62-78)	3.2 (2.4, 4.0), $P < 0.001$*		
C-CIM (Total score) (range) 0 to 100, higher better	MT + Bi-TENS	40(37-47)	44(40-49)	46(40-49)	1.7 (1.1, 2.3), $P < 0.001$*	3.0 (-0.4, 6.5), $P = 0.085$	0.8 (0.0, 1.7), $P = 0.051$
	Sham-MT + Bi-TENS	43(35-45)	44(36-47)	45(36-47)	0.9 (0.3, 1.5), $P = 0.006$		
C-SATIS-Stroke (Total score) (range) 0 to 1.03, higher better	MT + Bi-TENS	0.5(0.3-0.7)	0.6(0.4-0.7)	0.6(0.5-0.8)	0.13 (0.02, 0.24), $P = 0.03$	0.1 (-0.3,0.5), $P = 0.570$	0.1 (-0.1,0.1), $P = 0.802$
	Sham-MT + Bi-TENS	0.5(0.3-0.8)	0.5(0.4-0.9)	0.6(0.4-1.1)	0.12 (0.0, 0.2), $P = 0.04$		

*indicated significant difference ($P < 0.006$)

Note: CI, confidence interval; MD, mean difference; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

Table 7.4 Between-group Effects of MT + Bi-TENS and Sham-MT + Bi-TENS in People with Chronic Stroke (n = 60) (Post-Hoc Analysis)

Outcome Measures	1 Month (A_1) VS. Baseline(A_0)		2 Month (A_2) VS. Baseline(A_0)	
	Estimate (Standard Error)	*P* Value (95% CI)	Estimate (Standard Error)	*P* Value (95% CI)
		Primary Outcomes		
FMA-UE (Total score) (0 to 66, higher better)	1.8 (0.7)	$P = 0.009$ (0.5, 3.1)	5.2 (1.1)	$P < 0.001$ (3.1, 7.4)*
WMFT (Total score) (0 to 75, higher better)	1.6 (0.6)	$P = 0.006$ (0.5, 2.7)	3.7 (1.1)	$P = 0.001$ (1.6, 5.9) *
		Secondary Outcomes		
Grip Strength (kg) (Higher better)	1.2 (0.7)	$P = 0.073$ (0.1, 2.6)	1.7 (0.8)	$P = 0.035$ (0.1, 3.6)
Jacket Test (Second) (Lesser better)	-2.7 (1.0)	$P = 0.013$ (-4.7, -0.6)	-2.7 (1.1)	$P = 0.015$ (-4.8,-0.5)
C-UEFI (Total score) (0 to 59, higher better)	-1.2 (1.4)	$P = 0.389$ (-4.0, 1.6)	0.70 (1.6)	$P = 0.672$ (-2.6,4.0)

MAL (Amount of Use) (Total score) (Higher better)	6.3 (3.3)	*P* = 0.062 (-0.32, 13.0)	6.7 (4.4)	*P* = 0.130 (-2.1, 15.5)
MAL (Quality of Movement) (Total score) (Higher better)	2.9 (3.0)	*P* = 0.339 (-3.1, 8.9)	8.6 (3.8)	*P* = 0.029 (0.9, 16.2)
SIS (Total score) (Higher better)	-0.2 (1.1)	*P* = 0.832 (-2.4, 1.9)	-0.2 (1.3)	*P* = 0.901 (-2.7, 2.4)
C-CIM (Total score) (0 to 100, higher better)	0.9 (0.7)	*P* = 0.164 (-0.4, 2.3)	1.7 (0.9)	*P* = 0.047 (0.0, 3.5)
C-SATIS-Stroke (Total score) (0 to 1.03, higher better)	0.0 (0.0)	*P* = 0.916 (-0.1,0.1)	0.1 (0.1)	*P* = 0.657 (-0.2, 0.3)

*indicated significant difference ($P < 0.003$)

Note: CI, confidence interval; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

Table 7.5 Within-group Effects of MT + Bi-TENS and Sham-MT + Bi-TENS in People with Chronic Stroke (n = 60) (Post-Hoc Analysis)

Groups	1 Month (A_1) VS. Baseline(A_0)		2 Month (A_2) VS. Baseline(A_0)	
	Estimate (Standard Error)	P Value (95% CI)	Estimate (Standard Error)	P Value (95% CI)
		Primary Outcomes		
		FMA-UE (Total score): 0 to 66, higher better		
MT + Bi-TENS	5.6 (0.5)	$P < 0.001$ (4.7, 6.6) *	12.4 (0.8)	$P < 0.001$ (10.9, 13.9) *
Sham-MT + Bi-TENS	3.8 (0.5)	$P < 0.001$ (2.9, 4.8) *	7.2 (0.8)	$P < 0.001$ (5.6, 8.7) *
		WMFT (Total score):0 to 75, higher better		
MT + Bi-TENS	3.8 (0.4)	$P < 0.001$ (3.0, 4.5) *	8.4 (0.8)	$P < 0.001$ (6.9, 10.0)*
Sham-MT + Bi-TENS	2.2 (0.4)	$P < 0.001$ (1.4, 3.0)*	4.7 (0.8)	$P < 0.001$ (3.1, 6.2) *
		Secondary Outcomes		
		Grip Strength (kg): higher better		
MT + Bi-TENS	2.7 (0.5)	$P < 0.001$ (1.7, 3.6)*	4.1 (0.6)	$P < 0.001$ (3.0, 5.3)*
Sham-MT + Bi-TENS	1.4 (0.5)	$P = 0.005$ (0.4, 2.4)	2.4 (0.6)	$P < 0.001$ (1.2, 3.6)*
		Jacket Test (Second): lesser better		
MT + Bi-TENS	-4.3 (0.7)	$P < 0.001$ (-5.8, -2.9)*	-5.6 (0.8)	$P < 0.001$ (-7.1, -4.1)*

Sham-MT + Bi-TENS	-1.7 (0.7)	$P = 0.028$ (-3.1, -0.2)	-2.9 (0.8)	$P < 0.001$ (-4.5, -1.4)*
C-UEFI (Total score):0 to 59, higher better				
MT + Bi-TENS	3.2 (1.0)	$P < 0.001$ (1.3, 5.2)*	6.1 (1.1)	$P < 0.001$ (3.8, 8.4)*
Sham-MT + Bi-TENS	4.5 (1.0)	$P < 0.001$ (2.5, 6.4)*	5.4 (1.2)	$P < 0.001$ (3.1, 7.7)*
MAL(Amount of Use) (Total score): higher better				
MT + Bi-TENS	13.0 (2.3)	$P < 0.001$ (8.3, 17.7)*	22.4 (3.1)	$P < 0.001$ (16.3, 28.6)*
Sham-MT + Bi-TENS	6.7 (2.4)	$P = 0.007$ (1.9, 11.4)	15.7 (3.1)	$P < 0.001$ (9.4, 22.0)*
MAL(Quality of Movement) (Total score): higher better				
MT + Bi-TENS	9.8 (2.1)	$P < 0.001$ (5.6, 14.0)*	20.0(2.7)	$P < 0.001$ (14.6, 25.3)*
Sham-MT + Bi-TENS	6.9 (2.1)	$P = 0.002$ (2.6, 11.2)*	11.4 (2.7)	$P < 0.001$ (5.9, 16.9)*
SIS (Total score): higher better				
MT + Bi-TENS	4.2 (0.8)	$P < 0.001$ (2.6, 5.7)*	7.0 (0.9)	$P < 0.001$ (5.2, 8.8)*
Sham-MT + Bi-TENS	4.4 (0.8)	$P < 0.001$ (2.9, 5.9)*	7.2 (0.9)	$P < 0.001$ (5.3, 9.0)*
C-CIM (Total score): 0 to 100, higher better				

MT + Bi-TENS	1.9 (0.5)	$P < 0.001$ (1.0, 2.8)*	3.5 (0.6)	$P < 0.001$ (2.3, 4.7)*
Sham-MT + Bi-TENS	1.0 (0.5)	$P = 0.048$ (0.0, 1.9)	1.8 (0.6)	$P = 0.006$ (0.5, 3.0)
		C-SATIS-Stroke (Total score): 0 to 1.03, higher better		
MT + Bi-TENS	0.1 (0.1)	$P = 0.189$ (0.06, 0.30)	0.3 (0.1)	$P = 0.002$ (0.1, 0.5)*
Sham-MT + Bi-TENS	0.1 (0.0)	$P = 0.199$ (-0.06, 0.29)	0.2 (0.1)	$P = 0.013$ (0.1, 0.4)

*indicated significant difference ($P < 0.003$)

Note: CI, confidence interval; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

Table 7.6 The Carryover Effects of the Linear Mixed Models of Outcome Measures Across A_2 and A_{FU} in People with Chronic Stroke (n = 60)

Outcome Measures	Group	2 Month (A_2)	1 Month Follow-Up (A_{FU})	Time effect (MD (95%CI)), P Value	Group effect (MD (95%CI)), P Value	Interaction effect (MD (95%CI)), P Value
FMA-UE	MT + Bi-TENS	39(26-49)	39(26-50)	1.0 (-1.5, 3.8), P = 0.447	6.5 (0.6, 12.3), P = 0.030	0.5 (-4.1, 3.1), P = 0.789
(Total score) (range)	Sham-MT + Bi-TENS	31(20-43)	31(20-43)	0.5 (-2.1, 3.0), P = 0.708		
(0 to 66, higher better)						
WMFT	MT + Bi-TENS	42(28-58)	42(28-58)	0.1 (-2.7, 3.0), P = 0.927	4.7 (-1.7, 11.1), P = 0.150	0.1 (-4.0, 4.1), P = 0.974
(Total score) (range)	Sham-MT + Bi-TENS	36(22-42)	36(22-42)	0.1 (-2.8, 2.9), P = 0.963		
(0 to 75, higher better)						
Grip Strength	MT + Bi-TENS	9.6(5.0-19)	9.4(5.2-20)	0.1 (-0.5, 0.7), P = 0.667	3.9 (-0.2, 8.0), P = 0.062	0.1 (-0.5, 0.7), P = 0.772
(kg)(range)	Sham-MT + Bi-TENS	8.0(6.0-11)	8.0(6.0-10.1)	0.0 (-0.4, 0.4), P = 0.988		
(Higher better)						

Jacket Test (Second) (range) (Lesser better)	MT + Bi-TENS	16(14-22)	16(14-23)	0.0 (-0.2, 0.2), *P* = 0.841	1.8 (-2.3, 5.9), *P* = 0.381	-0.3 (-0.7, 0.0), *P* = 0.047
	Sham-MT + Bi-TENS	19(15-28)	20(15-28)	0.3 (0.1, 0.6), *P* = 0.010		
C-UEFI (Total score) (range) (0 to 59, higher better)	MT + Bi-TENS	46(39-50)	46(40-50)	0.2 (-0.2, 0.5), *P* = 0.370	0.7 (-4.2, 5.5), *P* = 0.787	0.0 (-0.5, 0.5), *P* = 0.983
	Sham-MT + Bi-TENS	44(39-50)	44(38-52)	0.2 (-0.2, 0.5), *P* = 0.362		
MAL(Amount of Use) (Total score) (range) (Higher better)	MT + Bi-TENS	31(15-65)	34(15-65)	1.1 (-4.1, 6.3), *P* =0.667	1.6 (-10.3, 13.5), *P* =0.789	0.5 (-6.9, 7.9), *P* =0.891
	Sham-MT + Bi-TENS	33(15-66)	37(15-66)	0.6 (-4.7, 5.9), *P* =0.817		
MAL(Quality of Movement) (Total score) (range)	MT + Bi-TENS	28(13-59)	30(13-59)	1.0 (-3.5, 5.5), *P* = 0.667	4.1 (-6.4, 14.5), *P* = 0.442	0.3 (-6.1, 6.8), *P* = 0.920
	Sham-MT + Bi-TENS	30(12-51)	30(12-51)	0.7 (-3.9, 5.2), *P* = 0.778		

(Higher better)						
SIS (Total score) (range) (Higher better)	MT + Bi-TENS	69 (65-75)	71(66-75)	0.7 (-0.9, 2.4), *P* = 0.392	0.6 (-3.2, 4.5), *P* = 0.747	0.5 (-1.9, 2.9), *P* = 0.670
	Sham-MT + Bi-TENS	70(62-78)	70(62-78)	0.2 (-1.5, 1.9), *P* = 0.807		
C-CIM (Total score) (range) (0 to 100, higher better)	MT + Bi-TENS	46(40-49)	46(40-49)	0.1 (-0.1, 0.1), *P* = 0.526	1.8 (-1.5, 5.2), *P* = 0.291	0.03 (-2.4, 2.4), *P* = 0.977
	Sham-MT + Bi-TENS	45(36-47)	45(36-48)	0.07 (-1.6, 1.8), *P* = 0.937		
C-SATIS-Stroke (Total score) (range) (0 to 1.03, higher better)	MT + Bi-TENS	0.6(0.5-0.8)	0.6(0.5-0.8)	0.0 (-0.2, 0.2), *P* = 0.870	0.0 (-0.4, 0.5), *P* = 0.871	0.0 (-0.3, 0.3), *P* = 0.865
	Sham-MT + Bi-TENS	0.6(0.4-1.1)	0.6(0.4-1.1)	0.0 (-0.2, 0.2), *P* = 0.938		

*indicated significant difference ($P < 0.003$)

Note: CI, confidence interval; MD, mean difference; MT, mirror therapy; Bi-TENS, bilateral transcutaneous electrical nerve stimulation; FMA-UE, Fugl-Meyer Assessment of Upper Extremity; WMFT, Wolf Motor Function Test; C-UEFI, Chinese Upper Extremity Functional Index; MAL, Motor Activity Log; SIS, Stroke Impact Scale; C-CIM, Chinese Community Integration Measure; C-SATIS-Stroke, Chinese SATIS-Stroke.

7.5 Discussion

This was the first study to investigate the combined effects of MT and Bi-TENS on the recovery of upper extremity motor function in people with chronic stroke compared with combined Sham-MT and Bi-TENS. Several key findings are as follows. First, compared with the Sham-MT + Bi-TENS group, people with chronic stroke had significantly greater between-group improvements in FMA-UE and WMFT scores at A_2. These effects persisted at A_{FU}. Second, compared with A_0, there were significant within-group improvements in FMA-UE, WMFT, paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, and C-CIM scores at both A_1 and A_2, and C-SATIS-Stroke score at A_2, in the MT + Bi-TENS group. These effects persisted at A_{FU}. Third, compared with A_0, there were significant within-group improvements in FMA-UE, WMFT, C-UEFI, MAL (Quality of Movement), and SIS scores at both A_1 and A_2, and paretic maximum grip strength, Jacket Test, and MAL (Amount of Use) scores at A_2, in the Sham-MT + Bi-TENS group. These effects persisted at A_{FU}.

7.5.1 The effects of MT + Bi-TENS in people with chronic stroke

Consistent with the results in sub-acute stroke survivors, chronic stroke survivors in this study also had significant differences in FMA-UE and WMFT scores at A_2 between two groups. As described in Chapter 6, the mechanisms underlying these beneficial effects of Bi-TENS on the recovery of motor function included increasing the excitability of transcallosal projections from the ipsilesionally to the contralesionally primary motor cortex by rebalancing interhemispheric inhibition (Cunningham et al., 2019) in people with stroke. The mechanisms underlying the beneficial effects of MT on the recovery of motor function included activating parts of the

mirror neuron system (e.g., inferior parietal lobule) to improve perceptual–motor control (Zhang et al., 2024), increasing the interhemispheric functional connectivity between the ipsilesionally and contralesionally primary motor cortex (Zhang et al., 2024), and increasing the attention of the affected extremity (Wasaka & Kakigi, 2012) in people with stroke.

Consistent with previous studies by our research team (Chen et al., 2022; Kwong et al., 2018), our results provided further evidence that the recovery of motor function of the paretic upper extremity can be significantly improved in people with stroke 6 months to 10 years after the first onset of stroke if appropriate interventions are applied. The critical time window for the recovery of motor function, characterized by the highest neuroplasticity in people with stroke, is between 3 and 6 months (Ballester et al., 2019). However, previous evidence has shown that appropriate interventions even in the chronic phase of stroke recovery can facilitate the recovery of upper extremity motor function (Ballester et al., 2019; Wingfield et al., 2022).

Our results had clinical significance in people with chronic stroke. The change in FMA-UE score (5.2) approached the estimated minimal clinically important difference of 5.25 for FMA-UE (Page et al., 2012). The change in WMFT score (3.7) reached the estimated minimal clinically important difference of 3 for WMFT (Lang et al., 2008). The 21% and 43% improvements in FMA-UE scores at A_1 and A_2, respectively, in the MT + Bi-TENS group provided further evidence that TENS combined with upper extremity exercises can exert greater positive effects on the recovery of upper extremity motor function in people with stroke compared with either stimulation alone or upper extremity exercise alone (Chen et al., 2022). The 12% and 31% improvements in WMFT scores at A_1 and A_2, respectively, in the MT + Bi-TENS group supported previous findings that upper extremity motor impairment was a

significant predictor for the recovery of upper extremity motor functions in people with stroke (Huang et al., 2014).

The improvements in FMA-UE and WMFT scores, representing the level of motor recovery in stroke survivors, probably explained the improvements in other outcome measures of motor functions, including maximum paretic grip strength and Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, C-CIM, and C-SATIS-Stroke scores, after 8-week treatment with MT + Bi-TENS. Indeed, improved motor functions of the paretic extremity are expected to allow stroke survivors to actively participate in daily life tasks, e.g., object manipulation and the use of the arm for gross motor activities of transferring, which can be expected to lead to a higher level of social participation in chronic stroke survivors.

Consistent with the results in people with sub-acute stroke reported in Chapter 6, the results of this study also demonstrated significant between-group improvements in FMA-UE and WMFT scores, as well as within-group improvements in other outcome measures. However, it might not be appropriate to make a direct comparison between the results in people with sub-acute and chronic stroke reported in Chapter 6 and in this chapter. In Chapter 6, all our subjects with sub-acute stroke had an additional 2.5-hour conventional therapy (including occupational therapy, speech therapy, and health education) provided by the Geriatric Day Hospital. Whether this intensive 2.5-hour conventional therapy affected the improvement of upper extremity motor function in people with sub-acute stroke was unclear. Thus, we separately reported the results of the studies on patients with sub-acute stroke and patients with chronic stroke in Chapter 6 and Chapter 7, respectively. Future research is warranted to investigate the additional effects of conventional therapy on the recovery of upper extremity motor function in people with sub-acute stroke.

7.5.2 The effects of Sham-MT + Bi-TENS in people with chronic stroke

In our study, the Sham-MT + Bi-TENS group showed significant within-group improvements in FMA-UE, WMFT, MAL (Quality of Movement), and SIS scores at both A_1 and A_2, and paretic maximum grip strength, Jacket Test, and MAL (Amount of Use) scores at A_2. The Sham-MT + Bi-TENS group received Bi-TENS while practicing bilateral upper extremity training but did not receive any MT (i.e., experiencing a visual illusion of enhanced function of the paretic extremity). Thus, the above-mentioned within-group improvements in the Sham-MT + Bi-TENS were probably attributable to Bi-TENS with bilateral upper extremity training.

Sham treatment is designed as an inactive procedure that closely resembles the active procedure in clinical trials without actually performing the treatment (Postalian, 2023). This study intended to investigate whether the addition of MT to Bi-TENS could exert synergistic effects to improve the recovery of motor function in stroke survivors. Hence, the Sham-MT treatment in our study was applied to mimic the MT treatment as closely as possible, allowing participants in both groups to perform symmetrical bilateral upper extremity exercises while imagining that the paretic side of the upper extremity was performing the same movements as the non-paretic side. Previous literature has shown the potential benefits of sham effects in sham-controlled trials, as the sham treatment was effective in altering the "subjective feeling" of the effect of treatment and induced strong physiological effects and meaningful symptomatic relief (Brim & Miller, 2013). The contribution of "subjective feeling" to the effect of sham treatment could not be determined in our study.

To date, no study has investigated the "pure" effect of Sham-MT. Whether Sham-MT can provide any therapeutic benefits for the recovery of upper extremity motor function in chronic stroke survivors is unclear. Future studies to investigate the neurophysiological, behavioral, and psychological responses to Sham-MT intervention are warranted.

7.5.3 Limitations

First, one month follow-up was conducted due to conditions of social unrest and pandemic. Hence, a longer-term follow-up should be examined in future studies. Second, the neurophysiological mechanisms about the addition of MT to Bi-TENS was not examined in this study. Further study in this area is warranted. Third, the results can only be applied to people with chronic stroke fulfilling our inclusion/exclusion criteria. Hence, our results have limited generalizability to all people with chronic stroke who have different levels of upper limb impairment. Fourth, the optimal dosage of the experimental protocol (e.g., TENS parameters, duration of the intervention) could not be determined in this study. Hence, Further study in this area is warranted about the optimal dosage. Fifth, compliance with MT and Sham-MT treatment was not recorded systematically. In addition, details of the actual treatment dosage, such as the number of repetitions performed during each treatment session, might have affected the overall effectiveness of the interventions. Thus, future studies should record compliance with treatment.

7.6 Conclusion

Compared with Sham-MT + Bi-TENS treatment, MT + Bi-TENS treatment induced greater increases in FMA-UE and WMFT scores at A_2 after 16 treatment sessions, in the people with

chronic stroke. These treatment effects were maintained at A_{FU}. Both MT + Bi-TENS and Sham-MT + Bi-TENS induced significant within-group improvements when compared with those at A_0 in the majority of the outcome measures after 8 and 16 sessions of treatment at A_1 and $A_{2,}$ respectively. These treatment effects were maintained at A_{FU}, 4 weeks after treatment ended.

CHAPTER EIGHT

Summary and conclusions of the thesis

8.1 Summary

Chapter 1 summarized the overview of prior research in people with stroke. Worldwide, the number of new first-time stroke cases each year is projected to increase to nearly 25 million by 2035. The sensorimotor impairment is the major impairment in stroke survivors, which encompasses muscle weakness, sensory deficits, spasticity, and loss of dexterity. The prevalence of upper extremity impairment in stroke survivors is reported range from 50% to 85% (Klamroth-Marganska et al., 2014; Pollock et al., 2014). In addition, previous studies have shown that mirror therapy (MT) (Bai et al., 2019; Choi et al., 2019) and transcutaneous electrical nerve stimulation (TENS) (Chuang et al., 2017; Chen et al., 2022) are effective treatments to improve the recovery of upper extremity motor function in stroke survivors.

In **Chapter 2**, several research gaps were identified in existing literature as follows:

(1) No consistent evidence about the synergistic effects of MT combined with electrical stimulation for improving the recovery of upper extremity motor function in people with stroke.

(2) Improvement in health-related quality of life is one of the ultimate goal in stroke rehabilitation. Although self-perceived functional recovery of upper extremity is important for indicating the status of upper extremity motor function, the effects or independent contributions of self-perceived functional recovery of upper extremity activity assessed by Upper Extremity Functional Index on the health-related quality of life assessed by Stroke Impact Scale in stroke survivors had not been explored.

(3) Reliability and validity of two outcomes, including Upper Extremity Functional Index (Chesworth et al., 2014) and SATIS-Stroke (Pereira et al., 2019), had not been culturally adapted and validated in Chinese stroke survivors; and

(4) No studies indicated the synergistic effects of MT + Bi-TENS to improve upper extremity impairment and the level of social participation in both sub-acute and chronic stroke survivors compared with Sham-MT combined with Bi-TENS.

In **Chapter 3**, an updated study had been conducted to investigate the synergistic effects of MT combined with electrical stimulation for improving the recovery of upper extremity motor function in people with stroke reported in the current literature. Results of 18 randomized controlled trials including 848 people with stroke demonstrated MT + electrical stimulation + conventional therapy was effective in improving the motor control of upper extremity, gross gripping function of upper extremity, and activity of daily living compared with conventional therapy alone, MT and conventional therapy, or electrical stimulation and conventional therapy. The results demonstrated that combined MT with ES is the effective modality for improving recovery of upper extremity recovery in stroke survivors.

In **Chapter 4**, the effect of self-perceived upper extremity motor function assessed by Upper Extremity Functional Index on health-related quality of life assessed by Stroke Impact Scale in stroke survivors was explored. The predictive model explained 60.3 % of the variance in health-related quality of life scores as assessed by Stroke Impact Scale. The Upper Extremity Functional Index was the strongest independent predictor of Stroke Impact Scale. The findings of this predictive model filled the gap in this study that the intervention targeting to improve

self-perceived upper extremity involving in daily life tasks could potentially improve health-related quality of life in stroke survivors.

In **Chapter 5**, psychometric properties of two outcome measures were investigated by a cross-sectional study, including translation and culturally adaption of Upper Extremity Functional Index (Chesworth et al., 2014) and SATIS-Stroke (Pereira et al., 2021; Pereira et al., 2019) in Chinese stroke survivors. The findings from this cross-sectional study demonstrated that the Chinese version of UEFI and SATIS-Stroke are reliable outcome measures to assess the self-perceived upper extremity motor function , and satisfaction level of daily life and social participation, respectively, in Chinese people with stroke. These two outcome measures were used in our main studies (reported in Chapter 6 and 7) to quantify the effects of MT with Bi-TENS on upper limb motor functions in people with stroke.

In **Chapter 6**, the randomized controlled trial were presented to explore whether that MT + Bi-TENS + conventional therapy was superior to Sham-MT + Bi-TENS + conventional therapy for improving upper extremity impairment and the level of social participation in sub-acute stroke survivors. Total 30 people with sub-acute stroke, of post-stroke duration from 3 weeks to 6 months, were allocated randomly into either the MT + Bi-TENS + conventional therapy or Sham-MT + Bi-TENS + conventional therapy group, and both groups were given to 30 minutes MT + Bi-TENS or Sham-MT + Bi-TENS and 2.5 hours convention therapy (standardized occupational therapy, speech therapy, and health education) with total 16 sessions. The findings demonstrated that, compared with Sham-MT + Bi-TENS + conventional therapy group, people with sub-acute stroke had significantly greater between-group improvement in FMA-UE scores and paretic maximum grip strength at both A_1 and A_2, and C-CIM scores at A_2 in MT + Bi-TENS + conventional therapy group. Compared with A_0, there

were significantly within-group improvements in FMA-UE, WMFT, paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, and C-CIM scores for people with sub-acute stroke in MT + Bi-TENS + conventional therapy group. Compared with A_0, there were significantly within-group improvements in FMA-UE, WMFT, MAL (Amount of Use), MAL (Quality of Movement) at both A_1 and A_2, and paretic maximum grip strength and SIS scores at A_2 for people with sub-acute stroke in Sham-MT + Bi-TENS + conventional therapy group. These effects persisted at A_{FU}.

In **Chapter 7**, results of another randomized controlled trial were presented that MT + Bi-TENS was superior to the Sham-MT + Bi-TENS for improving in upper extremity impairment and the level of social participation in chronic stroke survivors. Total 60 chronic stroke survivors (6 months to 10 years post stroke duration) were allocated randomly into either the MT + Bi-TENS or Sham-MT + Bi-TENS group, and both groups were given to 30 minutes MT + Bi-TENS or Sham-MT + Bi-TENS on 2 days per week for total 8 weeks. First, compared with Sham-MT + Bi-TENS group, people with chronic stroke had significantly greater between-group improvement in FMA-UE and WMFT scores at A_2. There were significantly within-group improvements in FMA-UE, WMFT, paretic maximum grip strength, Jacket Test, C-UEFI, MAL (Amount of Use), MAL (Quality of Movement), SIS, and C-CIM scores at both A_1 and A_2, and C-SATIS-Stroke score at A_2 for people with chronic stroke in MT + Bi-TENS group. There were significantly within-group improvements in FMA-UE, WMFT, C-UEFI, MAL (Quality of Movement), and SIS at both A_1 and A_2, and paretic maximum grip strength, Jacket Test, and MAL (Amount of Use) at A_2 for people with chronic stroke in Sham-MT + Bi-TENS. These effects persisted at A_{FU}.

8.2 Limitations and future directions

Due to the social unrest and several COVID-19 pandemic surges, the ongoing clinical study suspended for several episodes. In addition, stringent infectious control was enforced in all PolyU laboratories and in the Geriatric Day Hospital of Shatin Hospital under several COVID-19 pandemic surges from 2021 to 2023. Given the above-mentioned research environments, this thesis had several limitations.

First, the treatment effects and dosage of MT combined with Bi-TENS for improving the recovery of upper extremity motor function in stroke survivors had not been explored. We recommended further more studies in investigating the optimal dosage about the treatment effects and dosage response of MT combined with Bi-TENS for improving the recovery of upper extremity motor function in stroke survivors (Yap et al., 2023). Second, our participants were relatively cognitively intact and lower impaired motor function, which may have limited generalizability in different levels of motor function in stroke survivors. Hence, further research is needed to determine the suitability of applying the MT + Bi-TENS with severe upper extremity motor impairment. Third, the potential neurophysiological mechanisms to explain the synergistic effects of MT + Bi-TENS has not been investigated. Therefore, we encourage a future functional magnetic resonance imaging to examine the relationship between the visual, somatosensory, and motor cortex with or without MT and to determine the additional effects of MT on the recovery of motor function in stroke survivors. Fourth, one month follow-up was conducted due to conditions of social unrest and pandemic. Hence, a longer-term follow-up should be examined in future studies. Fifth, Sham-MT was used as comparison in the control group. The “pure” effects of Sham-MT on between-group or within-group improvements needs further investigation. Sixth, the compliances with MT or Sham-MT

treatment were not recorded systematically. In addition, the actual treatment dosage, such as the number of repetitions performed during each treatment session, might have affected the overall effects of the intervention. Thus, future studies should record the compliance with the treatments with MT or Sham-MT in people with stroke.

8.3 Implication on stroke rehabilitation

The main study showed that experimental group induced greater between-group improvements in FMA-UE and WMFT scores control group in people with sub-acute and chronic stroke. We also recommended combining MT with Bi-TENS as a safe, effective, and easy-to-administer intervention in improving upper extremity impairment, motor function, performance in daily life tasks, and social participation in people with sub-acute and chronic stroke. Our findings also revealed that interventions targeting on improving the self-perceived functional recovery of upper extremity in daily life activities could in turn leading to the improvement in health-related quality of life in people with stroke. We recommended using the Chinese version of Upper Extremity Functional Index and SATIS-Stroke as outcome measures for clinical application in stroke survivors.

APPENDICES

Appendix 3.1 Chapter 3 published on Disability and Rehabilitation (Final manuscript)

Effects of mirror therapy with electrical stimulation for upper limb recovery in people with stroke: a systematic review and meta-analysis

Introduction

Mirror therapy (MT), an effective adjunct intervention for recovering extremity motor function in people with stroke, creates the visual illusion that the paretic side moving with a normal movement pattern is the nonparetic side [1,2]. Electrical stimulation (ES) is an effective rehabilitation modality with a wide range of clinical applications for stimulating motor or sensory nerves or activating muscle responses [3,4]. Previous meta-analyses have shown that the use of MT or ES alone significantly improves upper limb motor function in people with stroke [5,6].

Two recent systematic reviews have provided evidence that MT combined with ES, as a priming technique, improves upper limb motor function recovery in people with stroke [7,8]. A meta-analysis by Luo et al. [7] evaluated the synergistic effects of MT combined with ES on upper limb recovery in people with subacute and chronic stroke. A subgroup analysis of two randomized controlled trials (RCTs) [9,10] demonstrated that, compared with MT alone, MT combined with electromyography (EMG)-triggered ES markedly improved functional recovery of the upper limb, as measured using the Fugl–Meyer Assessment (FMA), in people

with subacute stroke (Mean Difference (MD), 10.14; 95% CI, 5.27–15.01). However, no differences in recovery were detected between MT combined with mesh glove-afferent ES and MT alone in a subgroup analysis of people with chronic stroke [11,12].

In contrast to the meta-analysis results reported by Luo et al. [7] in a recent systematic review and meta-analysis conducted by Saavedra-García et al. [8] the pooled results from seven trials showed no significant differences in the effectiveness of combined MT and ES therapy, conventional therapy, MT alone, or ES alone at improving upper extremity motor function recovery, as assessed using the FMA, Action Research Arm Test (ARAT), and Box and Block Test (BBT), in people with stroke [9–11, 13–16]. One possible explanation for this discrepancy is that Saavedra-García et al. [8] pooled data from people with subacute and chronic stroke. Hence, differences in the synergistic effects of MT combined with ES in people with subacute and chronic stroke remain to be explored.

Although Luo et al. [7] and Saavedra-García et al. [8] systematic reviews provided a preliminary understanding of the effects of combined use of MT and ES on the recovery of upper limb function in people with stroke, three research questions remain unanswered. First, the synergistic effects of MT and transcutaneous electrical nerve stimulation (TENS) for improving upper limb motor function were not reviewed in Luo et al. [7] and Saavedra-García et al. [8] systematic reviews. In fact, a recent clinical trial [17] reported that MT combined with TENS could improve upper extremity motor function in people with stroke. Second, no previous study reviewed the synergistic effects of MT combined with ES for improving the participation level [e.g., activity of daily living (ADL)] of people with stroke. Third, the effects of combined use of MT and ES for improving upper extremity impairments, motor function

recovery and participation were not reviewed according to different post-stroke stages (acute/subacute compared with chronic).

Therefore, the objectives of this study were to: 1) examine whether MT with ES and CT (MT + ES + CT) is more effective in improving upper limb functional recovery in people with stroke compared with CT alone, ES and CT (ES + CT), and MT and CT (MT + CT) based on the International Classification of Functioning, Disability, and Health (ICF) framework; 2) identify whether MT combined with ES is more effective in improving upper limb functional recovery for people with acute/subacute stroke compared with chronic stroke.

Materials and methods

Protocol and registration

This systematic review and meta-analysis followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement [18]. The review protocol was registered in the International Prospective Register of Systematic Reviews database (CRD42023400726).

Eligibility criteria

Participants

Trials including people aged ≥ 18 years with a history of stroke (one or multiple) and in different phases of stroke recovery were included.

Interventions

Trials evaluating the synergistic effects of MT and peripheral nerve, or cutaneous ES were included.

Comparators

To provide a wider overview of the synergistic effects of MT and ES, the following three comparison groups were included.

1. Effects of MT with ES

MT + ES + CT versus CT alone would be compared to evaluate the summative effects of MT with ES.

2. Effects of MT

MT + ES + CT versus ES + CT would be compared to evaluate whether the summative effects of MT and ES are greater than the effects of ES alone.

3. Effects of ES

MT + ES + CT versus MT + CT would be compared to evaluate whether the summative effects of MT and ES are greater than the effects of MT alone.

Outcomes

Outcome measurements were divided into three domains according to the ICF framework [19,20] to provide meaningful results to clinical practice. If more than one validated measurement was identified in each domain, priority was given according to the following rules.

1. For the Body Function Domain, the primary outcome was upper limb motor control, as assessed by the FMA [20, 21], followed by any other validated measures.

2. For the Activity Domain, the primary outcome was upper limb gross gripping function, as assessed by the ARAT [20, 22], followed by any other validated measures.

3. For the Participation Domain, the primary outcome was the level of difficulty in using the most-affected upper extremity in ADL, as measured by the MAL [20, 23], followed by any other validated measures.

Studies

RCTs with parallel assignment or crossover designs were included. Only first-period data from studies with crossover designs were included to avoid potential period and carryover effects [24]. Studies published in English and Chinese peer-reviewed journals were included.

Excluded studies

Conference abstract, thesis, and case reports were excluded. Studies reporting data that could not be extracted from figures or graphs using WebPlotDigitizer; studies in which all groups received MT combined with ES; and studies in which MT was compared with sham MT or ES was compared with placebo ES were excluded.

Search strategy

An extensive literature search was conducted using the following 10 electronic databases: MEDLINE, Embase, Cochrane Library, Web of Science, Scopus, Physiotherapy Evidence Database, China Biology Medicine, China National Knowledge Infrastructure, Wan Fang, and VIP. ClinicalTrials.gov and the Chinese Clinical Trial Registry were also searched for unpublished trials. Databases and clinical registries were searched from their inception to January 2023. Additional studies were identified by screening the reference lists of relevant systematic reviews [7,8,25]. The search strategies used in this study are shown in Appendix A.

Study selection

Two independent authors (HP, CCCC) assessed the article titles and abstracts to identify studies investigating the effect of MT combined with ES on upper limb motor recovery in people with stroke. Full texts were assessed based on the eligibility criteria to identify articles to include in this systematic review. Any disagreements were resolved by discussion and/or consultation with the corresponding author.

Data extraction

Two authors (HP, WWLN) extracted the data independently using a standardized form. Any disagreements were resolved by discussion and/or consultation with the corresponding author.

Risk of bias Assessment

The trials included in the analysis were appraised by two authors (HP, SSLL) using version 2 of the Cochrane tool to assess the risk of bias [26]. The overall quality of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework [27].

Statistical analysis

All data analyses were performed using Review Manager version 5.3 (The Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark). For all continuous variables, the means, and standard deviations (SDs) of each group were analysed at the post-test time points. For studies with several evaluation points (e.g., 4, 8, and 12 weeks), only the longest time point was considered, because this point had the greatest clinical significance [28]. In studies where raw data were provided as median values or interquartile ranges, only normally distributed data were considered for inclusion in the analysis. The median values were considered equal to the mean values. The corresponding SDs of the interquartile ranges were calculated according to the following formula: SD = (upper limit − lower limit)/1.35 [24]. If the numerical data were provided as figures or graphs, WebPlotDigitizer (https:// apps.automeris.io/wpd/) was used to extract the data [29]. The mean difference (MD) and 95% CIs of random-effects models were calculated for an outcome evaluated by the same assessment tool. The effect sizes were analysed by calculating the standardized mean difference (SMD) and 95% CIs of the random-

effects models for an outcome evaluated by different assessment tools. The effect sizes were defined as small (< 0.2), moderate (0.2 to < 0.5), large (0.5 to < 0.8), or very large (> 0.8) [24,30,31].

Testing homogeneity

Chi-square test results with P-values < 0.05 were considered significantly heterogeneous. I^2 values were used to represent the degrees of heterogeneity, with values of 25%, 50%, and 75% denoting low, moderate, and high degrees of heterogeneity, respectively [24].

Subgroup analysis

The phases after stroke were categorized as acute (< 3 weeks), subacute (3 weeks to 6 months), or chronic (≥ 6 months). A predefined subgroup analysis was conducted according to the phase after stroke (acute/subacute versus chronic).

Sensitivity analysis

Sensitivity analyses were performed to identify the sources of heterogeneity with consideration of the stroke stage and risk of bias.

Regression analysis

Information regarding the duration of each training session, weekly frequency of the training session, and number of weeks in the entire training course were extracted [32]. The training

dosage was calculated as the duration of each training session multiplied by the frequency and the number of weeks of training. A regression meta-analysis was performed using STATA 15.0 (StataCorp, College Station, TX, USA) to explore the correlation between effect size and treatment dosage for the outcome variables assessed in more than 10 trials.

Publication bias

If the number of trials for a given outcome was more than 10, Egger's test was used to determine the probability of publication bias. The classic Fail-Safe N analysis was used for outcomes assessed in 10 or fewer trials [30].

Results

Search results

Two thousand eight hundred and sixty-three citations were retrieved from electronic databases, registry centers, and reference list searches, and 1,286 duplicates were removed. After the titles and abstracts were screened according to the inclusion and exclusion criteria, 88 full texts were assessed, and 16 articles were included in our systematic review and meta-analysis (Figure 1).

Study characteristics

Descriptive characteristics of the included studies are shown in Table 1.

Participants

The 16 included studies [9–17, 33–41] included 773 patients with stroke. The sample sizes ranged from 16 to 90 participants, and the mean ages ranged from 44.15 to 73.35 years. Most studies (*n*=11) assessed people with acute/subacute stroke (560 participants) [9,10,14,15,34–40], while five studies assessed people with chronic stroke (213 participants) [11–13,16,17]. According to the initial FMA upper extremity scores, the impairment levels ranged from moderate (3 studies, 107 patients) [11,12,16], to severe (11 studies, 577 patients) [9,10,14,17, 34–40]. Two studies [13,15] did not provide FMA-UE score details.

Interventions

The studies included in the analysis used MT combined with different types of ES. The ES modalities were functional electrical stimulation [10,14,15,38,39], neuromuscular electrical stimulation [34], EMG-triggered biofeedback electrical stimulation [9,13,35–37], somatosensory electrical stimulation [11,12,16], and TENS [39]. The length of the interventions ranged from 2 to 8 weeks, the treatment frequency ranged from 5 to 6 days per week, and the session lengths ranged from 20 to 120 min. The most commonly stimulated muscles were the extensor carpi radialis and extensor digitorum communis. The pulse width ranged from 200 to 500 μs, the frequency ranged from 20 to 60 Hz, and the intensity ranged from 0 to 90 mA. The treatment dosages (total minutes) ranged from 400 to 4,320 min. Only two studies [9,13] used bilateral ES, whereas all other studies used unilateral upper limb ES.

Ten studies used the physical therapy and occupational therapy [9,10, 17, 34-40] as the treatment components of CT. A total of two studies only used the physical therapy [13,14], and four studies in total [11,12,15,16] only used occupational therapy as the treatment component

of CT, respectively. The total training session of CT ranged from 20 to 240 minutes. The duration and training frequency of CT ranged from 3 to 8 weeks and 4 to 6 days per week, respectively.

Comparisons

MT with ES and CT was compared with MT and CT in nine studies [11, 12, 14–16, 34, 37–39], ES and CT in nine studies [9,10,14,15,34–36, 38, 40], and CT alone group in five studies [11,13,17,35,36]. In general, the comparison groups received similar treatment dosages as the combined therapy group.

Outcomes

In the Body Function Domain, 12 [9–12,14,17,34–40] and four [13,16,17,34] studies assessed upper limb motor control and spasticity using the FMA and Modified Ashworth Scale (MAS), respectively. In the Activity Domain, three [14–16] and seven [9–13,16,38] studies assessed upper limb gross gripping function and dexterity using the ARAT and BBT, respectively, and five [12–14,16,35] and four [9,17,37,39] studies measured functional mobility and ADL using the Functional Independence Measure (FIM) and Modified Barthel Index (MBI), respectively. One study [41] regarded the FIM and MBI as psychometrically similar measures of physical disability. Thus, we pooled the FIM and MBI results for the meta-analysis of ADL. Only two studies reported outcomes in the Participation Domain, assessing the level of difficulty in using the most-affected upper extremity in daily life using the MAL [11] and Stroke-Specific Quality of Life (SSQOL) [13] tools.

Methodological quality

Our methodological quality assessment of the included trials is provided in Table 2. All included studies showed a low risk of bias for two evaluation items: “missing outcome data” and “measurement of the outcome.” Nine included studies [9,11,12,14,15,17,37–39] had a low risk of bias regarding the randomization process, and the remaining seven studies [10,13,16,34–36,40] had some risk of bias concerning randomization methods. Two included studies [10,13] showed a high risk of bias for the evaluation item “deviations from the intended interventions,” whereas the remaining studies had a low risk of bias for this item. One included study [9] had a low risk of bias in the selection of the reported results, whereas the remaining studies had some risk of bias concerning elements of the study. In terms of overall quality, one included study [9] had a low risk of bias, two [10,13] had a high risk of bias, and the remaining studies had some risk of bias concerning characteristics of the study.

Effects of combined MT with ES and CT compared with CT alone group on body function, activity, and participation domain outcomes

Five included studies involving 225 participants contributed data on the effects of MT with ES and CT compared with CT alone group (Figure 2) [11,13,17,35,36]. The GRADE summary of findings for this comparison is shown in Table 3. Most studies were down-graded one level for a serious risk of bias, heterogeneity, and imprecision. The certainty of the evidence for the outcomes varied from very low to low. A large significant effect was observed favouring MT with ES and CT therapy, compared with CT alone group, for improving upper limb motor control in people with stroke (SMD, 1.89; 95% CI, 1.52–2.26; $p < 0.001$), with no heterogeneity ($I^2 = 0\%$, $p = 0.57$). There was no significant effect favouring MT with ES and CT compared

with CT alone group (MD, −0.76; 95% CI, −1.86–0.34; $p = 0.17$; $I^2 = 42\%$) for upper extremity spasticity. No significant effects were observed to favour MT with ES and CT for upper extremity dexterity, compared with CT alone group (SMD, −0.05; 95% CI, −0.58–0.49; $p = 0.86$; $I^2 = 0\%$). A large significant effect size was observed favouring MT with ES and CT therapy compared with CT alone group, for improving ADL (SMD, 1.17; 95% CI, 0.42–1.93; $p = 0.002$), with significant heterogeneity ($I^2 = 70\%$, $p = 0.04$).

One study [11] reported improvements in the level of difficulty in using the most-affected upper extremity in daily life, as assessed using the MAL, in the MT with ES and CT therapy group compared with CT alone group (SMD, 0.08; 95% CI, −0.65 to 0.81 for amount of use and SMD, 0.04; 95% CI, −0.69 to 0.77 for quality of movement). Another study [13] reported improvements in health-related quality of life, as assessed using the SSQOL tool, with MT with ES and CT compared with CT alone group (SMD, 0.47; 95% CI, −0.32 to 1.27).

Effects of combined MT with ES and CT compared with ES and CT on body function, activity, and participation domain outcomes

Nine included studies involving 300 participants contributed data on the effects of MT with ES and CT compared with ES and CT (Figure 3) [9,10,14,15,34–36,38,40]. The GRADE summary of findings for this comparison is shown in Table 4. Most studies were downgraded one level for a serious risk of bias and imprecision. The certainty of the evidence for the outcomes varied from low to moderate.

Moderate significant effects were observed favouring MT with ES and CT for improving upper limb motor control compared with ES and CT (SMD, 0.42; 95% CI, 0.11–0.73; $p = 0.008$; $I^2 =$

33%). One study [34] reported a greater reduction in spasticity with MT with ES and CT compared with ES and CT (MD, −0.15; 95% CI, −0.77 to 0.47). MT with ES and CT showed no significant effect, compared with ES and CT, on upper extremity gross gripping function in people with stroke (MD, 2.06; 95% CI, −3.42 to 7.55; $p = 0.46$; $I^2 = 8\%$). No significant effects were observed favouring MT with ES and CT therapy for improving upper extremity dexterity, compared with ES and CT (SMD, 0.43; 95% CI, −0.06 to 0.92; $p = 0.08$; $I^2 = 28\%$). No significant effects were found to favour MT with ES and CT, compared with ES and CT, for improving ADL (SMD, 0.48; 95% CI, −0.18 to 1.15; $p = 0.16$), with moderate heterogeneity ($I^2 = 61\%$, $p = 0.08$).

Effects of combined MT with ES and CT compared with MT and CT on body function, activity, and participation domain outcomes

Nine included studies involving 330 participants contributed data on the effects of MT with ES and CT compared with MT and CT(Figure 4) [11,12,14–16,34,37–39]. The GRADE summary of findings for this comparison is shown in Table 5. Most studies were downgraded one level for a serious risk of bias and imprecision. The certainty of the evidence for the outcomes was low. Moderate significant effects were observed to favour MT with ES and CT, compared with MT and CT, for improving upper limb motor control (SMD, 0.47; 95% CI, 0.04–0.89; $p = 0.03$; $I^2 = 65\%$). No significant effect was observed to favour MT with ES and CT, compared with MT and CT, for reducing spasticity (MD, 0.00; 95% CI, −0.18 to 0.18; $p = 1.0$; $I^2 = 0\%$). There was a significant effect favouring MT with ES and CT, compared with MT and CT, for improving upper extremity gross gripping function (MD, 6.47; 95% CI, 1.92–11.01; $p = 0.005$; $I^2 = 0\%$). No significant effect was observed favouring MT with ES and CT, compared with MT and CT for improving upper extremity dexterity (SMD, 0.32; 95% CI, −0.07 to 0.7; $p =$

0.11; I^2 = 13%). No significant effect was observed favouring MT with ES and CT, compared with MT and CT, for improving ADL (SMD, 0.44; 95% CI, −0.21 to 1.09; p = 0.19; I^2 = 76%), with highly significant heterogeneity (I^2 = 76%, p = 0.002). One study[11] reported a greater reduction in the level of difficulty in using the most-affected upper extremity in daily life, as assessed by the MAL, with MT with ES and CT compared with MT and CT (SMD, −0.2; 95% CI, −0.94 to 0.55 for the amount of use and SMD, −0.34; 95% CI, −1.09 to 0.41 for quality of movement).

Subgroup analysis

Only one comparison, MT with ES and CT versus MT and CT, had a sufficient number of studies (n = 7) for a subgroup analysis of people with subacute/acute or chronic stroke. Our analysis showed that, compared with MT and CT, MT with ES and CT was significantly more effective at improving upper limb motor control, as assessed by the FMA, in people with acute/subacute stroke (SMD, 0.66; 95% CI, 0.17–1.15; p = 0.009; I^2 = 65%) but not those with chronic stroke (SMD, −0.05; 95% CI, −0.54 to 0.44; p = 0.85; I^2 = 0%; Figure 5). The GRADE summary of findings for this comparison is shown in Table 6. Most studies were downgraded one level for a serious risk of bias and imprecision. The certainty of the evidence for the outcomes was low.

Sensitivity analysis

Sensitivity analyses were performed by removing four studies [16, 34, 35, 39]. There was only one instance in which performing a sensitivity analysis affected the primary meta-analysis with an opposite result. A minimal change in upper limb motor control for MT with ES and CT,

compared with MT and CT, was detected, and the result yielded non-significant effects between MT with ES and CT and MT and CT, with low heterogeneity (SMD, 0.30; 95% CI, −0.02 to 0.62; $p = 0.07$; $I^2 = 29\%$). The details are presented in Table 7.

Regression analysis

Only the FMA outcome variable had a sufficient number of trials ($n = 12$) to perform a correlation analysis. The meta-regression results showed that the training dosage of combined MT and ES was not significantly correlated with the pooled effect size for the FMA outcome variable ($r = 0.023$, $p = 0.398$).

Publication bias

As the number of included studies for each outcome was fewer than 10, the classic Fail-Safe N analysis was used to assess publication bias only for the FMA outcome. The details are presented in Table 8. According to this calculation, if the fail-safe N value exceeds 5 multiplied by K (the number of studies in the meta-analysis) plus 10, the results of the meta-analysis can be interpreted as robust [41]. However, a possibility of publication bias in our study was detected based on the calculations of the number of missing studies.

Discussion

This systematic review aimed to examine the synergistic effects of MT and ES on improving upper limb motor function recovery in people with stroke. The meta-analysis found low certainty evidence that MT with ES and CT was superior to CT alone therapy for improving

upper limb motor control, based on impairment level, ADL performance, based on activity level. Compared with ES and CT, MT with ES and CT resulted in significantly superior improvements in upper limb motor control, based on the impairment level, with low-certainty evidence. MT with ES and CT was significantly superior to MT and CT for improving upper limb motor control, based on the impairment level, and gross gripping function, based on the activity level, with low-certainty evidence. Subgroup analysis provided low-certainty evidence that, compared with MT and CT, MT with ES and CT had significant effects on upper limb motor control in people with acute/subacute but not chronic stroke.

Combined MT with ES and CT compared with CT alone group

Although the improvement in upper limb motor control did not reach a minimal clinically important change (10 points for sub-acute stroke and 4 points for chronic stroke when using the FMA) [42–44], our study showed that MT with ES and CT resulted in a greater improvement than CT alone group. As CT alone may also have additional effects in improving upper extremity impairment, which may lead to additional effects of MT with ES could not reach the minimal clinically important change in people with stroke in this study. However, two probable reasons may explain the statistically synergistic effect. First, from a motor mechanism perspective, two studies demonstrated that MT induced more focal primary motor cortex (M1) activation within the affected hemisphere and induced M1 activation in the unaffected hemisphere, facilitating a shift in M1 activation balance toward the affected hemisphere in people with stroke [45,46]. One functional magnetic resonance imaging (fMRI) study showed that ES induced greater M1 activation in the unaffected hemisphere [47], which indicated that the unaffected M1 may play a major role in compensating for motor deficits. According to the theory of motor primitives [48], the overall motor output is the sum of all levels of activation of each module. Hence, combined MT and ES jointly increase M1

activation in both unaffected and affected hemispheres, strongly activating the motor network [49] and maximizing the motor output to directly affect motor function recovery in people with stroke.

Second, from a sensory mechanism perspective, the modulation of sensory input has been regarded as a motor priming technique with projections from the sensory cortex to the motor cortex [50, 51]. This technique augments sensorimotor interactions and increases the tight anatomical coupling between somatosensory input and motor output [4,51,52]. Hence, effective sensory processing and integration play important roles in successful central motor control [51,53]. One fMRI study showed that combined visual and tactile stimulation significantly induced peak activation in both the primary sensory-motor cortex and the secondary somatosensory cortex [54]. Hence, combined MT and ES therapy simultaneously increases the proprioceptive and tactile inputs [51,55], activates the sensory cortex, and increases the number of sensory projections to the motor cortex to indirectly affect motor function recovery in people with stroke.

Although spasticity is defined as disordered sensorimotor control [56] and has a strong positive correlation with sensory deficits [57,58], we found that, compared with CT alone group, MT with ES and CT produced an insignificant reduction in upper limb spasticity in people with stroke. One probable reason for this result is that spasticity is a complex clinical sign that involves stretch reflex arc impairment and structural and component changes in muscle fibers and tendons [59]. Although combined MT and ES induces sensorimotor integration via proprioceptive sensory input to indirectly adjust central effects with a new plastic rearrangement [60], combined therapy may not have significant effects on muscle properties. Hence, combined MT and ES had limited efficacy for reducing upper limb spasticity. Moreover,

we cannot exclude the possibility that the use of CT alone has already reached its maximum effectiveness in improving spasticity. Hence, the addition of combined MT and ES had limited efficacy for reducing upper limb spasticity.

Our study showed that, compared with CT alone group, MT with ES and CT affected the Activity ICF domain, resulting in a significant improvement in ADL performance in people with stroke. CT training could add the effects in improving the performance of daily life activity tasks in people with stroke through increasing muscle strength and range of motion of upper extremity in people with stroke. On top of above reason, MT with ES can augment the additional effects in improvement in the ability of performing the daily life activities in people with stroke. According to the principles of sensorimotor learning [48], combined MT and ES increase the attention toward executing motor tasks with somatosensory input [45,48], which may improve the accuracy of performing daily activities for people with stroke. Hence, the improvement of upper extremity impairment through the combined use of MT, ES and CT could transfer to improve the ability in daily life tasks in people with stroke in this study. However, our study showed that MT with ES and CT were not superior to CT alone group for improving upper limb manual dexterity in people with stroke, based on the activity level. According to the motor learning principle of task specificity, upper limb manual dexterity requires both somatosensory input and sensory-based specific task skills training [48]. Hence, it is not surprising that combined MT and ES had limited efficacy for improving upper limb manual dexterity in people with stroke.

Combined MT with ES and CT compared with ES and CT

Our study showed that the addition of MT to ES and CT produced additional benefits on upper limb motor control, based on the impairment level, in people with stroke. Two probable reasons may explain these additional benefits. First, from a clinical perspective, viewing the reflection of self-generated movements in a mirror may increase attention toward the integration of vision and proprioception, which may increase the self-awareness and spatial efficiency of the affected upper limb [51]. Those positive effects may be helpful for counteracting learned non-use of the affected upper limb in people with stroke [51,61]. Second, from a mechanistic perspective, it has been confirmed that the observation of a mirror illusion may trigger the mirror neuron system (MNS) in humans [62,63]. The MNS involves both the classic motor system and M1, the primary somatosensory cortex, as the extended MNS [64]. The MNS has been proposed to be a neural substrate to prime the motor cortex via sensory input [65], which is related to the actions of understanding, imitation, and motor learning [64]. Hence, adding MT to ES and CT may provide additional benefits for upper limb motor control in people with stroke.

However, the addition of MT to ES and CT did not affect the Activity ICF domain to produce significant improvements in upper limb gross gripping function, dexterity, or ADL performance. One reason may explain these results. Although the addition of MT may increase the attention toward movement execution via somatosensory feedback [51], the people with stroke in our study had severe motor dysfunction, with FMA scores below 30 [28,66], and thus, they had difficulties in executing movements or task-based MT with efficient voluntary movements. Hence, the ability to sustain a grasp, effectively manipulate objects, and reacquire skilled movements essential to accomplish ADL could not be achieved by the addition of MT effects in our study.

Combined MT with ES and CT compared with MT and CT

Our study showed that adding ES to MT and CT produced additional significant benefits on upper limb motor control, based on the impairment level, in people with stroke. Two probable reasons may explain these additional benefits. First, from a clinical perspective, ES induces muscle contractions and produces a functionally useful motion during stimulation [51], which benefit the integration of task-based rehabilitation training. Meanwhile, ES increases the proprioceptive and tactile inputs to monitor the position of the body in space, which can help refine upper limb motor control [67]. Second, from a mechanistic perspective, ES increases the number of proprioceptive signals from evoked movements to activate the somatosensory cortex and induce motor motoneuronal excitability via sensorimotor coupling [68], which may facilitate more voluntary activation of relevant neuronal networks [68]. Hence, adding ES to MT and CT may provide additional benefits for upper limb motor control in people with stroke.

Although some studies have hypothesized that ES reduces spasticity by reducing stretch reflex excitability, modulating reciprocal inhibition, and increasing presynaptic inhibition [69], our study showed that the addition of ES produced no significant reduction in upper limb spasticity, as measured using the MAS, in people with stroke. One reason may explain this result. The validity of the MAS to assess spasticity has been challenged, as MAS is a subjective tool without standardized test conditions [70]. Meanwhile, it has been suggested that MAS measures hypertonia rather than spasticity [70]. Hence, future studies should use objective scales (e.g., neurophysiological tests) to confirm whether the addition of ES significantly reduces upper limb spasticity in people with stroke.

Our study showed that the addition of ES to MT and CT affected the Activity ICF domain, producing a significant improvement in upper limb gross gripping function. One probable reason for this result is that the addition of ES increases the strength of the flexor or extensor muscle, which can increase upper limb grip strength in people with stroke [71]. However, the improvement in upper limb gross gripping function did not translate into increased upper limb function in our study. The probable reason for this result is that upper limb dexterity and ADL require muscle strength in addition to high-level movement skill training. Hence, the complex movements required to accomplish ADL and manipulate objects were not improved by the addition of ES in our study.

Subgroup analysis

Our subgroup analysis demonstrated that, compared with MT and CT, MT with ES and CT had significant effects on upper limb motor control in people with acute/subacute but not chronic stroke. This finding indicates that early, rich multimodal sensory stimulation promotes motor function recovery in people with stroke. A previous fMRI study demonstrated only partial proportional passive and active somatosensory processing recovery early after a stroke, even if spontaneous recovery occurred [72], which indicates that people with acute/subacute stroke also have remaining sensory disorders. Another animal study assessing sensorimotor function recovery in a mouse model of early stroke showed that multisensory stimulation applied via enriched environments enhanced the resting-state functional connectivity of distinct brain regions involved in multisensory integration for the initiation and coordination of movements, resulting in a more rapid return to normal brain function and improvements in lost tactile proprioceptive function [73]. In the studies included in the present review, both laboratory and

clinical findings suggested that the enrichment of sensory training has important clinical significance for people with acute/subacute stroke.

Regression analysis

Our review is the first attempt to examine the relationship between the effect size and therapy dosage of MT combined with ES. No significant linear relationship between the effect size and the dosage was detected. Two factors may have contributed to this result. First, as there was a small number of included studies (n = 12), there may have been insufficient power to detect a significant correlation. Second, we used the total number of minutes of MT with ES as the training paradigm to explore the relationship; however, a novel measurement of dosage interactions with training effects warrants further investigation.

Strengths and limitations

Our study has several strengths. First, we used the ICF domains to integrate the biological, individual, and social dimensions of health based on three comparisons, which provided a comprehensive view of functional recovery achieved through the synergistic effects of MT combined with ES. Second, the GRADE assessment of each outcome will facilitate decision-making in clinical practice. Third, we explored the effects of combined therapy according to the time of stroke onset, demonstrating that patients with acute/subacute impairment may be the best candidates for combined MT and ES treatments.

We acknowledge that our study also has some limitations. First, defining an optimal treatment protocol may be crucial for determining the treatment effects [27]. However, the limited

number of included studies and the lack of details regarding ES parameters hindered the identification of an optimal treatment protocol. Second, knowing the order of priming and training is essential for determining the interaction direction [4]; however, the optimal order of MT and ES could not be determined due to limited details on the application sequence. Similarly, the type of ES that is most effective in combination with MT could not be explored due to the limited number of included studies. Thirdly, for the grade assessment, majority of studies assessed have high risk of bias with very low certainty of evidence. The included studies with high risk of bias may lead to the inaccurate of results with false positive effects and over-estimate the true effect. Hence, future studies should include studies with high methodological quality and low risk of bias to provide update evidence. Fourth, some reporting data could not be extracted from the figures or graphs leading to miss the relevant information, which leads to include a limited sample size for this meta-analysis. Hence, future studies should include more studies to provide more convincing evidence of the efficacy of MT combined with ES for upper extremity motor function recovery in people with stroke. Fifth, the duration of CT varied across the included studies, which may affect the comparisons between the intervention and control groups. However, the effects and parameters of CT on the recovery of upper extremity motor function were not explored as they are not the focus of the present study.

Conclusions

In conclusion, this review demonstrated that the combined use of MT and ES may be an effective priming technique for improving upper limb motor recovery in people with stroke. MT combined with ES may be more effective for upper limb recovery in patients with acute/subacute stroke than in those with chronic stroke. However, high-quality studies with

larger sample sizes are warranted to clarify the uncertain effects of MT combined with ES on different aspects of recovery after stroke.

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Author's contribution

Hong Pan conceived the study and drafted the manuscript. Tai Wa Liu, Raymond C.K. Chung and Charles W.K. Lai drafted the protocol and performed the literature search. Stefanie S.L. Lam, Winnie W.L. Ng, Charles C.C. Chan, and Maria W.S. Tang extracted and analysed data. Carol S.K. Li, Elsie Hui, Pei Ming Chen, and Jean Wu reviewed and commented on the manuscript draft. Shamay S.M Ng supervised the project. All authors have read and agreed to the published version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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References

[1] Ding L, Wang X, Chen SG, et al. Camera-Based mirror visual input for priming promotes motor recovery, daily function, and brain network segregation in subacute stroke patients. Neurorehabil Neural Repair. 2019;33(4):307–318. doi: 10.1177/1545968319836207.

[2] Selles RW, Michielsen ME, Bussmann JB, et al. Effects of a mirror-induced visual illusion on a reaching task in stroke patients: implications for mirror therapy training. Neurorehabil Neural Repair. 2014;28(7):652–659. doi: 10.1177/1545968314521005.

[3] Yang JD, Liao CD, Huang SW, et al. Effectiveness of electrical stimulation therapy in improving arm function after stroke: a systematic review and a meta-analysis of randomised controlled trials. Clin Rehabil. 2019;33(8):1286–1297. doi:10.1177/0269215519839165.

[4] Stoykov ME, Madhavan S. Motor priming in neurorehabilitation. J Neurol Phys Ther. 2015;39(1):33–42. doi: 10.1097/NPT.0000000000000065.

[5] Wattchow KA, McDonnell MN, Hillier SL. Rehabilitation interventions for upper limb function in the first four weeks following stroke: a systematic review and meta-analysis of the evidence. Arch Phys Med Rehabil. 2018;99(2):367–382. doi: 10.1016/j.apmr.2017.06.014.

[6] Zeng W, Guo YH, Wu GF, et al. Mirror therapy for motor function of the upper extremity in patients with stroke: a meta-analysis. J Rehabil Med. 2018;50(1):8–15. doi: 10.2340/16501977-2287.

[7] Luo ZH, Zhou YQ, He H, et al. Synergistic effect of combined mirror therapy on upper extremity in patients with stroke: a systematic review and meta-analysis. Front Neurol. 2020;11:155. doi: 10.3389/fneur.2020.00155.

[8] Saavedra-García A, Moral-Munoz JA, Lucena-Anton D. Mirror therapy simultaneously combined with electrical stimulation for upper limb motor function recovery after stroke: a systematic review and meta-analysis of randomized controlled trials. Clin Rehabil. 2021;35(1):39–50. doi: 10.1177/0269215520951935.

[9] Schick T, Schlake HP, Kallusky J, et al. Synergy effects of combined multichannel EMG-triggered electrical stimulation and mirror therapy in subacute stroke patients with severe or very severe arm/hand paresis. Restor Neurol Neurosci. 2017;35(3):319–332. doi: 10.3233/RNN-160710.

[10] Kim HJ, Lee GC, Song CH. Effect of functional electrical stimulation with mirror therapy on upper extremity motor function in poststroke patients. J Stroke Cerebrovasc Dis. 2014;23(4):655–661. doi: 10.1016/j.jstrokecerebrovas-dis.2013.06.017.

[11] Lin KC, Huang PC, Chen YT, et al. Combining afferent stimulation and mirror therapy for rehabilitating motor function, motor control, ambulation, and daily functions after stroke. Neurorehabil Neural Repair. 2014;28(2):153–162. doi: 10.1177/1545968313508468.

[12] Lee YY, Lin KC, Wu CY, et al. Combining afferent stimulation and mirror therapy for improving muscular, sensorimotor, and daily functions after chronic stroke: a randomized, Placebo-Controlled study. Am J Phys Med Rehabil. 2015;94 (10 Suppl 1):859–868. doi: 10.1097/PHM.0000000000000271.

[13] Kim JH, Lee BH. Mirror therapy combined with biofeedback functional electrical stimulation for motor recovery of upper extremities after stroke: a pilot randomized controlled trial. Occup Ther Int. 2015;22(2):51–60. doi: 10.1002/oti.1384.

[14] Mathieson S, Parsons J, Kaplan M, et al. Combining functional electrical stimulation and mirror therapy for upper limb motor recovery following stroke: a randomised trial. Eur J Physiother. 2018;20(4):244–249. doi: 10.1080/21679169.2018.1472635.

[15] Nagapattinam S, Babu VK, Kumar SN, et al. Effect of task specific mirror therapy with functional electrical stimulation on upper limb function for subacute hemiplegia. Int J Physiother. 2015;2(5):840–849.

[16] Lin KC, Chen YT, Huang PC, et al. Effect of mirror therapy combined with somatosensory stimulation on motor recovery and daily function in stroke patients: a pilot study. J Formos Med Assoc. 2014;113(7):422–428. doi: 10.1016/j.jfma.2012.08.008.

[17] Feng Q, Xu HY, Zhou YB, et al. Application of transcutaneous electrical acupoint stimulation combined with mirror therapy in rehabilitation nursing of patients with upper limb spasticity after stroke. Chin Nurs Res. 2021;35(16):2879–2883.

[18] Page MJ, McKenzie JE, Bossuyt PM, et al. The prisma 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71.

[19] Rauch A, Cieza A, Stucki G. How to apply the international classification of functioning, disability and health (ICF) for rehabilitation management in clinical practice. Eur J Phys Rehabil Med. 2008;44(3):329–342.

[20] Santisteban L, Térémetz M, Bleton JP, et al. Upper limb outcome measures used in stroke rehabilitation studies: a systematic literature review. PLoS One. 2016;11(5):e0154792. doi: 10.1371/journal.pone.0154792.

[21] Hernández ED, Galeano CP, Barbosa NE, et al. Intra- and inter-rater reliability of Fugl-Meyer assessment of upper extremity in stroke. J Rehabil Med. 2019;51(9):652–659. doi: 10.2340/16501977-2590.

[22] Yozbatiran N, Der-Yeghiaian L, Cramer SC. A standardized approach to performing the action research arm test. Neurorehabil Neural Repair. 2008;22(1):78–90. doi: 10.1177/1545968307305353.

[23] Uswatte G, Taub E, Morris D, et al. Reliability and validity of the upper-extremity motor activity log-14 for measuring real-world arm use. Stroke. 2005;36(11):2493–2496. doi: 10.1161/01.STR.0000185928.90848.2e.

[24] Higgins JPT, Green A. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration; 2011. Version 5.1.0 [updated March 2011] www. cochrane-handbook. org.

[25] Yang Y, Zhao Q, Zhang Y, et al. Effect of mirror therapy on recovery of stroke survivors: a systematic review and network meta-analysis. Neuroscience. 2018;390:318–336. doi: 10.1016/j.neuroscience.2018.06.044.

[26] Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. doi: 10.1136/bmj.l4898.

[27] Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011;64(4):383–394. doi: 10.1016/j.jclinepi.2010.04.026.

[28] Monte-Silva K, Piscitelli D, Norouzi-Gheidari N, et al. Electromyogram-related neuromuscular electrical stimulation for restoring wrist and hand movement in poststroke hemiplegia: a systematic review and meta-analysis. Neurorehabil Neural Repair. 2019;33(2):96–111. doi: 10.1177/1545968319826053.

[29] Drevon D, Fursa SR, Malcolm AL. Intercoder reliability and validity of WebPlotDigitizer in extracting graphed data. Behav Modif. 2017;41(2):323–339. doi: 10.1177/0145445516673998.

[30] Liu TW, Ng GYF, Chung RCK, et al. Cognitive behavioural therapy for fear of falling and balance among older people: a systematic review and meta-analysis. Age Ageing. 2018;47(4):520–527. doi: 10.1093/ageing/afy010.

[31] Goff AJ, De Oliveira Silva D, Merolli M, et al. Patient education improves pain and function in people with knee osteoarthritis with better effects when combined with exercise therapy: a systematic review. J Physiother. 2021;67(3):177–189. doi: 10.1016/j.jphys.2021.06.011.

[32] Yang F, Butler AJ. Efficacy of controlled whole-body vibration training on improving fall risk factors in stroke survivors: a meta-analysis. Neurorehabil Neural Repair. 2020;34(4):275–288. doi: 10.1177/1545968320907073.

[33] Mathieson S, Parsons J, Kaplan MS. Combining functional electrical stimulation with mirror therapy for the upper limb in people with stroke. Crit Rev Phys Rehabil Med. 2014;26(1-2):113–129. doi: 10.1615/CritRevPhysRehabilMed.2014010534.

[34] Yun GJ, Chun MH, Park JY, et al. The synergic effects of mirror therapy and neuromuscular electrical stimulation for hand function in stroke patients. Ann Rehabil Med. 2011;35(3):316–321. doi: 10.5535/arm.2011.35.3.316.

[35] Yao SZ, Gou LJ, Liu XD, et al. Clinical observation of mirror image therapy combined with electromyographic biofeedback therapy in promoting upper limb functional reconstruction of stroke patients with hemiplegia. Chin J Phys Med Rehabil. 2016;38(10):746–749.

[36] Wang LJ, Chen LZ, Ou Y, et al. Effects of mirror visual feedback and electromyographic biofeedback on upper extremity function in hemiplegics after stroke. Chin J Rehabil Theory Pract. 2015;21(2):202–205.

[37] Xu S, Li WT, Ji PP. Effect of mirror therapy combined with power-assisted electric stimulation on upper extremity motor function and activities of daily living in patients with early stroke. Pract J Card Cereb Pneumal Vascular Dis. 2020;28(8):89–93.

[38] Zhou YF, Chen QZ, Hu SH, et al. Effect of mirror feedback therapy of contralaterally controlled functional electrical stimulation on hand function of apoplectic hemiplegic patients. Rehabil Med. 2021;31(1):63–68.

[39] Lu Z. Effect of mirror image therapy combined with contralateral controlled functional electrical stimulation on early upper limb function of stroke patients with hemiplegia. J Nurs Rehabil. 2018;17(10):60–62.

[40] Chen J, Wu JS, Gu MX, et al. Effects of mirror therapy combined with electromyographic biofeedback on hand function in patients with stroke. J Neurosci Ment Health. 2015;15(6):602–604.

[41] Hobart JC, Lamping DL, Freeman JA, et al. Evidence-based measurement: which disability scale for neurologic rehabilitation? Neurology. 2001;57(4):639–644. doi: 10.1212/wnl.57.4.639.

[42] Arya KN, Verma R, Garg RK. Estimating the minimal clinically important difference of an upper extremity recovery measure in subacute stroke patients. Top Stroke Rehabil. 2011;18 Suppl 1(sup1):599–610. doi: 10.1310/tsr18s01-599.

[43] Ghaziani E, Couppé C, Siersma V, et al. Electrical somatosensory stimulation in early rehabilitation of arm paresis after stroke: a randomized controlled trial. Neurorehabil Neural Repair. 2018;32(10):899–912. doi: 10.1177/1545968318799496.

[44] Lundquist CB, Maribo T. The Fugl-Meyer assessment of the upper extremity: reliability, responsiveness, and validity of the Danish version. Disabil Rehabil. 2017;39(9):934–939. doi: 10.3109/09638288.2016.1163422.

[45] Michielsen ME, Selles RW, van der Geest JN, et al. Motor recovery and cortical reorganization after mirror therapy in chronic stroke patients: a phase II randomized controlled trial. Neurorehabil Neural Repair. 2011;25(3):223–233. doi: 10.1177/1545968310385127.

[46] Novaes MM, Palhano-Fontes F, Peres A, et al. Neurofunctional changes after a single mirror therapy intervention in chronic ischemic stroke. Int J Neurosci. 2018;128(10):966–974. doi:10.1080/00207454.2018.1447571.

[47] Wei WJ, Bai LJ, Wang J, et al. A longitudinal study of hand motor recovery after Sub-acute stroke: a study combined FMRI with diffusion tensor imaging. PLoS One. 2013;8(5):e64154. doi: 10.1371/journal.pone.0064154.

[48] Wolpert DM, Diedrichsen J, Flanagan JR. Principles of sensorimotor learning. Nat Rev Neurosci. 2011;12(12):739–751. doi: 10.1038/nrn3112.

[49] Foltys H, Krings T, Meister IG, et al. Motor representation in patients rapidly recovering after stroke: a functional magnetic resonance imaging and transcranial magnetic stimulation study. Clin Neurophysiol. 2003;114(12):2404–2415. doi: 10.1016/s1388-2457(03)00263-3.

[50] Asanuma H, Keller A. Neuronal mechanisms of motor learning in mammals. Neuroreport. 1991;2(5):217–224. doi:10.1097/00001756-199105000-00001.

[51] Bolognini N, Russo C, Edwards DJ. The sensory side of post-stroke motor rehabilitation. Restor Neurol Neurosci.2016;34(4):571–586. doi: 10.3233/RNN-150606.

[52] Fromm C, Wise SP, Evarts EV. Sensory response properties of pyramidal tract neurons in the precentral motor cortex and postcentral gyrus of the rhesus monkey. Exp Brain Res. 1984;54(1):177–185. doi: 10.1007/BF00235829.

[53] Nelles G, Spiekermann G, Jueptner M, et al. Reorganization of sensory and motor systems in hemiplegic stroke patients. A positron emission tomography study. Stroke.1999;30(8):1510–1516. doi: 10.1161/01.str.30.8.1510.

[54] Kwon HG, Jang SH, Lee MY. Effects of visual information regarding tactile stimulation on the somatosensory cortical activation: a functional MRI study. Neural Regen Res. 2017;12(7):1119–1123. doi: 10.4103/1673-5374.211191.

[55] Doyle S, Bennett S, Fasoli SE, et al. Interventions for sensory impairment in the upper limb after stroke. Cochrane Database Syst Rev. 2010;2010(6):CD006331.

[56] Demetrios M, Khan F, Turner-Stokes L, et al. Multidisciplinary rehabilitation following botulinum toxin and other focal intramuscular treatment for post-stroke spasticity. Cochrane Database Syst Rev. 2013;5(6):CD009689.

[57] Urban PP, Wolf T, Uebele M, et al. Occurence and clinical predictors of spasticity after ischemic stroke. Stroke. 2010;41(9):2016–2020. doi: 10.1161/STROKEAHA.110.581991.

[58] Wissel J, Manack A, Brainin M. Toward an epidemiology of poststroke spasticity. Neurology. 2013;80(3 Suppl 2):S13–S19. doi: 10.1212/WNL.0b013e3182762448.

[59] Leng Y, Lo WLA, Hu C, et al. The effects of extracorporeal shock wave therapy on spastic muscle of the wrist joint in stroke survivors: evidence from neuromechanical analysis. Front Neurosci. 2020;14:580762. doi: 10.3389/fnins.2020.580762.

[60] Veverka T, Hok P, Otruba P, et al. Botulinum toxin modulates posterior parietal cortex activation in post-stroke spasticity of the upper limb. Front Neurol. 2019;10:495. doi: 10.3389/fneur.2019.00495.

[61] Bolognini N, Russo C, Vallar G. Crossmodal illusions in neurorehabilitation. Front Behav Neurosci. 2015;9:212. doi:10.3389/fnbeh.2015.00212.

[62] Iacoboni M, Woods RP, Brass M, et al. Cortical mechanisms of human imitation. Science. 1999;286(5449):2526–2528. doi: 10.1126/science.286.5449.2526.

[63] Rizzolatti G, Fogassi L, Gallese V. Neurophysiological mechanisms underlying the understanding and imitation of action. Nat Rev Neurosci. 2001;2(9):661–670. doi: 10.1038/35090060.

[64] Pineda JA. Sensorimotor cortex as a critical component of an ‘extended’ mirror neuron system: does it solve the development, correspondence, and control problems in mirroring? Behav Brain Funct. 2008;4(1):47. doi: 10.1186/1744-9081-4-47.

[65] Zhang JJQ, Fong KNK, Welage N, et al. The activation of the mirror neuron system during action observation and action execution with mirror visual feedback in stroke: a systematic review. Neural Plast. 2018;2018:2321045. doi: 10.1155/2018/2321045.

[66] Fugl-Meyer AR, Jääskö L, Leyman I, et al. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. JRM. 1975;7(1):13–31. doi: 10.2340/1650197771331.

[67] Wu CW, van Gelderen P, Hanakawa T, et al. Enduring representational plasticity after somatosensory stimulation. Neuroimage. 2005; 27(4):872–884. doi: 10.1016/j.neuroimage.2005.05.055.

[68] Iftime-Nielsen SD, Christensen MS, Vingborg RJ, et al. Interaction of electrical stimulation and voluntary hand movement in SII and the cerebellum during simulated therapeutic functional electrical stimulation in healthy adults. Hum Brain Mapp. 2012;33(1):40–49. doi: 10.1002/hbm.21191..

[69] Mahmood A, Veluswamy SK, Hombali A, et al. Effect of transcutaneous electrical nerve stimulation on spasticity in adults with stroke: a systematic review and meta-analysis. Arch Phys Med Rehabil. 2019;100(4):751–768. doi: 10.1016/j.apmr.2018.10.016.

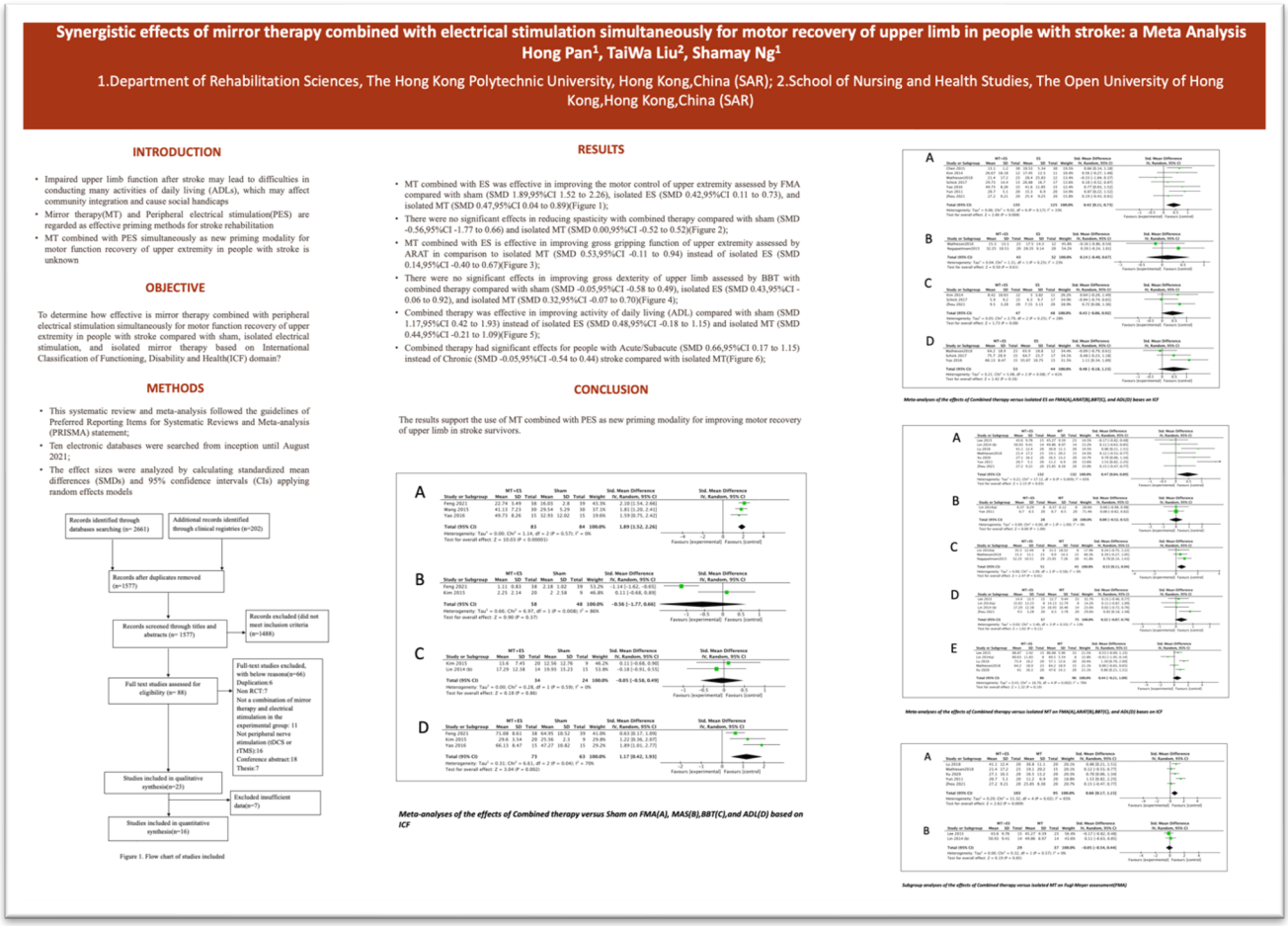
[70] Bakheit AM, Maynard VA, Curnow J, et al. The relation between ashworth scale scores and the excitability of the alpha motor neurones in patients with post-stroke muscle spasticity. J Neurol Neurosurg Psychiatry. 2003;74(5):646–648. doi: 10.1136/jnnp.74.5.646.

[71] Rosewilliam S, Malhotra S, Roffe C, et al. Can surface neuromuscular electrical stimulation of the wrist and hand combined with routine therapy facilitate recovery of arm function in patients with stroke? Arch Phys Med Rehabil. 2012;93(10):1715–1721. e1. doi: 10.1016/j.apmr.2012.05.017.

[72] Boccuni L, Meyer S, Kessner SS, et al. Is there full or proportional somatosensory recovery in the upper limb after stroke? Investigating behavioral outcome and neural correlates. Neurorehabil Neural Repair. 2018;32(8):691–700. doi:10.1177/1545968318787060.

[73] Hakon J, Quattromani MJ, Sjölund C, et al. Multisensory stimulation improves functional recovery and resting-state functional connectivity in the mouse brain after stroke. Neuroimage Clin. 2018;17:717–730. doi: 10.1016/j.nicl.2017.11.022.

Appendix 3.2 The poster of "Synergistic effects of mirror therapy combined with electrical stimulation for motor recovery of upper limb in people with stroke: a meta-analysis" demonstrated in 12th Pan-Pacific Conference on Rehabilitation.



Synergistic effects of mirror therapy combined with electrical stimulation simultaneously for motor recovery of upper limb in people with stroke: a Meta Analysis

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INTRODUCTION

- Impaired upper limb function after stroke may lead to difficulties in conducting many activities of daily living (ADLs), which may affect community integration and cause social handicaps
- Mirror therapy(MT) and Peripheral electrical stimulation(PES) are regarded as effective priming methods for stroke rehabilitation
- MT combined with PES simultaneously as new priming modality for motor function recovery of upper extremity in people with stroke is unknown

OBJECTIVE

To determine how effective is mirror therapy combined with peripheral electrical stimulation simultaneously for motor function recovery of upper extremity in people with stroke compared with sham, isolated electrical stimulation, and isolated mirror therapy based on International Classification of Functioning, Disability and Health(ICF) domain?

METHODS

- This systematic review and meta-analysis followed the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement;
- Ten electronic databases were searched from inception until August 2021;
- The effect sizes were analyzed by calculating standardized mean differences (SMDs) and 95% confidence intervals (CIs) applying random effects models

Figure 1. Flow chart of studies included

RESULTS

- MT combined with ES was effective in improving the motor control of upper extremity assessed by FMA compared with sham (SMD 1.89,95%CI 1.52 to 2.26), isolated ES (SMD 0.42,95%CI 0.11 to 0.73), and isolated MT (SMD 0.47,95%CI 0.04 to 0.89)(Figure 1);
- There were no significant effects in reducing spasticity with combined therapy compared with sham (SMD -0.56,95%CI -1.77 to 0.66) and isolated MT (SMD 0.00,95%CI -0.52 to 0.52)(Figure 2);
- MT combined with ES is effective in improving gross gripping function of upper extremity assessed by ARAT in comparison to isolated MT (SMD 0.53,95%CI -0.11 to 0.94) instead of isolated ES (SMD 0.14,95%CI -0.40 to 0.67)(Figure 3);
- There were no significant effects in improving gross dexterity of upper limb assessed by BBT with combined therapy compared with sham (SMD -0.05,95%CI -0.58 to 0.49), isolated ES (SMD 0.43,95%CI -0.06 to 0.92), and isolated MT (SMD 0.32,95%CI -0.07 to 0.70)(Figure 4);
- Combined therapy was effective in improving activity of daily living (ADL) compared with sham (SMD 1.17,95%CI 0.42 to 1.93) instead of isolated ES (SMD 0.48,95%CI -0.18 to 1.15) and isolated MT (SMD 0.44,95%CI -0.21 to 1.09)(Figure 5);
- Combined therapy had significant effects for people with Acute/Subacute (SMD 0.66,95%CI 0.17 to 1.15) instead of Chronic (SMD -0.05,95%CI -0.54 to 0.44) stroke compared with isolated MT(Figure 6);

CONCLUSION

The results support the use of MT combined with PES as new priming modality for improving motor recovery of upper limb in stroke survivors.

Meta-analyses of the effects of Combined therapy versus Sham on FMA(A), MAS(B),BBT(C),and ADL(D) based on ICF

Meta-analyses of the effects of Combined therapy versus Isolated ES on FMA(A),ARAT(B),BBT(C), and ADL(D) bases on ICF

Meta-analyses of the effects of Combined therapy versus Isolated MT on FMA(A),ARAT(B),BBT(C), and ADL(D) bases on ICF

Subgroup analyses of the effects of Combined therapy versus Isolated MT on Fugl-Meyer assessment(FMA)

Appendix 3.3 The headings and keywords used for literature searching

Search strategies
1."Stroke"[Mesh]
2. (((((Strokes [Title/Abstract]) OR (Cerebrovascular Accident [Title/Abstract])) OR (Cerebrovascular Apoplexy [Title/Abstract])) OR (Apoplexy, Cerebrovascular [Title/Abstract])) OR (Brain Vascular Accident [Title/Abstract])) OR (Apoplexy [Title/Abstract])
3.1 OR 2
4. "Cerebrovascular Disorders"[Mesh]
5. (((((Intracranial Vascular Disease [Title/Abstract]) OR (Intracranial Vascular Disorder [Title/Abstract])) OR (Cerebrovascular Disease [Title/Abstract])) OR (Brain Vascular Disorder [Title/Abstract])) OR (Cerebrovascular Occlusion [Title/Abstract])) OR (Cerebrovascular Insufficiency [Title/Abstract])
6. 4 OR 5
7. "Brain Ischemia"[Mesh]
8. ((Ischemic Encephalopathy [Title/Abstract]) OR (Cerebral Ischemia [Title/Abstract])) OR (Ischemia, Cerebral [Title/Abstract])
9.7 OR 8
10. "Cerebral Infarction"[Mesh]
11. ((((Cerebral Infarct [Title/Abstract]) OR (Infarct, Cerebral [Title/Abstract])) OR (Cerebral Infarction, Left Hemisphere [Title/Abstract])) OR (Subcortical Infarction [Title/Abstract])) OR (Posterior Choroidal Artery Infarction [Title/Abstract])
12.10 OR 11
13. "Intracranial Thrombosis"[Mesh]
14. ((Intracranial Thromboses [Title/Abstract]) OR (Cerebral Thrombus [Title/Abstract])) OR (Brain Thrombosis [Title/Abstract])

15.13 OR 14

16."Intracranial Embolism"[Mesh]

17. (Brain Embolism [Title/Abstract]) OR (Cerebral Embolism [Title/Abstract])

18.16 OR 17

19. "Cerebral Hemorrhage"[Mesh]

20. (((Cerebrum Hemorrhage [Title/Abstract]) OR (Cerebral Parenchymal Hemorrhage [Title/Abstract])) OR (Intracerebral Hemorrhage [Title/Abstract])) OR (Brain Hemorrhage, Cerebral [Title/Abstract])

21.19 OR 20

22. "Hemiplegia"[Mesh]

23. ((Monoplegia [Title/Abstract]) OR (Post-Ictal Hemiplegia [Title/Abstract])) OR (Crossed Hemiplegia [Title/Abstract])

24.22 OR 23

25.3 OR 6 OR 9 OR 12 OR 15 OR 18 OR 21 OR 24

26. ((electrotherapy [Title/Abstract]) OR (Electrical stimulation [Title/Abstract])) OR (stimulation, Electrical [Title/Abstract])

27. ((((((((((Mirror therapy[Title/Abstract]) OR (Mirror visual feedback[Title/Abstract])) OR (MVF[Title/Abstract])) OR (Mirror box[Title/Abstract])) OR (Mirror reflection[Title/Abstract])) OR (Mirror Neuron[Title/Abstract])) OR (Visual feedback[Title/Abstract])) OR (Mirror training[Title/Abstract])) OR (MT[Title/Abstract])) OR (Mirror[Title/Abstract])) OR (Mirror illusion[Title/Abstract])) OR (Mirror movement[Title/Abstract])

28. ((randomized controlled trial [Publication Type]) OR (randomized [Title/Abstract])) OR (placebo [Title/Abstract])

29. 25 AND 26 AND 27 AND 28

Appendix 4.1 Chapter 4 published on Disability and Rehabilitation (Final manuscript)

Self-perceived upper extremity motor function predicts health-related quality of life in chronic stroke survivors

Background

Stroke is characterised as a neurological deficit and is a leading cause of death and disability globally [1,2]. Stroke exerts various long-term adverse effects on mental, physical, and social aspects, affecting an individual's ability to participate in diverse life activities [3,4]. Health related quality of life (HRQOL) is defined as individuals' self-perceived well-being concerning the impact of health on their physical, mental, social, and cognitive functioning in various life domains [4,5]. HRQOL has been demonstrated to be a valid and crucial measure for evaluating the quality of life (QOL) and overall health status of patients with stroke [4,6]. After a stroke, both the HRQOL and well-being are substantially impaired [3]. Thus, to improve the overall health status of stroke survivors in various life domains, clinicians should identify the major determinants of HRQOL in these individuals.

The Stroke Impact Scale (SIS) is a comprehensive, stroke-specific, self-reported questionnaire widely used to evaluate disability and HRQOL in mild-to-moderate acute [7], subacute [8], and chronic [9] stroke survivors. Compared with other self-reported questionnaires used to assess QOL, including the 36-Item Short-Form Survey [10], the SIS covers more life domains, such as cognitive functioning, which is essential for the execution of daily life activities. Moreover, a study [11] demonstrated that SIS scores had good-to-excellent test–retest reliability, with intraclass correlation coefficients (ICCs) ranging from 0.79 to 0.93 in Chinese patients with

chronic stroke. The SIS scores have been reported to be significantly correlated with the Fugl–Meyer Assessment for Upper Extremity (FMA-UE) and Lower Extremity (FMA-LE; $r = 0.64$) [3], Berg Balance Scale ($r = 0.649$) [3], Functional Independence Measure ($r = 0.647$) [3], and Barthel Activities of Daily Living Index ($r = 0.82$) [8] scores in people with stroke.

Age [12], sex [12], side of hemiplegia [12], depression [12], anxiety [13], cognitive function [3], duration after onsets [14], stroke severity [15], upper and lower extremity functional status [3] have been identified as significant predictors of HRQOL outcomes in stroke survivors. Among those predictors, upper extremity (UE) motor function plays a critical role in the execution of daily life activities and contributes to manual dexterity for task specificity [12], thus enhancing leisure activities, social participation, and HRQOL [13]. UE motor functions can be evaluated using both observation-based and self-perceived outcome measures. Compared with observation-based outcome measures, self-report measures of UE function may provide additional insights because they reflect the stroke survivors' subjective views of current level of UE function [16], which could reflect their self-perceived efficacy and the areas of UE functions they want to improve. It enables clinicians to design and prescribe personalised rehabilitation interventions for people with stroke [16] with impaired UE functions. Moreover, the level of self-perceived UE function may not correspond to the observation-based UE function. For example, in a study conducted by Essers et al. [17], 18% and 23% of stroke survivors with high-level observed UE function (as measured using the FMA-UE) were found to have a low level of self-perceived motor function at 6- and 12-months post-stroke, respectively.

The UE Functional Index (UEFI) is initially used to evaluate the self-perceived difficulty in the performance of UE motor function in people with musculoskeletal disorders [18,19]. The

original 15-item English version of the UEFI was culturally adapted into Chinese (UEFI-C) and psychometrically tested using a cohort of community-dwelling people with stroke [20]. The UEFI-C demonstrated good test–retest reliability ($ICC_{3,1}$ = 0.872) and excellent internal consistency (Cronbach's α = 0.922) in Chinese patients with chronic stroke [20]. In addition, the UEFI-C had fair to good correlations with various stroke-specific impairment measures, including the FMA-UE (*r* = 0.423), Wolf Motor Function Test (WMFT) (*r* = 0.42), six-minute walk test (*r* = 0.519), Motor Activity Log (MAL) amount of use (*r* = 0.536), MAL quality of movement (*r* = 0.519), Activities-Specific Balance Confidence Scale (*r* = 0.633), and SIS (*r* = 0.217–0.759, except the memory subscale) scores in patients with chronic stroke [20].

The findings of the aforementioned studies indicate that (i) objective UE function plays a crucial predictive role in post-stroke HRQOL and (ii) self-perceived UE function majorly contributes to the ability to live independently and is separate from the role of objective UE function during stroke rehabilitation. Thus, this study investigated the relationships among HRQOL (as determined using the SIS), the objective motor impairments of the UE (as evaluated by paretic hand grip strength, FMA-UE, and WMFT scores); and the self-perceived UEFI scores. In addition, this study determined whether the UEFI score independently contributes to the SIS score and quantified its relative contribution to SIS scores in patients with chronic stroke.

Previous study [21] demonstrated the practices of bilateral movements simultaneously may result in a facilitation effect from the non-paretic side to the paretic side with a coordination unit in the brain, motor overflow and skill from one arm to another arm. Hence, those neurophysiological linkages demonstrate that bilateral UE training simultaneously may benefit motor learning and behaviour. There are many existing outcome measures evaluating UE motor

functions. However, they mainly assess UE motor functions unilaterally. For example, the MAL, in which the items focus on assessing the self-perceived UE motor functions on tasks of daily living only using the paretic arm. However, the UEFI mainly assesses the self-perceived UE motor functions on activities of daily living bilaterally, which reflects the amount of use of paretic upper extremity pragmatically. Hence, the UEFI is used to measure the self-perceived bilateral UE motor functions in this study.

Materials and methods

Participants

The assessment venue of this trial was a university-based rehabilitation centre. Community-dwelling chronic stroke survivors were recruited from local self-help groups or a community rehabilitation network through poster advertisements. Stroke survivors were included in the study if they (1) were aged between 50 and 80 years; (2) had experienced a single stroke, confirmed through magnetic resonance imaging or computed tomography, at least 1 year before the start of the study; (3) scored ≥ 7 on the Chinese version of the Abbreviated Mental Test [22]; (4) could speak Cantonese; (5) could initiate at least minimal anti-gravity movement in the shoulder of their paretic arm; and (6) could independently walk for at least 10 m with or without an assistive device. Stroke survivors were excluded if they (1) had any unstable medical conditions (e.g., angina pectoris) or other conditions that might impede the assessment process (e.g., dementia) and (2) had any aphasia or hearing impairment that might affect the data collection procedure.

We estimated the required sample size using linear regression model [23]. This linear regression model included four predictors (independent variables) with an effect size(d) of 0.6 corresponds approximately to an effect size (f) of 0.4 and a power of 0.8. Hence, a sample size of 85 was needed for this study. Considering a dropout rate of 10%, at least 95 participants were need for this study.

The study protocol was approved by the Departmental Research Committee of the Hong Kong Polytechnic University (approval number: HSEAR20210110002) and conducted in accordance with the Declaration of Helsinki (1975 and its revision in 1983) for human experimentation. All participants provided written informed consent to participate in this study.

Sociodemographic data

Three types of sociodemographic data were collected: (1) demographic data, including age, sex, body mass index (BMI), and living arrangements; (2) stroke-related variables, including years since stroke onset, cause of stroke, and hemiplegic side; and (3) mobility-related variables, including the use of walking aids.

Outcome measures

Paretic maximal grip strength

The maximal grip strength, a measure used to quantify extremity weakness and recovery in community-dwelling older adults and people with stroke [24,25], was evaluated using a JAMAR dynamometer (Sammons Preston Rolyan, Bolingbrook, IL, USA). The assessment

was conducted using the standardised position and instructions recommended by the American Society of Hand Therapists [25]. During the test, the participants were instructed to squeeze the dynamometer as hard as possible for 5 s in each of three trials, with a 60-s rest interval between consecutive trials [26]. The mean paretic hand grip strength from the three trials was calculated for data analysis. The maximal grip strength assessment has previously demonstrated excellent test–retest reliability (ICC = 0.91) for the paretic hand in chronic stroke survivors [27].

FMA-UE

The FMA-UE is used to evaluate UE motor control as an outcome measure of proximal to distal and synergistic to isolated movement behaviour in patients with stroke [28]. The assessment includes four subsections: (1) shoulder-arm, (2) wrist, (3) hand, and (4) coordination and speed [29]. Each item is scored on a 3-point scale ranging from 0 to 2, with the maximum total score being 66 [29]. A higher score indicates better motor control and a lower level of motor impairment [29]. The FMA-UE has demonstrated excellent inter-rater reliability (ICC = 0.97) and intra-rater reliability (ICC = 0.995–0.996) in chronic stroke survivors [29,30].

WMFT

The WMFT is used to evaluate the motor ability of patients with stroke who have moderate-to-severe UE motor deficits [31]. The WMFT yields three scores: a time score, which quantifies the speed of performance in seconds, a functional ability score, and a grip strength score [31]. Only the functional ability score was used for data analysis in this study. The functional ability

score is evaluated using a 6-point ordinal scale for 15 items, with a score of 0 indicating no attempt to use the paretic UE and a score of 5 indicating normal movement of the paretic UE [31]. The WMFT functional ability score has demonstrated excellent inter-rater reliability ($ICC_{3,1}$ = 0.97) [32], test–retest reliability ($ICC_{2,1}$ = 0.97) [33], and internal consistency (Cronbach's α = 0.92) [32] in patients with stroke.

UEFI

The Chinese version of the 15-item UEFI is used to evaluate the self-perceived difficulty in the performance of UE motor function of daily activity living in people with chronic stroke [20]. The items, which are rated on a 5-point adjectival response scale, assess the difficulty in performing UE activities, with scores of 4, 3, 2, 1, and 0 indicating no difficulty, a little bit of difficulty, moderate difficulty, quite a bit of difficulty, and extreme difficulty or inability to perform activity, respectively [20]. The total score of the UEFI-C ranges from 0 to 59, with a higher score indicating higher self-perceived UE activity functional recovery in patients with chronic stroke.

SIS

The SIS is a stroke-specific and self-reported outcome measure used to evaluate the subjective level of disability and HRQOL in patients with stroke [34]. The SIS assesses multidimensional stroke outcomes, including strength, hand function, ADLs/instrumental ADLs, mobility, communication, emotion, memory and thinking, participation, and stroke recovery [35]. For each domain, summative scores are calculated, ranging from 0 to 100, with a higher total score indicating a higher level of satisfactory functional recovery [36]. In this study, the total score

of SIS was calculated as the mean of the final scores of all of the domains (including stroke recovery) [37]. The SIS has demonstrated good test–retest reliability (ICC = 0.7–0.92), except for the emotion domain (ICC = 0.57), and excellent internal consistency (Cronbach's α = 0.90) in patients with stroke [34,38].

Statistical analysis

All data were analysed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk Test was used to assess data normality, and the significance level was set at α = 0.05 (two-tailed). For the multiple regression analysis, we calculated the Bonferroni-corrected threshold to decrease the risk of a type I error with five outcome measures tested on the same participants. The demographic data are summarised using descriptive statistics. The correlation between SIS scores and other outcome measures was examined using Pearson's and Spearman's correlation coefficients for normally and nonnormally distributed data, respectively. Partial correlation coefficients were calculated to examine the relationships between SIS scores and grip strength, FMA-UE, WMFT, and UEFI scores after adjustment for sociodemographic parameters (i.e., age, paretic side, and use of walking aids). Multiple linear regression with a forced entry method was used to determine the proportion of variability in HRQOL (as a dependent variable, SIS scores) explained by the independent variables (grip strength, FMA-UE, WMFT, and UEFI scores). This analysis was conducted to identify variables that exhibited the most predictive power for SIS scores (the largest standardised regression coefficients).

Results

Characteristics of the participants

The characteristics of the participants are listed in Table 1. This study included 53 (56%) men and 42 (44%) women with two types of strokes (ischemic stroke, n = 65; haemorrhagic stroke, n = 30). The mean age of the participants was 63.84 ± 6.4 years, and their average duration after stroke onset was 6.66 ± 4.35 years. Forty-five and 50 participants experienced left and right hemiplegia, respectively. The BMI was 25.24 ± 11.51 kg/m2. Furthermore, 85 (89%) participants lived with others, and 69 (73%) of them required a walking aid. The mean SIS score was 59.77 ± 17.58, indicating that the chronic stroke survivors perceived a moderate health impact on their everyday life [38,39]. The mean grip strength score for the paretic UE was 14.34 ± 8.24 kg, indicating that the participants experienced weakness in the isometric muscular strength of the hand and forearm in the chronic phase after stroke [40]. The mean FMA-UE, UEFI, and WMFT scores were 44.59 ± 18.12, 46.02 ± 11.22, and 51.68 ± 21.2, respectively, indicating a limited full UE capacity in the participants [41].

Relationships between SIS scores and other variables

The correlation between SIS scores and other variables is presented in Table 2. Age and the use of walking aids were positively correlated with SIS scores ($r = -0.276$, $p = 0.007$ and $r = -0.324$, $p = 0.001$, respectively). The scores of grip strength (paretic side), FMA-UE, WMFT (paretic side), and UEFI exhibited a significantly moderate to strong positive correlation with SIS scores ($r = 0.544$– 0.687, $p < 0.001$). The partial correlation between SIS scores and other variables is shown in Table 3. After the adjustment of the effects of sociodemographic parameters, such as age, paretic side, and use of walking aids, the scores of grip strength

(paretic side), FMA-UE, WMFT (paretic side), and UEFI still demonstrated a significantly fair to strong positive correlation with SIS scores ($r = 0.439–0.629$, $p < 0.001$).

A combined multiple linear regression model including use of walking aids, grip strength, FMA-UE, WMFT (paretic side), and UEFI scores predicted 60.3% (6, 81 = 23.06, $p < 0.001$) of the variance in SIS scores (Table 4). Among all of the independent variables, grip strength and self-perceived UE motor function (as assessed using the UEFI) were identified as significant predictors of HRQOL (as determined by the SIS) in the participants. Among the three significant independent predictors, the UEFI score was the best predictor of SIS scores in the participants, as indicated by the magnitude of the standardised regression coefficient ($\beta = 0.487$, $p < 0.001$; Table 4).

Discussion

This is the first study to investigate the contribution of self-perceived UE motor function to HRQOL in chronic stroke survivors. Our predictive model revealed that paretic maximal grip strength significantly contributed to HRQOL in the community-dwelling chronic stroke survivors. This finding aligns with that reported in the recent literature. Moreover, our model suggests that among various upper limb motor function assessments, the level of self-perceived UE motor function was the most significant predictor of HRQOL in the participants. Our findings enhance the current understanding of the importance of administering interventions aimed at improving self-perceived UE motor function to improve HRQOL in chronic stroke survivors.

HRQOL and other outcome measures

Our correlation analysis revealed that paretic maximal grip strength, FMA-UE, WMFT, and UEFI scores exhibited a significant moderate to strong positive correlation with SIS scores. Sociodemographic variables, namely age, paretic side, and use of walking aids, were significantly associated with SIS scores.

A decrease in grip strength is associated with a reduction in physical activity and energy expenditure and loss of independence in performing ADLs [25]. Thus, an improvement in paretic maximal grip strength would enhance upper limb performance and health-related status in ADLs. The FMA primarily assesses neural motor control, evaluating the proximal-to-distal and synergistic-to-isolated movements [31]. The WMFT evaluates the upper limb motor ability, which includes both upper limb strength and dexterity [31]. These components are essential for upper limb functional performance in ADLs and for achieving independent living [42]. Thus, improvements in upper limb motor control, dexterity, and coordination would enhance HRQOL. Among all of the independent variables, the UEFI had the strongest correlation with HRQOL. A possible explanation for this finding is that the UEFI assesses self-perceived difficulty in performing upper limb motor functions, effectively reflecting the ability and usage of the upper limb in ADLs from the patient's perspective [20]. This could indicate HRQOL in the upper limb activity domain of SIS scores with high accuracy.

In terms of sociodemographic variables, age and the use of walking aids exhibited a significant but fair negative correlation with SIS scores. Consistent with the findings of previous studies [43,44], old age may be associated with low physical functioning due to decreased tolerance to intense rehabilitation and slow functional recovery [13], potentially leading to the less frequent use of the UE in HRQOL. However, age alone may account for only a small amount of

variation in functional outcomes and HRQOL in chronic stroke survivors [43]. Thus, age alone was weakly correlated with functional recovery and HRQOL in these individuals. For upper extremity, a greater use of walking aids may lead to a decreased use of paretic side of upper extremity for activity tasks in daily life and the declines in sensorimotor functions, such as the motor control and joint proprioception [45,46]. For lower extremity, some studies [46–49] demonstrated that the regularly greater use of walking aids would reduce the balance and falls efficacy, reduce the hemiplegic muscle activity, and unload the hip joints. Hence, the use of walking aids might be negatively correlated with HRQOL in chronic stroke survivors. Consistent with the findings of a previous study [50], our study demonstrated that the paretic side had a weak relationship with HRQOL. Although the right or left paretic side may be correlated with body neglect, spatial disorientation, or communication problems, which may affect the HRQOL of patients with stroke, these problems may be associated with orientation, motor performance, and self-awareness. Thus, the paretic side was only fairly correlated with HRQOL.

Self-perceived UE motor function independently predicts HRQOL

The final model explained 60.3% of the variance in SIS scores. The results of multiple linear regression analysis revealed that self-perceived UE motor function (measured by UEFI scores) made the highest contribution to HRQOL (as determined by SIS scores) in the chronic stroke survivors, explaining 18.8% of the variance. Two possible reasons can explain the substantial contribution of the UEFI scores to SIS scores. First, the UEFI contains two categories of ADL assessments: basic and instrumental [51]. Basic ADLs involve skills required to manage one's basic physical needs, including grooming, dressing, transferring, ambulating, eating, and personal hygiene. Instrumental ADLs pertain to more complex abilities related to living

independently in society, which may include food preparation, housekeeping, laundry, and managing finances and modifications. After a stroke, engaging in basic and instrumental ADLs is crucial for regaining functional capabilities required to live independently within a home and community [52]. Moreover, the mobility, defined as an individual's capacity to move around effectively in the environment, is significantly correlated with gait, balance, or ambulatory capacity and includes some daily life tasks, such as transferring, sitting up, standing, and walking [53,54]. The regaining of mobility would be an important factor in being independent for daily life activities and social participation. The basic and instrumental ADLs of the UEFI involves in body transferring, maintaining balance, and walking with upper extremities daily life tasks of laundering clothes, preparing food, lifting a bag of groceries, and vacuuming. Thus, higher performance in basic and instrumental ADLs may lead to higher HRQOL and participation in chronic stroke survivors, which may explain the significant contribution of the UEFI scores to SIS scores. Hence, this finding suggests that it is essential for the assessment and prescription of basic and instrumental ADLs rehabilitation programs in order to improve the HRQOL of people with stroke.

The second possible reason for the significant contribution of the UEFI is its capability to assess self-perceived UE functional motor performance. This self-perceived assessment of post-stroke impairments, restrictions, and recovery is a prominent trend in stroke rehabilitation. It focuses on identifying patients' needs and preferences [55], aiming to engage them in clinical decision-making [56]. HRQOL is associated with the subjective assessment of an individual's well-being in terms of both physical and mental health and their correlation with health conditions and social support [57]. The UEFI includes the self-perceived assessments of basic and instrumental ADLs required to maintain independence and participation with a sense of fulfilment [58], which can effectively reflect and capture patients' perceptions of their HRQOL

[59]. Thus, the UEFI score can independently predict the SIS score. Approximately 90% of stroke survivors experience varying levels of UE paresis, including low grip strength [12]. This can impede their ability to use the UE to perform various daily life and self-care activities, such as manipulating, gripping, grasping, holding objects' surfaces, eating, and bathing [40, 60]. Thus, higher paretic grip strength may contribute to improved HRQOL in patients with stroke.

The objective outcome measures of UE motor control (FMA-UE) and motor function (WMFT) could not predict HRQOL in our chronic stroke survivors in the regression model. This finding appears to contradict the results of previous studies [3,61]. Two possible reasons can explain this nonsignificant relationship. First, both the FMA and WMFT assess only the motor control and function of the paretic UE. However, ADLs are often the execution of living tasks bimanually [12]. Some studies [40,62] have demonstrated that the nonparetic side of the UE was the best predictor of daily life activities in stroke survivors. Thus, evaluating only the paretic UE may not accurately predict HRQOL in chronic stroke survivors. Second, both the FMA and WMFT assess only the motor control of the UE and simple motor functions without any specific task skills training or bimanual practice, which are crucial for ADLs, respectively. Hence, this finding suggests that it is essential for assessing the self-perceived level of bilateral coordination of UE in order to improve the HRQOL of people with stroke. In addition, the use of UEFI can provide insights for clinicians to design personalised training for UE rehabilitation targeting on the performance of basic and instrumental ADLs of people with stroke, such as washing hair and using cell phones.

This study has several limitations that should be addressed. First, although multiple linear regression predicted 60.3% of the variance in SIS scores, approximately 39.7% of the variance remained unexplained by the regression model. Thus, future studies should consider including

other relevant factors, such as lower extremity mobility function and cognition, to better explain variations in HRQOL. Second, the causal relationship could not be identified due to the cross-sectional study design. Thus, controlled clinical trials should be conducted to determine whether improving self-perceived UE motor function can enhance HRQOL in chronic stroke survivors. Third, the participants in this study were active members of local self-help groups, which may limit the representativeness and generalisability of the findings. Thus, future studies should verify whether these findings can be applicable to a broader population of patients with stroke (e.g., those with subacute stroke). Fourth, the results indicate that UE daily life activities significantly contributed to HRQOL in chronic stroke survivors. However, whether basic or instrumental ADLs have a greater impact on HRQOL in these individuals remains unclear. Thus, future studies should quantify the significant contributions of basic and instrumental ADLs to HRQOL in chronic stroke survivors.

Conclusions

The key finding of this study is that self-perceived UE motor function is an independent predictor of HRQOL in chronic stroke survivors, accounting for 18.8% of the variance in SIS scores. The entire model explained 60.3% of the variance in SIS scores. This finding indicates that self-perceived basic and instrumental ADLs should be considered as crucial factors that can enhance HRQOL and participation among chronic stroke survivors.

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Ethics approval

The ethical approval was obtained from the Departmental Research Committee of the Hong Kong Polytechnic University (Approval number: HSEARS20210110002).

Author contributions

S.S.M.N. conceived the original idea and T.W.L. planned the experiments. H.P., S.S.L.L., C.S.K.L., C.C.C.C., R.C.K.C., C W.K.L., W.W.L.N., M.W.S.T., and E.H. carried out the experiments, performed the analytic calculations and S.S.M.N., T.W.L., and J.W. supervised the project. H.P. wrote the manuscript. All authors discussed the results and contributed to the final manuscript.

Disclosure statement

The authors declared no potential conflicts of interests regarding to the research, authorship, and publication of this article.

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References

[1] Campbell BCV, Khatri P. Stroke. Lancet. 2020;396(10244): 129–142. doi:10.1016/S0140-6736(20)31179-X.

[2] Hankey GJ. Stroke. Lancet. 2017;389(10069):641–654. doi:10.1016/S0140-6736(16)30962-X.

[3] Chen CM, Tsai CC, Chung CY, et al. Potential predictors for health-related quality of life in stroke patients undergoing inpatient rehabilitation. Health Qual Life Outcomes. 2015;13(1):118. doi:10.1186/s12955-015-0314-5.

[4] Ali A, Tabassum D, Baig SS, et al. Effect of exercise interventions on health-related quality of life after stroke and transient ischemic attack: a systematic review and meta-analysis. Stroke. 2021;52(7):2445–2455. doi:10.1161/STROKEAHA.120. 032979.

[5] Barclay-Goddard R, Lix LM, Tate R, et al. Health-related quality of life after stroke: does response shift occur in self-perceived physical function? Arch Phys Med Rehabil. 2011;92(11):1762–1769. doi:10.1016/j.apmr.2011.06.013.

[6] Hobart JC, Williams LS, Moran K, et al. Quality of life measurement after stroke: uses and abuses of the sf-36. Stroke. 2002;33(5):1348–1356. doi:10.1161/01.str.0000015030. 59594.b3.

[7] Duncan PW, Bode RK, Lai SM, et al. Rasch analysis of a new stroke-specific outcome scale: the stroke impact scale. Arch Phys Med Rehabil. 2003;84(7):950–963. doi:10.1016/ s0003-9993(03)00035-2.

[8] MacIsaac R, Ali M, Peters M, et al. Derivation and validation of a modified short form of the stroke impact scale. J Am Heart Assoc. 2016;5(5):e003108. doi:10.1161/JAHA.115.003108.

[9] Carod-Artal FJ, Ferreira Coral L, Stieven Trizotto D, et al. Self-and proxy-report agreement on the stroke impact scale. Stroke. 2009;40(10):3308–3314. doi:10.1161/STROKEAHA.109. 558031.

[10] Zhang Y, Qu B, Lun SS, et al. The 36-item short form health survey: reliability and validity in chinese medical students. Int J Med Sci. 2012;9(7):521–526. doi:10.7150/ijms.4503.

[11] Qi MH, Tao YQ, Wang LY, et al. Translation and psychometric evaluation of the stroke impact scale 3.0 for proxy in Chinese version. Journal of Clinical Rehabilitative Tissue Engineering. 2007;11(30):5920–5924. Doi:CNKI: SUN: XDKF.0.2007-30-018.

[12] Lieshout E, van de Port IG, Dijkhuizen RM, et al. Does upper limb strength play a prominent role in health-related quality of life in stroke patients discharged from inpatient rehabilitation? Top Stroke Rehabil. 2020;27(7):525–533. doi:10.1080/ 10749357.2020.1738662.

[13] Morris JH, van Wijck F, Joice S, et al. Predicting health related quality of life 6 months after stroke: the role of anxiety and upper limb dysfunction. Disabil Rehabil. 2013;35(4):291–299. doi:10.3109/09638288.2012.691942.

[14] Shinohara Y, OASIS Study Group. Factors affecting health-related quality of life assessed with the sf-36v2 health survey in outpatients with chronic-stage ischemic stroke in Japan–cross-sectional analysis of the oasis study. Cerebrovasc Dis. 2010;29(4):361–371. doi:10.1159/000281834.

[15] Jeong BO, Kang HJ, Bae KY, et al. Determinants of quality of life in the acute stage following stroke. Psychiatry Investig. 2012;9(2):127–133. doi:10.4306/pi.2012.9.2.127.

[16] Reeves M, Lisabeth L, Williams L, et al. Patient-reported outcome measures (proms) for acute stroke: rationale, methods and future directions. Stroke. 2018;49(6):1549–1556. doi:10.1161/STROKEAHA.117.018912.

[17] Essers B, Van Gils A, Lafosse C, et al. Evolution and prediction of mismatch between observed and perceived upper limb function after stroke: a prospective, longitudinal, observational cohort study. BMC Neurol. 2021;21(1):488. doi:10.1186/s12883-021-02493-1.

[18] Chesworth BM, Hamilton CB, Walton DM, et al. Reliability and validity of two versions of the upper extremity functional index. Physiother Can. 2014;66(3):243–253. doi:10.3138/ptc.2013-45.

[19] Hamilton CB, Chesworth BM. A rasch-validated version of the upper extremity functional index for interval-level measurement of upper extremity function. Phys Ther. 2013;93 (11):1507–1519. doi:10.2522/ptj.20130041.

[20] Pan H, Ng SSM, Liu TW, et al. Psychometric properties of the Chinese (cantonese) version of the upper extremity functional index in people with chronic stroke. Front Neurol. 2023;14:989403. doi:10.3389/fneur.2023.989403.

[21] Demartino AM, Rodrigues LC, Gomes RP, et al. Manual dexterity is associated with use of the paretic upper extremity in community-dwelling individuals with stroke. J Neurol Phys Ther. 2021;45(4):292–300. doi:10.1097/NPT. 0000000000000365.

[22] Hodkinson H. Evaluation of a mental test score for assessment of mental impairment in the elderly. Age Ageing. 1972;1(4):233–238. doi:10.1093/ageing/1.4.233.

[23] Guan TY, Alam MK, Rao MB. Sample size calculations in simple linear regression: a new approach. Entropy (Basel). 2013;25(4):611. doi:10.3390/e25040611.

[24] Bertrand AM, Fournier K, Wick Brasey MG, et al. Reliability of maximal grip strength measurements and grip strength recovery following a stroke. J Hand Ther. 2015;28(4):356–362; quiz 363. doi:10.1016/j.jht.2015.04.004.

[25] Abizanda P, Navarro JL, García-Tomás MI, et al. Validity and usefulness of hand-held dynamometry for measuring muscle strength in community-dwelling older persons. Arch Gerontol Geriatr. 2012;54(1):21–27. doi:10.1016/j.archger.2011.02.006.

[26] Innes E. Handgrip strength testing: a review of the literature. Aus Occup Therapy J. 1999;46(3):120–140. doi:10.1046/ j.1440-1630.1999.00182.x.

[27] Boissy P, Bourbonnais D, Carlotti MM, et al. Maximal grip force in chronic stroke subjects and its relationship to global upper extremity function. Clin Rehabil. 1999;13(4):354–362. doi:10.1191/026921599676433080.

[28] Fugl-Meyer AR, Jääskö L, Leyman I, et al. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. JRM. 1975;7(1):13–31. doi:10.1186/1743-0003-7-60.

[29] Gladstone DJ, Danells CJ, Black SE. The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties. Neurorehabil Neural Repair. 2002;16(3):232–240. doi:10.1177/154596802401105171.

[30] Duncan PW, Propst M, Nelson SG. Reliability of the fugl-meyer assessment of sensorimotor recovery following cerebrovascular accident. Phys Ther. 1983;63(10):1606–1610. doi:10.1093/ptj/63.10.1606.

[31] Edwards DF, Lang CE, Wagner JM, et al. An evaluation of the wolf motor function test in motor trials early after stroke. Arch Phys Med Rehabil. 2012;93(4):660–668. doi:10.1016/j.apmr.2011.10.005.

[32] Morris DM, Uswatte G, Crago JE, et al. The reliability of the wolf motor function test for assessing upper extremity function after stroke. Arch Phys Med Rehabil. 2001;82(6):750–755. doi:10.1053/apmr.2001.23183.

[33] Whitall J, Savin DN, Jr., Harris-Love M, et al. Psychometric properties of a modified wolf motor function test for people with mild and moderate upper-extremity hemiparesis. Arch Phys Med Rehabil. 2006;87(5):656–660. doi:10.1016/j.apmr. 2006.02.004.

[34] Vellone E, Savini S, Fida R, et al. Psychometric evaluation of the stroke impact scale 3.0. J Cardiovasc Nurs. 2015;30(3):229– 241. doi:10.1097/JCN.0000000000000145.

[35] Gjellesvik TI, Becker F, Tjønna AE, et al. Effects of high-intensity interval training after stroke (the hiit stroke study) on physical and cognitive function: a multicenter randomized con-

trolled trial. Arch Phys Med Rehabil. 2021;102(9):1683–1691. doi:10.1016/j.apmr.2021.05.008.

[36] Wang TC, Tsai AC, Wang JY, et al. Caregiver-mediated intervention can improve physical functional recovery of patients with chronic stroke: a randomized controlled trial. Neuro- rehabil Neural Repair. 2015;29(1):3–12. doi:10.1177/1545968314532030.

[37] Norouzi-Gheidari N, Hernandez A, Archambault PS, et al. Feasibility, safety, and efficacy of a virtual reality exergame system to supplement upper extremity rehabilitation post-stroke: a pilot randomized clinical trial and proof of principle. Int J Environ Res Public Health. 2019;17(1):113. doi:10.3390/ijerph17010113.

[38] Duncan PW, Wallace D, Lai SM, et al. The stroke impact scale version 2.0. Evaluation of reliability, validity, and sensitivity to change. Stroke. 1999;30(10):2131–2140. doi:10.1161/01.str. 30.10.2131.

[39] Guidetti S, Ytterberg C, Ekstam L, et al. Changes in the impact of stroke between 3 and 12 months post-stroke, assessed with the stroke impact scale. J Rehabil Med. 2014; 46(10):963–968. doi:10.2340/16501977-1865.

[40] Ademoyegun AB, Mbada CE, Sonuga OA, et al. Does grip strength of the less-affected side of ischemic stroke survivors influences performance of self-care activities? Bull Fac Phys Ther. 2022;27(1):1–11. doi:10.1186/s43161-022-00090-y.

[41] Hoonhorst MH, Nijland RH, van den Berg JS, et al. How do fugl-meyer arm motor scores relate to dexterity according to the action research arm test at 6 months poststroke? Arch Phys Med Rehabil. 2015;96(10):1845–1849. doi:10.1016/j.apmr. 2015.06.009.

[42] Lundquist CB, Maribo T. The fugl-meyer assessment of the upper extremity: reliability, responsiveness and validity of the Danish version. Disabil Rehabil. 2017;39(9):934–939. doi :10.3109/09638288.2016.1163422.

[43] Bagg S, Pombo AP, Hopman W. Effect of age on functional outcomes after stroke rehabilitation. Stroke. 2002;33(1):179–185. doi:10.1161/hs0102.101224.

[44] Sturm JW, Donnan GA, Dewey HM, et al. Quality of life after stroke: the North East melbourne stroke incidence study (nemesis). Stroke. 2004;35(10):2340–2345. doi:10.1161/01.STR. 0000141977.18520.3b.

[45] Maguire CC, Sieben JM, Lutz N, et al. Replacing canes with an elasticated orthotic-garment in chronic stroke patients - The influence on gait and balance. A series of N-of-1 trials. J Bodyw Mov Ther. 2020;24(4):203–214. doi:10.1016/j.jbmt. 2020.06.006.

[46] Son SM, Kwon JW, Nam SH, et al. Adverse effects of motor-related symptoms on the ipsilateral upper limb according to long-term cane usage. NeuroRehabilitation. 2012;31(2):137–141. doi:10.3233/NRE-2012-0782.

[47] Ajemian S, Thon D, Clare P, et al. Cane-assisted gait biomechanics and electromyography after total hip arthroplasty. Arch Phys Med Rehabil. 2004;85(12):1966–1971. doi:10.1016/j. apmr.2004.04.037.

[48] Maguire C, Sieben JM, Frank M, et al. Hip abductor control in walking following stroke – the immediate effect of canes, taping and TheraTogs on gait. Clin Rehabil. 2010;24(1):37–45. doi:10.1177/0269215509342335.

[49] Bateni H, Maki BE. Assistive devices for balance and mobility: benefits, demands, and adverse consequences. Arch Phys Med Rehabil. 2005;86(1):134–145. doi:10.1016/j.apmr.2004.04.023.

[50] de Haan RJ, Limburg M, van der Meulen JH, et al. Quality of life after stroke. Impact of stroke type and lesion location. Stroke. 1995;26(3):402–408. doi:10.1161/01.str.26.3.402.

[51] Ghaffari A, Rostami HR, Akbarfahimi M. Predictors of instrumental activities of daily living performance in patients with stroke. Occup Ther Int. 2021;2021:6675680–6675687. doi:10.1155/2021/6675680.

[52] Juniper AR, Connor LT. Self-perceived adl/iadl function is influenced by residual neurological impairment, aphasia, and anxiety. Can J Occup Ther. 2022;89(3):307–314. doi:10.1177/00084174221098876.

[53] Khan F, Abusharha S, Alfuraidy A, et al. Prediction of factors affecting mobility in patients with stroke and finding the mediation effect of balance on mobility: a cross-sectional study. Int J Environ Res Public Health. 2022;19(24):16612. doi:10.3390/ijerph192416612.

[54] Lamberti N, Straudi S, Malagoni AM, et al. Effects of low-intensity endurance and resistance training on mobility in chronic stroke survivors: a pilot randomized controlled study. Eur J Phys Rehabil Med. 2017;53(2):228–239. doi:10.23736/ S1973-9087.16.04322-7.

[55] Martín-Sanz MB, Salazar-de-la-Guerra RM, Cuenca-Zaldivar JN, et al. Person-centred care in individuals with stroke: a qualitative study using in-depth interviews. Ann Med. 2022;54(1):2167–2180. doi:10.1080/07853890.2022.2105393.

[56] Chen YW, Lin KC, Li YC, et al. Predicting patient-reported outcome of activities of daily living in stroke rehabilitation: a machine learning study. J Neuroeng Rehabil. 2023;20(1):25. doi:10.1186/s12984-023-01151-6.

[57] Ran L, Jiang X, Li B, et al. Association among activities of daily living, instrumental activities of daily living and health-related quality of life in elderly yi ethnic minority. BMC Geriatr. 2017;17(1):74. doi:10.1186/s12877-017-0455-y.

[58] Ravensbergen WM, Timmer IL, Gussekloo J, et al. Self-perceived functioning and (instrumental) activities of daily living questionnaires after a hip fracture: do they tell the same story? Age Ageing. 2022;51(11):afac259. doi:10.1093/ageing/afac259.

[59] Brekke MF, la Cour K, Brandt Å, et al. The association between adl ability and quality of life among people with advanced cancer. Occup Ther Int. 2019;2019:2629673–2629610. doi:10.1155/2019/2629673.

[60] Ekstrand E, Lexell J, Brogårdh C. Grip strength is a representative measure of muscle weakness in the upper extremity after stroke. Top Stroke Rehabil. 2016;23(6):400–405. doi:10.1080/10749357.2016.1168591.

[61] Franceschini M, Goffredo M, Pournajaf S, et al. Predictors of activities of daily living outcomes after upper limb robot-assisted therapy in subacute stroke patients. PLoS One. 2018;13(2):e0193235. doi:10.1371/journal.pone.0193235.

[62] Yi Y, Shim JS, Oh BM, et al. Grip strength on the unaffected side as an independent predictor of functional improvement after stroke. Am J Phys Med Rehabil. 2017;96(9):616–620. doi:10.1097/PHM.0000000000000694.

Appendix 4.2 The poster of "Self-perceived upper extremity motor function predicts health-related quality of life in chronic stroke survivors" demonstrated in 2023 Rehabilitation Medicine Society of Australia and New Zealand 6th Annual Scientific Meeting.

Appendix 5.1 Chapter 5 published on Frontiers in Neurology (Final manuscript)

Psychometric properties of the Chinese (Cantonese) version of the Upper Extremity Functional Index in people with chronic stroke

Introduction

Stroke is a common disability in adults, with an estimated 9.6 million ischaemic strokes and 4.1 million haemorrhagic strokes occurring globally each year (1), representing a large economic burden (2). Approximately 80–85% of people with stroke have some degree of upper extremity sensorimotor impairment (3, 4), such as loss of motor control and sensory and proprioceptive deficits (5). Such impairment can directly impact upper extremity- related activities of daily living (ADLs) and social participation in people with stroke (6).

Compared with observational and objective outcome measures, patient-reported outcome measures (PROMs) provide additional value and unique insights into motor recovery after stroke (7). PROMs have been used to screen, monitor progress, and facilitate patient-centered care by gaining insights into patients' views of their physical symptoms, functional abilities and overall psychosocial wellbeing related to their health status (7, 8). Moreover, PROMs can provide data to elucidate the differential effects of interventions based on patients' perspectives. These data can be analysed to inform rehabilitation programme design to address patients' needs and preferences and improve the quality and efficiency of stroke rehabilitation (9–11). Thus, clinicians need a reliable and valid region-specific PROM that can be used to establish patients' paretic upper limb functions at baseline and monitor patients' progress as a result of treatment.

There are several existing PROMs commonly used to assess the upper limb function of people with stroke, e.g., the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire (12), the Stroke Impact Scale (SIS) (13), the Motor Activity Log (MAL) (14), and the Dexterity Questionnaire-24 (DextQ-24) (15). However, these PROMs have limited abilities to capture region-specific upper extremity function (12–15). For example, the DASH questionnaire has been questioned for containing different factors in the contents as the body functions are included (e.g., arm, shoulder, or hand pain) (12, 16). The SIS contains some items unrelated to upper limb-specific tasks, including mood-, language- and memory- related ADL items (13, 16). The MAL is time-consuming because it contains 30 items to assess the amount of use of the more-affected arm and the quality of movement during functional activities (7). The DextQ-24 has 12 out of 24 items evaluating the unimanual upper limb movements of the paretic side in people with chronic stroke and not focus on assessing the upper limb function bilaterally that is particularly important when performing activities of daily living in real-life situations (15).

The Upper Extremity Functional Index (UEFI) is a 20-item, region-specific PROM initially designed to assess upper extremity function in people with musculoskeletal disorders (17, 18). A 15- item version of the UEFI was later developed to increase the reliability and validity as a single-construct interval-level measure of upper extremity function in individuals with upper extremity musculoskeletal disorders (19). The original (English) version of the 15-item UEFI has demonstrated excellent test–retest reliability (intraclass correlation coefficient [ICC]2,1 = 0.95, ICC = 0.94) and excellent internal consistency (person separation index = 0.94) in people with upper extremity musculoskeletal disorders (17, 19).

The UEFI could serve as a region-specific PROM to assess upper extremity function in people with stroke. The UEFI has been translated into several languages for different patient populations. For example, the English (17, 20), Arabic (21), and Turkey (22) versions have been used to assess upper extremity musculoskeletal disorders, the English version has been used for breast cancer (23), and the Arabic version has been used for chronic obstructive pulmonary disease (24). However, the UEFI has not been translated into Chinese, and its psychometric properties have not been examined in Chinese people with stroke. Additionally, the correlations between the 15-item UEFI mean scores and other stroke-related outcome measures have not been evaluated. Thus, the objectives of the current study were to translate and culturally adapt the 15-item UEFI to develop a Chinese (Cantonese) version (C-UEFI) and evaluate the psychometric properties of the C-UEFI for use in assessing upper extremity functional recovery among community-dwelling people with chronic stroke in Hong Kong.

Materials and methods

Study design

This study was conducted from January to June 2021 in accordance with the Guidelines for Reporting Reliability and Agreement Studies (25) and the Declaration of Helsinki. Ethical approval was obtained from the Departmental Research Committee of the Hong Kong Polytechnic University (Approval number: HSEARS20210110002). All participants provided written informed consent to participate in this study.

Translation and cross-cultural adaptation

The permission to translate the original English UEFI into Chinese was obtained from the authors of the UEFI. Forward and backward translation and cross-cultural adaptation of the UEFI were performed in accordance with the international guidelines proposed by Beaton et al. (26), which comprise five steps (Figure 1). A panel of six experts was assembled, including two physiotherapists with more than 15 years of clinical experience in stroke rehabilitation, two nurses with more than 10 years of clinical experience and two healthcare professionals. The expert panel rated the experiential, conceptual, semantic, and idiomatic equivalence of each UEFI item using a 4-point Likert scale rating: 1 = not relevant, 2 = somewhat relevant, 3 = quite relevant and 4 = highly relevant. Ratings of 3 or 4 were dichotomised as relevant and 1 or 2 as irrelevant. Among the 15 items, item 7 of the UEFI (driving) was modified into "use of upper limbs in manipulating the shopping cart to buy commodities in the store" for the C-UEFI because it is uncommon for people living in Hong Kong to own a private vehicle.

The pilot C-UEFI was then produced and tested on 10 people with chronic stroke and five healthy controls. All 15 pilot trial participants agreed that the pilot version was fluent, clear, and comprehensible. After the pilot study, no further revision was needed, and the final C-UEFI was established. Finally, we tested the psychometric properties of the C-UEFI.

Setting and sampling

We recruited 101 people with stroke (58 male, 43 female) from a local self-help group via poster advertisements. People with stroke were included in the study if they: (1) were 50–80 years old; (2) suffered a single stroke that was confirmed by magnetic resonance imaging or computed tomography at least 1 year before the start of the study; (3) scored 7 or higher in the

Chinese version of the Abbreviated Mental Test (27); (4) could speak Chinese (Cantonese); (5) had volitional control of their non-paretic arm; (6) could induce at least minimal anti-gravity movement in the shoulder of their paretic arm; (7) had at least 5◦ of wrist extension in the anti-gravity position; and (8) could walk independently for at least 10 m with or without an assistive device. People with chronic stroke were excluded if they: (1) had any other unstable medical conditions (e.g., angina pectoris, pain, or arthritis) or other conditions with medications that may intervene the upper limb function (e.g., Parkinson's disease or Multiple Sclerosis); and (2) had any aphasia or hearing impairment that would affect the data collection procedure.

We recruited 50 healthy older adults (14 male, 36 female) aged 50–80 years with stable health as the control group. People with any comorbid neurological, cardiovascular, or musculoskeletal disease that might affect the assessment were excluded.

The 15-item UEFI has demonstrated excellent test–retest reliability (ICC2,1 = 0.95) in people with upper extremity musculoskeletal disorders (19). However, its reliability in people with stroke has not been evaluated. Assuming that an ICC value for assessing test–retest reliability of the 15-item UEFI in people with stroke was 0.9, a sample size of ≥46 subjects was required to achieve 80% power to detect an ICC of 0.9 with a null hypothesis ICC of 0.8 and a significance level of 0.05. To evaluate the ability of the C-UEFI to discern differences between different groups, ≥ 50 people with chronic stroke and ≥ 50 healthy controls were required with a CA0 value of 0.3 and CA1 value of 0.7 (28). A sample of >100 people with chronic stroke were regarded as reasonable based on the exploratory factor analysis (EFA) estimation (29). Thus, 101 people with stroke were recruited for this study.

Data collection

All assessments were performed in a university-affiliated neurorehabilitation laboratory. The study objectives and assessment procedures were explained to the participants. After obtaining informed consent, the participants completed a demographic data extraction form.

On day 1, the demographic data of the chronic stroke group ($N = 101$) were collected, and the group completed the C-UEFI. The participants also completed the Fugl-Meyer Assessment of Upper Extremity (FMA-UE), Wolf Motor Function Test (WMFT), Six-Minute Walk Test (6MWT), MAL, Activity-Specific Balance Confidence (ABC) scale, IADL scale, Survey of Activities and Fear of Falling in the Elderly (SAFFE), SIS and Community Integration Measure (CIM) in a randomized order. At least 5 min of rest was allowed between each assessment. After a 7-day interval (day 2), 50 people with chronic stroke were randomly selected from the 101 participants who completed the day 1 assessment, to complete the C-UEFI again to assess test–retest reliability by the same rater who conducted the assessment in day 1.

The healthy control group only completed the C-UEFI on day 1, and their data were used to determine the C-UEFI cut-off scores for people with stroke.

Outcome measures

Upper Extremity Functional Index

The 15-item UEFI retains the rating scale of the 20-item UEFI for all items except item 9 “doing up buttons,” which was modified to a scale from 0 to 3 points based on the Rasch analysis (17). The lowest anchor of item 9, extreme difficulty or unable to perform activity, has

the same weight as the other items (=0), but the next two response options are equally weighted: quite a bit of difficulty (=1) and moderate difficulty (=1). The last two response options are weighted as follows: a little bit of difficulty (=2) and no difficulty (=3). All other items are scored using a 5-point adjectival response scale to rate difficulty in performing upper extremity activities: 0 = extreme difficulty or unable to perform activity, 1 = quite a bit of difficulty, 2 = moderate difficulty, 3 = a little bit of difficulty, and 4 = no difficulty.

Fugl-Meyer Assessment of Upper Extremity

The FMA-UE is used to evaluate upper limb motor function impairment in people with stroke (30). The FMA-UE comprises 33 items measuring the reflex, movement and coordination of the shoulder, elbow, forearm, wrist, and hand (30). Each item is scored on a 3-point scale from 0 to 2, with a maximum possible score of 66 (30). A higher score indicates a lower level of motor impairment (30). The FMA-UE has demonstrated excellent intra-rater reliability (ICC = 0.995–0.996) and inter-rater reliability (ICC = 0.97) in people with chronic stroke (30, 31).

Wolf Motor Function Test

The WMFT is used to assess upper extremity motor function after stroke (32). The scale includes 17 items, comprising 15 function-based tasks and two strength-based tasks. The WMFT yields three scores: a functional ability score, a time score, which quantifies the speed of performance in seconds, and a grip strength score (32). Only the functional ability score was used for the correlation analysis. The functional ability score is rated using a 6-point ordinal scale on 15 items, with a maximum score of 75. A score of 0 indicates no attempt to use the more affected upper extremity, and a score of 5 indicates that movement of the affected upper

extremity appears normal (32). The WMFT functional ability score has demonstrated good inter-rater reliability (ICC3,1 = 0.93) and internal consistency (Cronbach's α = 0.92) in people with stroke (33).

Six-Minute Walk Test

The 6MWT is used to assess walking endurance (34), a significant predictor of community ambulation and integration in people with stroke (35, 36). Participants were instructed to walk back and forth along a 20-m corridor, covering as much distance as possible in 6 min, taking rests as needed. The maximum distance covered was recorded (36). The 6MWT has demonstrated good inter-rater reliability (ICC = 0.78), inter-rater reliability (ICC = 0.75) and excellent test–retest reliability ($ICC_{2,1}$ = 0.98) in people with stroke (35, 36).

Motor Activity Log

The MAL is used to assess the amount of use (AOU) and quality of movement (QOM) of the paretic arm and hand during ADLs in patients with chronic stroke (15). For each item of AOU and QOM, the scores range from 0 to 5, with total scores ranging from 0 to 150 (15). The MAL has demonstrated excellent internal consistency for AUO (Cronbach's α = 0.88) and QOM (Cronbach's α = 0.91) (15) and excellent test–retest reliability for AOU (r = 0.70–0.85) and QOM (r = 0.61–0.71) in people with stroke (15).

The Activity-Specific Balance Confidence Scale

The ABC scale, a 16-item questionnaire, is used to assess subjective balance confidence in daily activities (37). The items are rated on a scale from 0 to 100. A score of 0 represents no confidence, and a score of 100 represents complete confidence. The total ABC score is calculated by adding the individual item scores together and dividing by the total number of items (38). The ABC scale has demonstrated good test–retest (ICC = 0.85) and high internal consistency (Cronbach's $\alpha = 0.97$) in people with chronic stroke (38).

The Lawton Instrumental Activities of Daily Living Scale

The Lawton IADL scale (14), a self-reported questionnaire, is used to assess the more complex ADLs necessary for living in a community (39). The instrument is most useful for identifying how a person is functioning at present and assessing improvement or deterioration over time. The IADL scale measures nine function items using a 3-point ordinal scale (0 = unable to do, 1 = with assistance, 2 = independent). The IDAL scale has demonstrated excellent inter-rater reliability ($ICC_{2,1} = 0.99$) and test–retest reliability (ICC = 0.9) and good internal consistency (Cronbach's $\alpha = 0.86$) in older adults (14).

The Survey of Activities and Fear of Falling in the Elderly

The SAFFE is used to assess the role of fear of falling in activity restriction (40). Fear of falling during the performance of 11 activities is assessed by asking respondents to rate how worried they are about falling during each activity on a 3-point Likert scale (0 = not at all worried, 1 = a little worried, 2 = somewhat worried and 3 = very worried). The total score is the unweighted sum of the 11 items (range: 0–33), with a higher score indicating more fear (41, 42). The

SAFFE has demonstrated good internal consistency reliability (Cronbach's α = 0.95) in Chinese older adults (40, 41).

Stroke Impact Scale

The SIS is a self-reported questionnaire used to assess the subjective level of disability and health-related quality of life after stroke (13). The SIS comprises 59 items in eight domains and an extra question on stroke recovery. Each item is rated on a 5-point Likert scale in terms of the difficulty in completing each item. The summative scores are generated for each domain, ranging from 0 to 100. The SIS has demonstrated good test–retest reliability (ICC = 0.7–0.92), except for the emotion domain (ICC = 0.57), and good internal consistency (Cronbach's α = 0.90) in people with stroke (13, 43).

Community Integration Measure

The CIM assesses the level of community integration using 10 items rated on a 5-point scale, with the total score ranging from 10 to 50 (44). A higher score indicates a higher level of community integration. The Chinese version of the CIM has demonstrated good test–retest reliability (ICC = 0.84) and internal consistency (Cronbach's α = 0.84) in people with chronic stroke (44).

Statistical analysis

All data were analysed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). The level of confidence for significance was set as $\alpha = 0.05$. The Shapiro–Wilk test was used to assess data normality. Independent t-tests and Mann–Whitney U tests were used to compare between-group differences in the parametric and non-parametric data of demographics and variables of interest, respectively. Statistically significant differences between the expected and observed frequencies in categorical variables were calculated using the chi-square test.

Test-retest reliability was assessed using the $ICC_{3,1}$. The model was based on the two-way mixed effects model and the single-rater type (45, 46). The reliability was defined as excellent (ICC > 0.90), good (ICC: 0.75–0.90), moderate (ICC: 0.50–0.75) and poor (ICC < 0.50) (46). Internal consistency was evaluated using Cronbach's α coefficient, which was rated as follows: very good (0.90–0.95), good (0.80–0.89), fair (0.70–0.79), weak (0.60–0.69) and unacceptable (<0.60) (47). The standard error of measurement (SEM) relative to the total score was rated as follows: very good (<5%), good (5– 10%), doubtful (>10–20%) and negative (>20%) (48). SEM was calculated as standard deviation (SD) × $\sqrt{}$ (1 − r) (49).

The minimal detectable change (MDC) was calculated as SD × 1.96 × $\sqrt{2}$ (1 − r) (50) at a 95% confidence interval, where SD denotes the standard deviation of the baseline total UEFI score, and r denotes the test–retest reliability coefficient. Standardized response mean (SRM) was calculated as the ratio of change from pre-test to post-test divided by the standard deviation of the change scores. SRM > 0.8, 0.5–0.8, or 0.2–<0.5 indicate large, moderate, and low responsiveness, respectively (51).

Spearman's ρ and Pearson's correlation analyses were used to detect correlations between outcome variables for non-normally and normally distributed data, respectively. Correlation

strength was rated as follows: good to excellent ($r > 0.75$), moderate to good ($r = 0.50–0.75$), fair ($r = 0.25–0.49$) and little to no correlation ($r < 0.25$) (52). In order to confirm whether C-UEFI has the ability to determine the difference in the upper limb functions between the people with stroke with upper extremity activity limitations and health older adults, the known-group validity was applied to compare the C-UEFI scores between the stroke group and healthy group. The independent t-tests and Mann–Whitney U tests were used for parametric and non-parametric data analysis, respectively.

Both EFA and confirmatory factor analysis (CFA) were used to identify the components of the C-UEFI. Principal component analysis and a scree plot were used to determine the optimal number for factor extraction, and promax rotation was used to enhance the interpretability of the factors. In the EFA, the items with factor loadings >0.3 were considered meaningful (53), and these data were input into the CFA model. The commonly used indices were estimated to fit the model of interest according to the following criteria: the comparative fit index >0.95, the Tucker– Lewis index >0.9, the root mean square error approximation <0.06 and the ratio of chi-square to degrees of freedom ($\chi 2 /df < 3.0$) (54).

A receiver operating characteristics (ROC) curve and the areas under the curve (AUCs) were used to determine the optimal cut- off of C-UEFI and the accuracy of ability of C-UEFI to classify the upper extremity activity limitations in people with stroke. The true positive rate and false positive rate were plotted to generate the receiver operating characteristics (ROC) curve to evaluate the performance of C-UEFI as a classifier to distinguish the upper limb functions between the people with stroke with upper extremity activities limitations and healthy subjects. After number of possible cut-off values obtained, the Youden index analysis was performed to identify the optimal cut-off point of the C-UEFI in distinguishing the level of

upper extremity activity limitations in people with stroke and their healthy counterparts (55). Area under the curve (AUC) values of <0.5, 0.5–0.7, 0.7–0.8, 0.8–0.9 and >0.9 indicate no, poor, acceptable, excellent, and outstanding discrimination, respectively (56). Youden's index was used to determine the trade- off between maximizing sensitivity and specificity.

Results

The translation and cross-cultural adaptation process

"There were only minor linguistic discrepancies between the translators during the forward-backward translation process and resolved through consensus. Our expert panel confirmed the cultural relevancy and linguistic equivalence of the pilot version of Chinese (Cantonese) version of UEFI. The pilot results demonstrated that the fluency, clarity, and comprehensibility of pilot version was good."

Participant characteristics

A total of 151 participants (101 people with chronic stroke and 50 healthy older adults) were recruited for this study. Their mean ages were 63.82 (SD 6.4) and 61.58 (7.56) years, respectively (Table 1).

Reliability, responsiveness, and validity

The $ICC_{3,1}$ value is shown in Table 2. The test–retest $ICC_{3,1}$ for the C-UEFI total score was 0.872 (95% CI: 0.798–0.920, $P < 0.001$). The test–retest ICC3,1 for the C-UEFI items ranged from 0.22 (95% CI: −0.023–0.439, $P = 0.038$) to 0.771 (95% CI: 0.651–0.854, $P < 0.001$). The internal consistency (Cronbach's α) of the C-UEFI was 0.922 (Table3). The SEM and MDC were 3.6 and 9.98, respectively. The SRM was 0.51 (95% CI: 0.09–0.89).

The C-UEFI total scores and item scores of the stroke group and healthy group were compared using the known- group validity. The healthy group demonstrated higher levels of upper extremity functional activity than the stroke group (Table 4).

Correlations with other outcome measures

For our stroke participants, their overall C-UEFI mean score showed significant positive correlations with the FMA-UE, WMFT, ABC scale, MAL, Lawton IADL scale, SIS and CIM mean scores ($r = 0.217–0.759$, $P < 0.05$) and with the distance covered in the 6MWT ($r = 0.519$, $P < 0.001$). Their overall C- UEFI mean score also showed a significant negative moderate correlation with the SAFFE mean score ($r = −0.551$, $P < 0.001$) (Table 5).

Factor analysis

The Kaiser–Meyer–Olkin measure was 0.886, which indicated sufficient C-UEFI items for the factor analysis. Bartlett's test of sphericity was significant, showing that the factor analysis was satisfactory. The EFA suggested a two-factor model, which explained 58.434% of the total variance (Table 6). The CFA model is presented in Figure 2 and Table 7. Items 13, 6, 8, 14, 15, 7, 12, 1, and 5 were specified to load on the "Basic Daily Activity" factor, and items 2, 3, 10,

11, 9, and 4 were specified to load on the "Advanced Functional Activity" factor. Although some parameters of the CFA did not reach the significance threshold, this model displayed an acceptable fit, with a χ 2 /df of 2.27 ($P < 0.001$), a robust comparative fit index of 0.872, a robust Tucker–Lewis index of 0.849 and a robust root mean square error approximation of 0.113. The inter-factor correlation between the two subscales was significant ($r = 0.78$). The Cronbach's α values for the two subscales (α1 = 0.922; α2 = 0.774) and the total score (α = 0.921) were acceptable.

Distinguishing cut-off score

A C-UEFI cut-off score of 57.5 was identified. The receiver operating characteristic curve yielded an AUC of 0.921, with a sensitivity of 89.1% and a specificity of 84% of 1.721 of Youden's index, respectively, and with positive predictive value of 91.8% and negative predictive value of 79.2%, separately (Table 8, Figure 3).

Discussion

This is the first study to extend the use of the UEFI to assess the region-specific PROM of the level of upper extremity function in community-dwelling people with stroke. In summary, the C-UEFI demonstrated good test–retest reliability and excellent internal consistency in people with chronic stroke. People with stroke scored lower than healthy controls on all items of the C-UEFI. The C-UEFI score was significantly correlated with the scores of FMA- UE, WMFT, ABC scale, MAL, Lawton IADL scale, SAFFE, SIS, and CIM and with the distance covered in the 6MWT. Our study also demonstrated that 57.5 was the optimal cut-off UEFI score to differentiate between people with stroke and healthy older adults according to upper extremity

function. A two-factor structure comprising “Basic Daily Activity” and “Advanced Functional Activity” was confirmed by factor analysis.

UEFI scores in people with chronic stroke

In our study, the PROM of upper extremity function of people with stroke was significantly lower than that of healthy controls on all items of the C-UEFI. Stroke-specific impairments of upper and lower extremities include muscle weakness, spasticity, and impaired motor control (57), which are caused by insufficient motor unit recruitment, reduced muscle motor unit firing rates (58), and poor voluntary activation (59). These impairments may worsen the ability of people with stroke to execute specific ADL movements, resulting in poorer C-UEFI scores compared with healthy older adults.

UEFI reliability

This was the first study to investigate the reliability of the C- UEFI for assessing people with chronic stroke. The good test– retest reliability ($ICC_{3,1}$ = 0.872) indicates that the C-UEFI is a reliable outcome measure for clinical use in Chinese people with chronic stroke. This finding is consistent with previous studies showing excellent test–retest reliability of the English version in people with upper extremity musculoskeletal disorders ($ICC_{2,1}$ = 0.95, ICC = 0.94) (17, 19). Three reasons may explain the good results achieved. First, we recruited people with chronic stroke (post-stroke duration of 6.74 ± 4.42 years), which indicates that the potential functional recovery of their upper extremity activity has plateaued, resulting in low variability in the test–retest performance. Second, our standardized experimental protocol and well-trained raters may have helped minimize measurement error. Third, the 7-day test–retest

interval adopted in our study is suitable for minimizing learning effects and preventing changes in the conditions of participants.

The Cronbach's α coefficients were excellent for the individual items (Cronbach's α = 0.912–0.923) and total scores (Cronbach's α = 0.922) of the C-UEFI, indicating good correlations between each item. This finding is consistent with previous studies that reported excellent internal consistency in people with upper extremity musculoskeletal disorders (Cronbach's α = 0.94) (19). The high internal consistency of the C-UEFI may indicate that individual items measured the same concept and domain.

The measurement error of the C-UEFI in people with chronic stroke was quantified in this study using SEM and MDC. The SEM (3.6) represents 6.1% of the C-UEFI score range, indicating that the measurement error of the C-UEFI represents only a small portion of the total scale range. The MDC (9.98) represents 16.9% of the total score range, which is similar to the MDC (8.1) previously reported in people with upper extremity musculoskeletal disorders (19). The MDC indicates that a change of at least 9.98 is required to be considered a true change in the level of upper extremity functional activity in people with chronic stroke. The C-UEFI cut-off score (57.5) distinguishing between people with chronic stroke and healthy older adults in this study markedly surpasses the calculated MDC (9.98). This between-group disparity suggests that the difference was genuine and not caused by measurement error.

The SRM of C-UEFI in people with stroke shown a moderate degree responsiveness from two evaluations, which indicates the C-UEFI could be used to detect the people with stroke's upper extremity activity limitations.

Correlations with other outcome measures

A significant fair correlation was detected between C-UEFI and FMA-UE scores. FMA-UE scores reflect neural motor control, including upper extremity muscle performance and gross gripping function, which are essential components of the level of upper extremity functional activity (60). Hence, it is expected that people with stroke with a high FMA-UE score would achieve a high C-UEFI score.

Expectedly, the C-UEFI score showed significant correlations with WMFT and MAL scores. The WMFT is a quantitative outcome measure of upper extremity motor ability in people with stroke, mainly rating upper extremity strength and dexterity (32), similar to some items of the C-UEFI. The MAL is a semi-structured interview used to assess arm function during 30 daily functional tasks (15). The C-UEFI and MAL items assessing upper extremity functional activities in ADLs are similar. Hence, the C-UEFI and MAL share similar contents and the same ICF construct.

The C-UEFI score showed significant correlations with the distance covered in the 6MWT and the ABC scale scores. The 6MWT assesses the distance walked in 6min as a sub-maximal test of aerobic capacity or exercise endurance (35). The ABC scale is a self-reported outcome measure of balance confidence in performing various daily activities without losing balance or experiencing a sense of unsteadiness (37). Aerobic capacity, walking endurance and balance performance in daily activities are beneficial for coordinating the upper extremity to execute specific activities in some items of the C-UEFI, e.g., items 2, 3, 7, and 15. Hence, the C-UEFI scores were significantly positively correlated with the distance covered in the 6MWT and the ABC scale scores.

Our study demonstrated that the C-UEFI score showed a significant positive good to excellent correlation with the Lawton IADL scale score. The Lawton IADL scale evaluates the ability to perform complex ADLs necessary for independent living in the community (39), and the C-UEFI evaluates functional activities using the upper extremities in ADLs. Thus, the C- UEFI and Lawton IADL scale share similar contents and the same ICF construct and domain. Our study also demonstrated that the C-UEFI showed a significant negative moderate to good correlation with the SAFFE. The SAFFE was developed as an outcome measure to evaluate avoidance behaviour due to fear of falling by quantifying self-perceived and observable ADLs and instrumental ADLs (41). Thus, reduced upper extremity mobility could increase the fear and risk of falling in people with stroke.

The C-UEFI score was significantly correlated with the SIS score, except for the memory evaluation. The SIS is used to evaluate the health-related quality of life in the upper extremity activity domain (13). Higher UEFI scores reflect increased use of the upper limbs in ADLs and thus higher SIS scores. The C-UEFI score was also significantly correlated with the CIM score. CIM is a subjective outcome measure of community integration and considers the self-reported subjective feelings of participants (44). Hence, improving upper extremity mobility could increase participation in daily activities, which could enhance community integration.

Factor analysis

Our study used factor analysis to explore the components of the C-UEFI. A two-factor structure was identified according to the EFA, namely, “Basic Daily Activity” and “Advanced Functional Activity,” which was confirmed by the CFA. The “Basic Daily Activity” dimension (items 13, 6, 8, 14, 15, 7, 12, 1, and 5) mainly evaluates basic ADLs, which require basic

movements. The "Advanced Functional Activity" dimension (items 2, 3, 10, 11, 4, and 9) mainly evaluates instrumental ADLs, which require more complex skills and coordination. The factor analysis revealed the option to split the C-UEFI questionnaire into two parts: basic ADLs and instrumental ADLs. Future studies are needed to provide further evidence on the psychometric properties of the newly derived subscales. Moreover, some items (e.g., 6, 7, 8, and 14) in the "Basic Daily Activity" dimension also involve the application of instruments. Future studies using Rasch analysis are needed to provide a more robust conclusion regarding this two-factor structure model.

Optimal cut-off score

Our results showed that a UEFI score of 57.5 was sufficiently sensitive for discriminating between people with chronic stroke and healthy older adults (AUC = 0.921; sensitivity = 88.1%; specificity = 84% of Youden's index). The high AUC indicates excellent accuracy of the C-UEFI in discriminating between those two groups. Thus, the C-UEFI is a sensitive and specific test for identifying people with stroke who have upper extremity functional activity limitations.

Limitations

Several limitations of this study should be acknowledged. First, our participants were recruited from a local self-help group for people with stroke, and those who attend such groups may have a relatively high level of functional mobility. Future studies should include participants with lower levels of functional mobility to increase the generalisability of our results to the stroke population. Second, stroke incidence is associated with age, doubling with each decade after 55 years (61), only people aged ≥ 50 years were recruited in this study. Thus, the results in our

study only apply to those participants who fulfilled our inclusion criteria. Future research is needed to verify whether the C-UEFI could be extended to those who are younger. Third, compared with men, women with stroke tend to be more disabled, and there may be sex differences in the levels of upper extremity functional activity (62). Thus, future studies should evaluate differences in the levels of upper extremity functional activity between men and women with chronic stroke.

Conclusions

The results of this study demonstrate that the C-UEFI is a reliable, valid, sensitive, and specific clinical test for evaluating functional recovery of upper extremity activity in people with chronic stroke.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Departmental Research Committee of The Hong Kong Polytechnic University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

HP and SN contributed to the conception and design of the study. HP, TL, JT, and TW collected the data and organized the database and wrote the first draft of the manuscript. HP, SN, and TL performed the statistical analysis. All the authors contributed to manuscript revision, read, and approved the submitted version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1.BCV, Khatri P. Stroke. Lancet. (2020) 396:129– 42. doi: 10.1016/S0140-6736(20)31179-X

2. Sevick LK, Ghali S, Hill MD, Danthurebandara V, Lorenzetti DL, Noseworthy T, et al. Systematic review of the cost and cost-effectiveness of rapid endovascular therapy for acute ischemic stroke. Stroke. (2017) 48:2519–26. doi: 10.1161/STROKEAHA.117.017199

3. Wattchow KA, McDonnell MN, Hillier SL. Rehabilitation interventions for upper limb function in the first 4 weeks following stroke: a systematic review and meta-analysis of the evidence. Arch Phys Med Rehabil. (2018) 99:367– 82. doi: 10.1016/j.apmr.2017.06.014

4. Santisteban L, Térémetz M, Bleton JP, Baron JC, Maier MA, Lindberg PG. Upper limb outcome measures used in stroke rehabilitation studies: a systematic literature review. PLoS ONE. (2016) 11:e0154792. doi: 10.1371/journal.pone.0154792

5. Pollock A, Farmer SE, Brady MC, Langhorne P, Mead GE, Mehrholz J, et al. Interventions for improving upper limb function after stroke. Cochrane Database Syst Rev. (2014) 2014:CD010820. doi: 10.1002/14651858.CD010820.pub2

6. Veerbeek JM, Kwakkel G, van Wegen EE, Ket JCF, Heymans MW. Early prediction of outcome of activities of daily living after stroke: a systematic review. Stroke. (2011) 42:1482–8. doi: 10.1161/STROKEAHA.110.604090

7.Stewart JC, Cramer SC. Patient-reported measures provide unique insights into motor function after stroke. Stroke. (2013) 44:1111– 6. doi: 10.1161/STROKEAHA.111.674671

8. Moloney J, Walshe M, Regan J. Patient reported outcome measures in dysphagia research following stroke: a scoping review and qualitative analysis. Dysphagia. (2022) 38:181–90. doi: 10.1007/s00455-022-10448-y

9. van Lieshout EC, Visser-Meily JMA, Nijland RH, Dijkhuizen RM, Kwakkel G. Comparison of self-reported vs. observational clinical measures of improvement in upper limb capacity in patients after stroke. J Rehabil Med. (2020) 52:jrm00051. doi: 10.2340/16501977-2661

10. Price-Haywood EG, Harden-Barrios J, Carr C, Reddy L, Bazzano LA, Driel MLV. Patient-reported outcomes in stroke clinical trials 2002–2016: a systematic review. Qual Life Res. (2019) 28:1119–28. doi: 10.1007/s11136-018-2053-7

11. Reeves M, Lisabeth L, Williams L, Katzan I, Kapral S, Deutsch A, et al. Patient- reported outcome measures (proms) for acute stroke: rationale, methods and future directions. Stroke. (2018) 49:1549–56. doi: 10.1161/STROKEAHA.117.018912

12. Dalton E, Lannin NA, Laver K, Ross L, Ashford S, McCluskey A, et al. Validity, reliability and ease of use of the disabilities of arm, shoulder and hand questionnaire in adults following stroke. Disabil Rehabil. (2017) 39:2504– 11. doi: 10.1080/09638288.2016.1229364

13. Vellone E, Savini S, Fida R, Dickson VV, Melkus GD, Carod-Artal FJ, et al. Psychometric evaluation of the stroke impact scale. J Cardiovasc Nurs. (2015) 30:229– 41. doi: 10.1097/JCN.0000000000000145

14. van der Lee JH, Beckerman H, Knol DL, de Vet HCW, Bouter LM. Clinimetric properties of the motor activity log for the assessment of arm use in hemiparetic patients. Stroke. (2004) 35:1410–4. doi: 10.1161/01.STR.0000126900.24964.7e

15. Dehmiyani A, Taghizadeh G, Azad A, Goudarzi S, Jamali S, Hejazi Shirmand M, et al. Psychometric properties of dexterity questionnaire-24 in Iranian chronic stroke survivors. Top Stroke Rehabil. (2022) 29:201–7. doi: 10.1080/10749357.2021. 1970451

16. Hill B, Bialocerkowski A, Williams G. Do patient reported outcome measures capture actual upper limb recovery? Int J Ther Rehabil. (2014) 21:558– 9. doi: 10.12968/ijtr.2014.21.12.558

17. Chesworth BM, Hamilton CB, Walton DM, Benoit M, Blake TA, Bredy H, et al. Reliability and validity of two versions of the upper extremity functional index. Physiother Can. (2014) 66:243–53. doi: 10.3138/ptc.2013-45

18. Arumugam V, MacDermid JC. Clinimetrics: upper extremity functional index. J Physiother. (2018) 64:125. doi: 10.1016/j.jphys.2018.01.003

19. Hamilton CB, Chesworth BM. A rasch-validated version of the upper extremity functional index for interval-level measurement of upper extremity function. Phys Ther. (2013) 93:1507–19. doi: 10.2522/ptj.20130041

20. Hadadi M, Ebrahimi S, Sarvestani M, Mozafari M. Correspondence: upper extremity functional index. J Physiother. (2020) 66:278. doi: 10.1016/j.jphys.2020.09.004

21. Aljathlani MF, Alshammari MO, Alsuwaygh MA, Al-Mutairi M, Aljassir FF, Bindawas SM, et al. Cross-cultural adaptation and validation of the Arabic version of the upper extremity functional index. Disabil Rehabil. (2021) 38:1– 7. doi: 10.1080/09638288.2021.1947396

22. Aytar A, Yuruk ZO, Tuzun EH, Baltaci G, Karatas M, Eker L. The upper extremity functional index (uefi): cross-cultural adaptation, reliability, and validity of the turkish version. J Back Musculoskelet Rehabil. (2015) 28:489– 95. doi: 10.3233/BMR-140545

23. Binkley JM, Stratford P, Kirkpatrick S, Farley CR, Okoli J, Gabram S. Estimating the reliability and validity of the upper extremity functional index in women after breast cancer surgery. Clin Breast Cancer. (2018) 18:e1261–7. doi: 10.1016/j.clbc.2018.02.008

24. Alnahdi AH, Albarrati A. The upper extremity functional index: reliability and validity in patients with chronic obstructive pulmonary disease. Int J Environ Res Public Health. (2021) 18:10608. doi: 10.3390/ijerph182010608

25. Kottner J, Audige L, Brorson S, Donner A, Gajewski B, Hróbjartsson A, et al. Guidelines for reporting reliability and agreement studies (grras) were proposed. Int J Nurs Stud. (2011) 48:661–71. doi: 10.1016/j.ijnurstu.2011.01.016

26. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. (2000) 25:3186– 91. doi: 10.1097/00007632-200012150-00014

27. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. Age Ageing. (1972) 1:233–8. doi: 10.1093/ageing/1.4.233

28. Bujang MA, Omar ED, Baharum NA. A review on sample size determination for cronbach's alpha test: a simple guide for researchers. Malays J Med Sci. (2018) 25:85–99. doi: 10.21315/mjms2018.25.6.9

29. Arafat SY, Chowdhury HR, Qusar M, Hafez MA. Cross cultural adaptation and psychometric validation of research instruments: a methodological review. J Behav Health. (2016) 5:129–36. doi: 10.5455/jbh.20160615121755

30. GladstoneDJ, DanellsCJ, BlackSE. The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties. Neurorehabil Neural Repair. (2002) 16:232–40. doi: 10.1177/154596802401105171

31. Duncan PW, Propst M, Nelson SG. Reliability of the fugl-meyer assessment of sensorimotor recovery following cerebrovascular accident. Phys Ther. (1983) 63:1606– 10. doi: 10.1093/ptj/63.10.1606

32. Edwards DF, Lang CE, Wagner JM, Birkenmeier R, Dromerick AW. An evaluation of the wolf motor function test in motor trials early after stroke. Arch Phys Med Rehabil. (2012) 93:660–8. doi: 10.1016/j.apmr.2011.10.005

33. Morris DM, Uswatte G, Crago JE, Cook EW, Taub E. The reliability of the wolf motor function test for assessing upper extremity function after stroke. Arch Phys Med Rehabil. (2001) 82:750–5. doi: 10.1053/apmr.2001.23183

34. Cederberg KLJ, Sikes EM, Bartolucci AA, Motl RW. Walking endurance in multiple sclerosis: meta-analysis of 6-min walk test performance. Gait Posture. (2019) 73:147–53. doi: 10.1016/j.gaitpost.2019.07.125

35. Macchiavelli A, Giffone A, Ferrarello F, Paci M. Reliability of the 6-min walk test in individuals with stroke: systematic review and meta-analysis. Neurol Sci. (2021) 42:81–7. doi: 10.1007/s10072-020-04829-0

36. Liu J, Drutz C, Kumar R, McVicar L, Weinberger R, Brooks D, et al. Use of the 6-min walk test post-stroke: is there a practice effect? Arch Phys Med Rehabil. (2008) 89:1686–92. doi: 10.1016/j.apmr.2008.02.026

37. Mak MK, Lau AL, Law FS, Cheung CC, Wong IS. Validation of the Chinese translated activities-specific balance confidence scale. Arch Phys Med Rehabil. (2007) 88:496–503. doi: 10.1016/j.apmr.2007.01.018

38. Botner EM, Miller WC, Eng JJ. Measurement properties of the activities-specific balance confidence scale among individuals with stroke. Disabil Rehabil. (2005) 27:156– 63. doi: 10.1080/09638280400008982

39. GrafC.TheLawtoninstrumentalactivitiesofdailylivingscale.AmJNurs.(2008) 108:52–62. doi: 10.1097/01.NAJ.0000314810.46029.74

40. Lachman ME, Howland J, Tennstedt S, Jette A, Assmann S, Peterson EW. Fear of falling and activity restriction: the survey of activities and fear of falling in the elderly (safe). J Gerontol B Psychol Sci Soc Sci. (1998) 53:P43– 50. doi: 10.1093/geronb/53B.1.P43

41. Chou KL, Yeung FK, Wong EC. Fear of falling and depressive symptoms in Chinese elderly living in nursing homes: fall efficacy and activity level as mediator or moderator? Aging Ment Health. (2005) 9:255–61. doi: 10.1080/13607860500114035

42. Hornyak V, Brach JS, Wert DM, Hile E, Studenski S, VanSwearingen JM. What is the relation between fear of falling and physical activity in older adults? Arch Phys Med Rehabil. (2013) 94:2529–34. doi: 10.1016/j.apmr.2013.06.013

43. Duncan PW, Wallace D, Lai SM, Johnson D, Embretson S, Laster LJ. The stroke impact scale version 20 Evaluation of reliability, validity, and sensitivity to change. Stroke. (1999) 30:2131–40. doi: 10.1161/01.STR.30.10.2131

44. Liu TW, Ng SS, Ng GY. Translation and initial validation of the Chinese (Cantonese) version of community integration measure for use in patients with chronic stroke. Biomed Res Int. (2014) 2014:623836. doi: 10.1155/2014/623836

45. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. (1979) 86:420–8. doi: 10.1037/0033-2909.86.2.420

46. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. (2016) 15:155–63. doi: 10.1016/j.jcm.2016.02.012

47. Pereira GS, Silva SM, Júlio CE, Thonnard J, Bouffioulx E, Corrêa JCF, et al. Translation and cross-cultural adaptation of satis-stroke for use in Brazil: a satisfaction measure of activities and participation in stroke survivors. Biomed Res Int. (2019) 2019:8054640. doi: 10.1155/2019/8054640

48. Ostelo RW, de Vet HC, Knol DL, van den Brandt PA. 24-item roland-morris disability questionnaire was preferred out of six functional status questionnaires for post-lumbar disc surgery. J Clin Epidemiol. (2004) 57:268–76. doi: 10.1016/j.jclinepi.2003.09.005

49. Stratford PW. Estimating the standard error of measurement from reliability studies. Physiother Can. (2004) 56:27–30. doi: 10.2310/6640.2004. 15377

50.Haley SM, Fragala-Pinkham MA. Interpreting change scores of tests and measures used in physical therapy. Phys Ther. (2006) 86:735– 43. doi: 10.1093/ptj/86.5.735

51. Portney LG, Watkins MP. Foundations of Clinical Research: Applications to Practice. London: Pearsons (2013).

52. Ng SSM, Liu TW, Chan CY, Chan ICW, Chu JCL, Poon HCH, et al. Reliability and validity of the long-distance corridor walk among stroke survivors. J Rehabil Med. (2020) 52:jrm00062. doi: 10.2340/16501977-2691

53. Floyd FJ, Widaman KF, Butcher JN. Factor analysis in the development and refinement of clinical assessment instruments. Psychol Assess. (1995) 7:286– 99. doi: 10.1037/1040-3590.7.3.286

54. Babyak MA, Green SB. Confirmatory factor analysis: An introduction for psychosomatic medicine researchers. Psychosom Med. (2010) 72:587–97. doi: 10.1097/PSY.0b013e3181de3f8a

55. Brincks J, Jorgensen JB, Giese IE, Palle ML, Callesen J, Johnsen E, et al. A study of the discriminative properties of the six-spot step test in people with Parkinson's disease at the risk of falling. NeuroRehabilitation. (2019) 45:265–72. doi: 10.3233/NRE-192801

56. Liu TW, Ng SSM, Tan MP. Assessing the fall risks of community-dwelling stroke survivors using the short-form physiological profile assessment (s-ppa). PLoS ONE. (2019) 14:e0216769. doi: 10.1371/journal.pone.0216769

57. Ng SS, Shepherd RB. Weakness in patients with stroke: Implications for strength training in neurorehabilitation. Phys Ther Rev. (2000) 5:227– 38. doi: 10.1179/108331900786166650

58. Gemperline JJ, Allen S, Walk D, Rymer WZ. Characteristics of motor unit discharge in subjects with hemiparesis. Muscle Nerve. (1995) 18:1101– 14. doi: 10.1002/mus.880181006

59. Horstman AM, Beltman MJ, Gerrits KH, Koppe P, Janssen TW, Elich P, et al. Intrinsic muscle strength and voluntary activation of both lower limbs and functional performance after stroke. Clin Physiol Funct Imag. (2008) 28:251– 61. doi: 10.1111/j.1475-097X.2008.00802.x

60. Lundquist CB, Maribo T. The fugl-meyer assessment of the upper extremity: reliability, responsiveness and validity of the Danish version. Disabil Rehabil. (2017) 39:934–9. doi: 10.3109/09638288.2016.1163422

61. Ng SSM, Liu TW, Tsoh J, Chen PM, Cheng TS, Cheung MCH, et al. Psychometric properties of the trail walking test for people with stroke. Front Neurol. (2022) 13:821670. doi: 10.3389/fneur.2022.821670

62. Gall S, Phan H, Madsen TE, Reeves M, Rist P, Jimenez M, et al. Focused update of sex differences in patient reported outcome measures after stroke. Stroke. (2018) 49:531–5. doi: 10.1161/STROKEAHA.117.018417

Appendix 5.2 Chapter 5 published on Disability and Rehabilitation (Final manuscript)

Testing the psychometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke

Background

Stroke is a common cause of disability in adults. Approximately 9.6 million cases of ischemic stroke and 4.1 million cases of haemorrhagic stroke are reported globally each year [1]; thus, stroke imposes a large economic burden, with direct and indirect costs totalling $33.0 billion annually (2011 USD) [2]. Stroke can cause serious physical impairments, including impaired motor control and sensory and proprioceptive deficits [3], which are often persistent and result in disability. These impairments can directly impact the daily activities and social participation of people with stroke [4,5]. The main goals of stroke rehabilitation are to restore the patient's ability to live independently and improve their levels of activity and social participation [6].

According to the International Classification of Functioning, Disability and Health (ICF), the activity domain refers to the capacity to execute and perform specific actions and tasks in daily living, and the participation domain refers to involvement in life situations [7,8]. The activity and participation domains can be expressed as a single list of nine elements: learning and applying knowledge; general tasks and demands; communication; mobility; self-care; domestic life; interpersonal interactions and relationships; major areas, such as corporate and economic life; and community, social and civic life [9,10]. Activity and participation can be measured in various ways, such as through experienced difficulty or the degree of assistance required or the degree of patient performance in activities and life situations [11]. Tse et al. [9] and Kossi et

al. [10] reviewed the existing outcome measures for assessing the activity and participation levels of individuals with stroke. The most commonly used outcome measures [e.g., Stroke Impact Scale (SIS), Assessment of Life Habits] rate the activity and participation of people with stroke in terms of the difficulties they experience.

However, subjective satisfaction with regard to activity and participation in the actual environments experienced by stroke survivors is an overlooked area in stroke rehabilitation. Satisfaction is a latent variable in terms of activity and participation [11]. Satisfaction can be defined as a state of enthusiasm or pleasure felt when achieving a goal, whereas failure to achieve that goal can lead to dissatisfaction [4]. The satisfaction level of people with stroke corresponds to their perception of their performance in activities and life situations that meet their needs [12]. Measuring perceived subjective satisfaction can provide healthcare practitioners with the information required to identify the needs of people with stroke, plan and implement interventions, assess the effectiveness of interventions and adjust those interventions if necessary [13].

SATIS-Stroke was developed to measure the satisfaction of people with chronic stroke in terms of their activity and participation in the environments they experience [11]. SATIS-Stroke operationalises the nine elements of the ICF activity and participation domains [4] to assess both the effort required and the pleasure experienced upon performing the tasks addressed in the items of the questionnaire [4]. SATIS-Stroke has excellent intra-rater (intraclass correlation coefficient $[ICC]_{2,1} = 0.90$, ICC = 0.93) and inter- rater ($ICC_{2,1} = 0.89$, ICC = 0.90) reliabilities, excellent internal consistency (Cronbach's a = 0.93–0.94), good correlation with the Brazilian Portuguese version of the Stroke-Specific Quality of Life scale in people with chronic stroke ($r = 0.74$, $p < 0.05$) [4,7], excellent test–retest reliability (ICC = 0.98) and good correlation

with the English and French versions of the Barthel Index in people with chronic stroke (r = 0.74 , P <0.05) [12].

SATIS-Stroke has been translated into Brazilian Portuguese [4,7], French [12] and English [12], and the reliability of these versions has been tested in people with chronic stroke. However, SATIS-Stroke has not been translated to Cantonese or culturally adapted to the Chinese population, and its psychometric properties have not been assessed in Chinese people with chronic stroke. Although the mean SATIS-Stroke scores were shown to have significant correlations with Barthel Index scores [12] and the Stroke-Specific Quality of Life scale [4], the correlations with outcome measures in the body function domain have not been assessed. Thus, the current study aimed to (1) translate SATIS- Stroke to Cantonese (C-SATIS-Stroke) and culturally adapt it to assess the satisfaction levels of Chinese people with chronic stroke in terms of activity and social participation, and (2) investigate the psychometric properties of C-SATIS-Stroke, namely the reliability [internal consistency, test–retest reliability and standard error of measurement (SEM)], measurement error (minimal detectable change), validity (known-group validity), correlations with other outcome measures, optimal cut-off score [receiver operating characteristic (ROC) curve analysis, sensitivity and specificity] and ceiling and floor effects among Chinese people with chronic stroke.

Materials and methods

Study design

This cross-sectional clinical study was conducted according to the Guidelines for Reporting Reliability and Agreement Studies [14]. All human experiments were performed according to

the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to study initiation. Translation and cross-cultural adaptation Permission was obtained from the author of SATIS-Stroke to translate the original English version to Cantonese. Forward and backward translation and cross-cultural adaptation were performed following the internationally accepted guidelines recommended by Beaton et al. [15]. The following steps were taken (Figure 1).

Step 1

The English version of SATIS-Stroke was translated into Cantonese by two independent bilingual translators whose native language is Chinese (Cantonese). One translator is a physiotherapist with more than 15 years of clinical experience in rehabilitation, and the other is a professional translator with no background in medicine or rehabilitation. They independently translated the English version of SATIS-Stroke into two initial Cantonese drafts (D1 and D2).

Step 2

The original English version of SATIS-Stroke and the two initial drafts (D_1 and D_2) were reviewed by the same translators involved in Step 1. Any discrepancies between D_1 and D_2 were discussed, and a consensus version was drafted ($D_{1–2}$).

Step 3

Next, the $D_{1–2}$ version was backward translated by two different independent translators blinded to the original version of SATIS- Stroke. One translator is a physiotherapist with more than 20

years of clinical experience in rehabilitation, and the other is a professional translator with no background in medicine or rehabilitation. Both translators are fluent in Cantonese and English. This step yielded two independent back-translated versions (BD_1 and BD_2). BD_1 and BD_2 were compared with the original English version to determine the validity of the translated version. The Cantonese version (C-SATIS-Stroke) was then generated.

Step 4

A panel of five experts – two physiotherapists with more than 15 years of clinical experience in rehabilitation, two nurses with more than 10 years of nursing experience, and two healthcare professionals – was convened. The expert panel evaluated C-SATIS-Stroke for cultural equivalence to the original English version in terms of content, semantics and conceptual and technical discrepancies. No discrepancies were identified in the back-translated version; hence, a pilot version of C-SATIS-Stroke was established.

Step 5

The pilot C-SATIS-Stroke was administered to 10 Chinese people with chronic stroke and five healthy older adults to ascertain its fluency, clarity, and comprehensibility. After completing the items of the pilot C-SATIS-Stroke, the participants were interviewed to discuss their opinions regarding the perceived limitations of the scale and any questions they had about each item of the questionnaire. No revisions to the pilot C-SATIS-Stroke were required, and the final C-SATIS-Stroke was established. The psychometric properties of the final C-SATIS-Stroke were tested using a larger sample.

Sample size determination

The sample size was derived using a formula for testing and estimating the coefficient alpha proposed by Bonett [16], with an a-value of 0.05, a b-value of 0.1, a k-value (number of items) of 36, a Cronbach's a (CA0) value of 0.0 at null hypothesis, an expected Cronbach's a (CA1) value of 0.7 and a power value of 0.90. Based on this analysis, a minimum of 30 people with chronic stroke were required for internal consistency. According to the guidelines of quality criteria for questionnaires [17], 50 people with chronic stroke were recruited for the test–retest analysis. To evaluate the ability of C-SATIS-Stroke to distinguish between different groups, a minimum of 50 people with chronic stroke and 50 healthy controls were required, with a CA0 value of 0.3 and a CA1 value of 0.7 [18]. To make a more robust decision about the correlations of C-SATIS-Stroke with other outcome measures [4,19], 101 people with chronic stroke were recruited for the study [20].

Participants

People with stroke (n =101) were recruited from a local rehabilitation network through poster advertisements. Participants were included if they (1) were aged 50–80 years, (2) were able to speak Chinese, (3) diagnosed with stroke using MRI or CT at least 1 year prior to the start of the study, (4) scored > 7 on the Chinese version of the Abbreviated Mental Test and (5) could walk independently for at least 10 m with or without an assistive device. Potential participants were excluded if they had (1) unstable medical conditions or (2) aphasia or hearing impairments that could affect data collection. Fifty healthy older adults aged 50–80 years with stable health were recruited as the control group. Those with neurological defects or cardiovascular disease that could affect proper assessment were excluded.

Data collection

All assessments were performed at a university-affiliated neurorehabilitation research laboratory. After providing informed consent, the participants completed a demographic data extraction form. On Day 1, the demographic data of all 101 participants were collected, and C-SATIS-Stroke was administered. The participants completed the Fugl–Meyer Assessment of the Upper Extremity (FMA-UE) and Lower Extremity (FMA-LE), Five Times Sit-to-Stand (FTSTS) test, Timed Up and Go (TUG) test, Six-Minute Walk Test (6MWT), Wolf Motor Function Test (WMFT), Berg Balance Scale (BBS), Activity-specific Balance Confidence (ABC) scale, Survey of Activities and Fear of Falling in the Elderly (SAFFE), Stroke Impact Scale (SIS) and Community Integration Measure (CIM) in a randomised order. After a 7-day interval (Day 2), 50 of the 101 people with stroke who participated in the Day-1 assessment were randomly selected to retake C-SATIS-Stroke for the test–retest reliability evaluation. The control participants only completed C-SATIS-Stroke on Day 1; their data were used to determine the known-group validity and cut-off scores. The known-group validity of C-SATIS-Stroke was determined according to the satisfaction levels that distinguish people with stroke from healthy older adults.

Outcome measures

SATIS-Stroke

SATIS-Stroke is used to assess the level of satisfaction of people with stroke in terms of activity and social participation in the environments they experience [11]. SATIS-Stroke has 36 items, and each item is rated on a 4-point scale, ranging from “0 = very dissatisfied” (individuals

unable to perform activities with assistance) to “3 = very satisfied” (individuals who can perform activities easily and independently) [12]. The activities and life situations not encountered in the previous 30 days can be marked “not applicable” or scored “0” [4]. For the total score, it is not sufficient to make quantitative comparisons because a unit progression in the total score does not necessarily indicate the same progression in satisfaction throughout the continuum. Such comparisons require a measurement unit that is constant and reproducible throughout the range of the variable measured [13]. Hence, the total SATIS- Stroke raw score (range: 0–108) has been transformed into a linear measure on a unidimensional scale expressed in ‘logits’ (5.11 to 5.08) using the Rasch model [11] to avoid measurement errors and increase the reliability of the general measure of satisfaction [4]. A higher value in logits corresponds to a higher degree of satisfaction in terms of activity and social participation. In addition, the transformation table provided by Pereira [4] can be used to identify which values in logits should be considered to obtain raw SATIS-Stroke scores.

FMA

The FMA is considered one of the most comprehensive quantitative assessment tools for evaluating motor function impairment in the upper and lower extremities in people with stroke [21]. The motor domain of FMA comprises 50 items measuring the reflex, movement and coordination of the shoulder, elbow, forearm, wrist, hand, hip, knee, and ankle [21]. Each item is scored on a 3- point scale ranging from 0 to 2, with maximum possible scores of 66 and 34 for the upper and lower limbs, respectively [21]. A higher score indicates a lower level of motor impairment [21]. The FMA has excellent intra-rater reliability (total score ICC = 0.98–0.99; upper extremity motor sub-score ICC = 0.995–0.996; lower extremity motor sub-score ICC =

0.96) and inter-rater reliability (total score ICC = 0.96; upper extremity motor sub-score ICC = 0.97; lower extremity motor sub-score ICC = 0.92) in people with chronic stroke [21,22].

FTSTS test

The FTSTS test is used to assess functional lower limb muscle strength in people with chronic stroke [23]. The FTSTS test measures the time taken to complete five repetitions of the sit-to-stand action. All sit-to-stand actions are performed on a chair nearly 43cm in height and 47.5 cm in depth, without an armrest. The average of three measurements is considered for analysis. The FTSTS test has shown excellent intra-rater reliability (ICC = 0.97–0.98), inter-rater reliability (ICC = 0.99) and test–retest reliability (ICC = 0.98–0.99) in people with chronic stroke [23].

TUG test

The TUG test is an objective clinical measurement used to assess functional mobility [24]. Individuals are instructed to rise from a chair, walk 3 m, turn, walk back and sit down. The time (in seconds) taken to complete the task is measured twice with a stopwatch. The mean time of two trials is calculated and recorded. The TUG test has shown excellent reliability (ICC = 0.95) in people with chronic stroke [24].

6MWT

The 6MWT is commonly used as a standardised outcome measure of exercise tolerance and functional walking capacity following stroke. The 6MWT has also been shown to be a

significant predictor of community ambulation and integration in individuals with stroke [25,26]. Participants are instructed to walk back and forth along a 20-m corridor, covering the maximum distance possible in 6 min and taking rest as needed. The maximum distance covered is then recorded [26]. The 6MWT has shown good intra- rater reliability (ICC = 0.78), interrater reliability (ICC = 0.75) and excellent test–retest reliability ($ICC_{2,1}$ = 0.98) in people with stroke [25,26].

WMFT

The WMFT is commonly used to assess upper extremity motor function after stroke [27]. This scale includes 17 items - 15 function- based tasks and two strength-based tasks - and yields three scores: a functional ability score, a time score (which quantifies the speed of performance in seconds) and a grip strength score [27]. The functional ability score is used for correlation data analysis. The functional ability score is calculated from 15 items rated on a 6-point ordinal scale, where 0 indicates no attempt to use the more affected upper extremity, and 5 indicates that the movement of the affected upper extremity may be normal. The maximum score is 75 [27]. The WMFT has good inter-rater reliability ($ICC_{3,1}$ = 0.93) and internal consistency (Cronbach's a = 0.92) in people with stroke [28].

BBS

The BBS measures functional balance in older adults and people with various disorders, including stroke [29]. The BBS comprises 14 items, scored from 0 to 4, with total scores between 0 and 56. A higher score indicates better balance. The BBS has shown excellent inter-

rater reliability (ICC = 0.95) and test–retest reliability ($ICC_{3,1}$ = 0.98) in people with chronic stroke [29].

ABC scale

The ABC scale is a 16-item outcome measure used to assess subjective balance confidence in daily activities [30]. The items are rated from 0 to 100. A score of 0 represents no confidence, and a score of 100 represents complete confidence. The total ABC score for each participant is calculated by summing the scores of individual items and then dividing the total by the number of items [31]. The ABC scale has shown good test–retest reliability (ICC = 0.85) and high internal consistency (Cronbach's a = 0.97) in people with chronic stroke [31].

SAFFE

SAFFE was developed to assess the effect of the fear of falling on activity restriction [32]. SAFFE assesses the respondent's fear of falling while performing 11 activities. Each activity is rated on a 4- point Likert scale (0 = not at all worried, 1 = slightly worried, 2 = somewhat worried and 3 = extremely worried). The total score on the scale is an unweighted sum of these 11 items, ranging from 0 to 33, with a higher score indicating increased fear [33,34]. SAFFE has shown good internal consistency (Cronbach's a = 0.95) among older Chinese adults [32,33].

SIS

The SIS is a self-reported questionnaire used to assess the subjective level of disability and health-related quality of life after stroke [35]. The SIS includes 59 items in eight domains and an extra question on stroke recovery. The difficulty an individual with stroke experiences in completing each item is rated on a 5-point Likert scale, ranging from "1 = unable to complete the item" to "5 = no difficulty experienced." Summative scores ranging from 0 to 100 are generated for each domain. The SIS has shown good test–retest reliability (ICC = 0.7–0.92), except in the emotion domain (ICC = 0.57), in people with stroke [35,36].

CIM

The CIM assesses the level of community integration [6]. The CIM has 10 items, and each item is rated on a 5-point scale, with total scores ranging from 10 to 50. Higher scores indicate higher levels of community integration. The Chinese version of the CIM has shown good test–retest reliability (ICC = 0.84) and internal consistency (Cronbach's a = 0.84) in people with chronic stroke [6].

Statistical analysis

The data were analysed using SPSS software version 26.0 (IBM Corporation, Armonk, NY, United States). The level of significance was set at a = 0.05. The Shapiro–Wilk statistic was applied to check data normality. Independent t-tests and Mann–Whitney U tests were used to assess between-group differences for parametric and non-parametric demographic data, respectively. Statistically significant differences between the expected and the observed frequencies in the categorical variables were calculated using the chi-square test.

The test–retest reliability was assessed using $ICC_{3,1}$, i.e., the ICC based on the 2-way mixed-effects model and single-rater type, according to the terminology proposed by Shrout and Fleiss [37,38]. Reliability was defined as excellent (ICC > 0.90), good (ICC = 0.75–0.90), moderate (ICC = 0.50 – 0.75) or poor (ICC < 0.50) [38]. Internal consistency was evaluated using Cronbach's a, which was rated as follows: 0.90 – 0.95 = very good, 0.80 to < 0.90 = good, 0.70 to < 0.80 = fair, 0.60 to < 0.7 = weak, and < 0.60 = unacceptable [7]. Item-level agreement and the weighted kappa value were used for item-level retest analysis. The kappa coefficient was defined as perfect (0.81–1), substantial (0.61–0.8), moderate (0.41–0.6), fair (0.21–0.4), slight (0.01–0.2) and poor (0) agreement [39]. The standard error of measurement (SEM) relative to the total score was rated as very good (< 5%), good (5% – 10%), doubtful (10% – 20%) or negative (> 20%) [40]. SEM was calculated using the formula SD * $\sqrt{(1-r)}$[41].

Minimal detectable changes (MDCs) are the minimal levels of changes that are not caused by chance variations in measurement and can be calculated using the formula SD×1.96×$\sqrt{2(1-r)}$ [42] at 95% confidence intervals. SD denotes the standard deviation of the baseline total C-SATIS-Stroke score, and *r* denotes the test–retest reliability coefficient.

Correlations between C-SATIS-Stroke and stroke-specific outcome measures were evaluated under the structure of the ICF framework. The body structure and function domain included the FMA, FMA-UE, FMA-LE and FTSTS test. The activity domain included the TUG test, 6MWT, WMFT, BBS, ABC scale and SAFFE. The participation domain included the SIS and CIM. Spearman's rho and Pearson's correlation coefficient were used to analyse the correlations between stroke-specific outcome variables for non-normally and normally distributed data, respectively. The correlation strength was rated as good to excellent ($r > 0.75$), moderate to good ($r = 0.50 – 0.75$), fair ($r = 0.25 – 0.49$), or little or no correlation ($r < 0.25$)

[43]. To compare C-SATIS-Stroke scores between people with stroke and healthy controls, the known- group validity was evaluated using independent t-tests and Mann–Whitney U tests for parametric and non-parametric data, respectively.

ROC curves were applied to identify the optimal cut-off score to distinguish people with stroke from healthy older adults using C-SATIS-Stroke. Area under the curve (AUC) values of < 0.5, $0.5 – 0.7$, $0.7 – 0.8$, $0.8 – 0.9$ and > 0.9 indicate no, poor, acceptable, excellent and outstanding discrimination, respectively [40]. Youden's index was used to determine the trade-off between maximum sensitivity and specificity.

Ceiling and floor effects were calculated according to the percentages of participants with the highest (ceiling) and lowest (floor) scores, respectively. Ceiling and/or floor effects for each item are considered to exist when at least 15% of the participants obtain the maximum or minimum scores, respectively [17].

Results

Translation and cross-cultural adaptation

SATIS-Stroke was translated from English to Chinese (Cantonese) using the standardised translation procedure. No ambiguity was reported by the bilingual translators or participants during pilot testing. Our expert panel also confirmed the cultural relevancy and linguistic equivalence of the Chinese (Cantonese) version of SATIS-Stroke.

Participant characteristics

A total of 101 people with chronic stroke and 50 healthy older adults were recruited; the mean ages of the participants were 63.82 (SD 6.4) and 61.58 (SD 7.56) years, respectively (Table 1). There were no differences in mobility status between the stroke and control groups (Table 2).

Reliability and measurement error (SEM and MDC)

The $ICC_{3,1}$ for the test–retest reliability was 0.913 for the total C- SATIS-Stroke score (95% CI: 0.861–0.946, $P < 0.001$) and ranged from 0.836 (95% CI: 0.827–0.845, $p < 0.001$) to 0.854 (95% CI: 0.845–0.862, $p < 0.001$) for the individual C-SATIS-Stroke items (Supplementary Table I). The weighted kappa value was 0.212–0.622 (Table 3). The internal consistency (Cronbach's a) of C-SATIS-Stroke was 0.959 (Table 4). The SEM and MDC were 63 (0.36 in logits) and 78 (1.0 in logits), respectively.

Known-group validity

Known-group validity was evaluated to compare the C-SATIS-Stroke total scores and item scores between people with stroke and healthy controls. The control group demonstrated higher levels of satisfaction in terms of activity and social participation (Table 5), except on item 17 (participating in spousal relationships).

Correlations with other outcome measures

The correlations between C-SATIS-Stroke scores and stroke-specific outcome measures are shown in Table 6. The mean C-SATIS- Stroke scores were not significantly correlated with the mean FMA, FTSTS, TUG test, WMFT or BBS scores or the 6MWT distance. The C-SATIS-Stroke scores had significant positive fair-to-moderate correlations with the ABC, SIS and CIM scores and a significant negative moderate correlation with the SAFFE score.

Cut-off score

A C-SATIS-Stroke cut-off score of 80 (1.035 in logits) was identified. The ROC curve yielded an AUC of 0.779, with a sensitivity of 77% and specificity of 72% of Youden's index (Figure 2).

Ceiling and floor effects

Except for items 2, 8, 9, 29, 31 and 36, all items had ceiling effects higher than the acceptable standards (≥ 15%). No floor effects were identified (Table 7).

Discussion

Our study reports the first translation of the original SATIS-Stroke version into Cantonese. In the present study, C-SATIS-Stroke demonstrated excellent test–retest reliability and internal consistency in people with stroke. Except for item 17 (i.e., participation in spousal relationships), the healthy controls had higher levels of satisfaction regarding social participation for all items than did people with chronic stroke. The C-SATIS-Stroke scores were significantly correlated with the ABC and SAFFE scores in the activity domain and the

SIS and CIM scores in the participation domain. To differentiate the levels of satisfaction and social participation between people with stroke and healthy controls, we propose a score of 80 as the optimal C-SATIS-Stroke cut-off score. C-SATIS- Stroke had ceiling effects but not floor effects.

Test–retest reliability

The excellent test–retest reliability of both the total ($ICC_{3,1}$ = 0.913) and individual item ($ICC_{3,1}$ = 0.845–0.856) scores indicates that C-SATIS-Stroke is a reliable outcome measure for clinical use among Chinese people with chronic stroke. These findings are consistent with those of two previous studies reporting good inter-observer and intra-observer reliability ($ICC_{2,1}$ = 0.89–0.90 and 0.90–0.93, respectively) [4,7]. These excellent results may be attributable to two reasons. First, people with chronic stroke (6.74 ± 4.42 years) whose potential functional recovery may have plateaued were included in our study, which may explain the low test–retest variability. Second, our standardised experimental protocol and the explicit instructions shared by our well-trained raters might have helped to minimise measurement errors. The strength of agreement amongst the 36 items of the C-SATIS- Stroke was slight to substantial. The relatively consistent responses from participants may indicate that the translation and cultural adaptation was appropriate.

Internal consistency

Cronbach's a coefficients were excellent for the individual items (Cronbach's a = 0.957–0.961) and the total scores (Cronbach's a = 0.959) of C-SATIS-Stroke, indicating that all individual items had good internal consistency. Our results are consistent with Pereira et al. [7], who

reported good internal consistency among the SATIS-Stroke items (Cronbach's a = 0.93–0.94 for individual scores). The high internal consistency among the C-SATIS-Stroke items may indicate that the individual items were within the same concept and domain. Whether this high internal consistency is due to item redundancy warrants further investigation.

SEM and MDC

We quantified the measurement error of C-SATIS-Stroke in people with chronic stroke using the SEM and MDC. The SEM reported in this study was 63, equivalent to 0.36 in logits, representing approximately 3.5% of the total C-SATIS-Stroke score (0.36 in logits/10.19 in logits). This finding is consistent with Pereira et al. [4], who reported that 62 was equivalent to 0.31 in logits, representing 3.04% of the total SATIS-Stroke score (0.31 in logits/10.19 in logits). Our SEM result indicates that the measurement error represents only a small portion of the total C-SATIS-Stroke score range.

The MDC in this study was 78, equivalent to 1.0 in logits, representing 9.8% of the total score range, similar to a previous report that 88 was equivalent to 1.49 in logits, representing 14.62% of the total SATIS-Stroke score [4]. Furthermore, our MDC result indicates that a C-SATIS-Stroke score of at least 78 (1.0 in logits) is required to be considered a true change in the respondent's satisfaction levels in terms of activity and social participation. The difference in the cut-off score of C-SATIS-Stroke [1.035 (in logits)] between people with stroke and healthy controls surpassed the calculated MDC [1.0 (in logits)]. This between-group disparity suggests a genuine difference rather than a measurement error.

Known-group validity

For all items of C-SATIS-Stroke except 17, the satisfaction levels in terms of activity and social participation among people with stroke were significantly lower than those among healthy controls. A possible reason may be that people with stroke may experience cognitive and physical deterioration (motor disabilities, sensory deficits, aphasia or mood disorders) [44], which may worsen their ability to execute movements, perform activities of daily living (ADL) and participate in social events compared with healthy older adults. However, our stroke participants had mild levels of functional impairment (FMA-UE = 44.70, FMA-LE mean score = 26.12), which might not have affected bonding between couples. This could explain why no significant difference was noted for item 17 of C-SATIS-Stroke between the two groups.

Correlations with other outcome measures

Contrary to our expectations, the C-SATIS-Stroke scores were not correlated with the FMA scores, FTSTS scores, TUG scores, 6MWT distance or WMFT scores in the body structure and function and activity domains. These results were consistent with those of a previous study by Bouffioulx [45], who reported that body functions and manual ability could predict only 43% of the variation in SATIS-Stroke measures during the chronic stroke stage. The respondents' levels of satisfaction in terms of activity and social participation depend on complex interactions between personal (cognitive status, motivation, adaptability, etc.), functional and environmental factors (health services, financial support, patient's habits, etc.) [45], not just body functions and activities.

The C-SATIS-Stroke score was significantly correlated with the ABC scores but not the BBS scores in the activity domain. These differences could be due to the differences in the balance

assessment targets between the BBS and ABC. The BBS evaluates functional balance and fall risk during specifically designed movements [46] and may not interact with contextual factors, such as the patients' social (e.g., human assistance) and physical (e.g., technical assistance) environments [45]. In contrast, the ABC scale assesses a person's self-perceived level of confidence in their ability to maintain the balance required for performing ADL [30]. Most ADLs in the ABC scale are social activities (e.g., getting in and out of a car, walking up and down stairs, sweeping the floor), which may explain why the C-SATIS-Stroke score was correlated with the ABC score in this study.

To our knowledge, our study is the first to demonstrate that C-SATIS-Stroke scores are significantly correlated with SAFFE scores. SAFFE is an outcome measure used to evaluate fear avoidance behaviours caused by the fear of falling by quantifying self-perceived and observable ADLs and instrumental ADLs [33,47]. Thus, an increased fear of falling may lead to self-induced restriction in physical activity participation, in turn reducing the satisfaction levels in terms of independence in ADLs measured by the C- SATIS-Stroke.

Our study is also the first to explore the correlation between the C-SATIS-Stroke and SIS scores. The results demonstrated that seven domains of SIS had significant fair correlations with C- SATIS-Stroke and the participation domain had a significant moderate correlation. SIS is a self-report questionnaire that evaluates disability and health-related quality of life after stroke [48]. C- SATIS-Stroke is used to evaluate the satisfaction with activity and participation of people with stroke in their real-life environments. In addition to assessing ADLs and physical function, SIS also assesses impairment in the cognitive domain, memory and thinking [49]. Some studies using regression analysis showed that muscle strength and mobility respectively predicted 32% and 39% of the variance in social participation in people with

chronic stroke [50], emotional aspects predicted only 10% of the variance in social participation in people with chronic stroke [51] and cognitive ability had a low correlation with social participation in people with subacute stroke [52]. However, some personal factors (e.g., motivation or adaptability) and environmental factors (e.g., health services, financial support or the habits of people with stroke) would also be important interaction components with social participation [45]. Hence, the strength, memory, thinking, emotion, communication, ADL, mobility and hand function domains assessed by SIS only showed significant fair correlations with the C-SATIS-Stroke score.

As expected, the C-SATIS-Stroke scores had significant moderate correlations with the SIS and CIM scores in the participation domain. The participation domain of SIS mainly evaluates social ADLs, and its significant moderate correlation with C-SATIS-Stroke may be attributable to the use of the same ICF construct and domain and similar evaluation contents. CIM is a subjective outcome measure of community integration that considers the self-reported subjective feelings of participants [6]. In contrast, C-SATIS-Stroke is a subjective outcome measure of satisfaction with activities and participation. In addition, personal perceptions and social factors play an important role in patients' subjective feelings during social participation [45]. Both C-SATIS-Stroke and CIM consider not only the patient's perceptions of social participation but also the environmental factors that affect stroke recovery.

Optimal cut-off score

Our results showed that a score of 80 (1.035 in logits) is sensitive for separating people with chronic stroke from healthy older adults, with an AUC of 0.779, sensitivity of 77% and specificity of 72% of Youden's index. The AUC indicates that the C-SATIS-Stroke is

acceptably accurate in discriminating between those two groups. Thus, the C-SATIS-Stroke is a sensitive and specific test for identifying people with stroke who have limitations in activity and social participation.

Ceiling and floor effects

C-SATIS-Stroke had ceiling effects but not floor effects, which might be attributable to two possibilities. First, we sampled people with chronic stroke in stable physical condition and with maximum functional recovery, which may have enabled them to have a greater acceptance of and adaptation to ADLs, leading to higher satisfaction scores. Second, the participants in this study used walking aids (e.g., sticks or small- or large-based quadripod canes), which may have led to more participation in social activities and reduced their difficulties in performing ADLs, thus increasing their perceived satisfaction level.

Limitations

Several limitations of this study need to be acknowledged. First, only 50 healthy older adults and 101 people with chronic stroke participated in the reliability, validity, and correlation analyses. The limited sample size hindered our ability to conduct advanced analyses, such as factor analysis. Hence, studies with a larger sample size are needed to draw more robust conclusions regarding the psychometric properties of this questionnaire. Second, our participants were recruited from a local self-help group and had high levels of motor function recovery. Future studies should include participants with lower levels of motor function recovery to ensure that the results can be generalised to the general stroke population. Third, the participants included in the correlation analysis were only matched by age. Future studies

are needed to determine whether the subjective level of satisfaction with activities and social participation is affected by other parameters, such as gender or BMI. Fourth, as the incidence of stroke is associated with age and doubles each decade after 55 years [44], only participants ≥ 50 years old were recruited for this study. Additional investigations should explore and confirm the applicability of C- SATIS-Stroke to younger people with stroke.

Conclusions and clinical implications

The final version of C-SATIS-Stroke exhibited satisfactory semantic, idiomatic, cultural, and conceptual equivalence to the original version. C-SATIS-Stroke exhibited excellent reliability and validity and could differentiate between people with stroke and healthy controls in terms of their levels of satisfaction with activity and social participation. These findings will facilitate the identification of limitations and restrictions that Chinese people with chronic stroke may experience in activities and social participation. However, high-quality studies with larger sample sizes are warranted to clarify the uncertain aspects of C-SATIS-Stroke as a tool for evaluating Chinese people with chronic stroke.

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Ethical approval

Ethical approval was obtained from the Departmental Research Committee of the Hong. Kong Polytechnic University (Approval number: HSEARS20210110002).

Author contributions

S.S.M.N. conceived the original idea and T.W.L. planned the experiments. H.P., J.T., S.S.L.L., C.S.K.L., C.C.C.C., and C.Y.Y.L. carried out the experiments, performed the analytic calculations and S.S.M.N. and T.W.L.W supervised the project. H.P. wrote the manuscript. All authors discussed the results and contributed to the final manuscript.

Disclosure statement

The authors declared no potential conflicts of interest regarding the research, authorship, and publication of this article.

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References

[1] Campbell BCV, Khatri P. Stroke. Lancet. 2020;396(10244): 129–142.

[2] Sevick LK, Ghali S, Hill MD, et al. Systematic review of the cost and cost-effectiveness of rapid endovascular therapy for acute ischemic stroke. Stroke. 2017;48(9):2519–2526.

[3] Pollock A, Farmer SE, Brady MC, et al. Interventions for improving upper limb function after stroke. Cochrane Database Syst Rev. 2014;2014(11):CD010820.

[4] Pereira GS, Corrêa FI, Júlio CE, et al. Clinimetric properties of the satis-stroke questionnaire in the brazilian population: A satisfaction assessment measure addressing activities and participation after a stroke. Braz J Phys Ther. 2021; 25 (6): 719-726.

[5] Veerbeek JM, Kwakkel G, van Wegen EE, et al. Early prediction of outcome of activities of daily living after stroke: a systematic review. Stroke. 2011;42(5):1482–1488.

[6] Liu TW, Ng SS, Ng GY. Translation and initial validation of the Chinese (Cantonese) version of community integration measure for use in patients with chronic stroke. Biomed Res Int. 2014; 2014: 623836.

[7] Pereira GS, Silva SM, Julio CE, et al. Translation and cross-cultural adaptation of SATIS-Stroke for use in Brazil: a satisfaction measure of activities and participation in stroke survivors. Biomed Res Int. 2019; 2019: 8054640.

[8] Rauch A, Cieza A, Stucki G. How to apply the International Classification of Functioning, Disability and Health (ICF) for rehabilitation management in clinical practice. Eur J Phys Rehabil Med. 2008;44(3):329–342.

[9] Tse T, Douglas J, Lentin P, et al. Measuring participation after stroke: a review of frequently used tools. Arch Phys Med Rehabil. 2013;94(1):177–192.

[10] Kossi O, Amanzonwe ER, Thonnard JL, et al. Applicability of International Classification of Functioning, Disability and Health-based participation measures in stroke survivors in Africa: a systematic review. Int J Rehabil Res. 2020;43(1): 3–11.

[11] Bouffioulx E, Arnould C, Vandervelde L, et al. Changes in satisfaction with activities and participation between acute, post-acute and chronic stroke phases: a responsiveness study of the SATIS-Stroke questionnaire. J Rehabil Med. 2010;42(10):944–948.

[12] Bouffioulx E, Arnould C, Thonnard JL. SATIS-Stroke: a satisfaction measure of activities and participation in the actual environment experienced by patients with chronic stroke. J Rehabil Med. 2008;40(10):836–843.

[13] Bouffioulx E. Satisfaction with activity and participation in patients with stroke [dissertation]. Prom: Universtity of Groningen; 2011.

[14] Kottner J, Audige L, Brorson S, et al. Guidelines for reporting reliability and agreement studies (GRRAS) were proposed. Int J Nurs Stud. 2011;48(6):661–671.

[15] Beaton DE, Bombardier C, Guillemin F, et al. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000;25(24):3186–3191.

[16] Bonett DG. Sample size requirements for comparing two alpha coefficients. Appl Psychol Measure. 2003;27(1):72–74.

[17] Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health statusquestionnaires. J Clin Epidemiol. 2007;60(1):34–42.

[18] Bujang MA, Omar ED, Baharum NA. A review on sample size determination for Cronbach's alpha test: a simple guide for researchers. Malays J Med Sci. 2018;25(6):85–99.

[19] Hobart JC, Cano SJ, Warner TT, et al. What sample sizes for reliability and validity studies in neurology? J Neurol. 2012; 259(12):2681–2694.

[20] Arafat SY, Chowdhury HR, Qusar M, et al. Cross cultural adaptation & psychometric validation of research instruments: a methodological review. J Behav Health. 2016;5(3): 129–136.

[21] Gladstone DJ, Danells CJ, Black SE. The Fugl-Meyer Assessment of motor recovery after stroke: a critical review of its measurement properties. Neurorehabil Neural Repair. 2002;16(3):232–240.

[22] Duncan PW, Propst M, Nelson SG. Reliability of the Fugl- Meyer Assessment of sensorimotor recovery following cerebrovascular accident. Phys Ther. 1983;63(10):1606–1610.

[23] Mong Y, Teo TW, Ng SS. 5-Repetition sit-to-stand test in subjects with chronic stroke: reliability and validity. Arch Phys Med Rehabil. 2010;91(3):407–413.

[24] Ng SS, Hui-Chan CW. The timed up & go test: its reliability and association with lower-limb impairments and locomotor capacities in people with chronic stroke. Arch Phys Med Rehabil. 2005;86(8):1641–1647.

[25] Macchiavelli A, Giffone A, Ferrarello F, et al. Reliability of the six-minute walk test in individuals with stroke: systematic review and meta-analysis. Neurol Sci. 2021;42(1):81–87.

[26] Liu J, Drutz C, Kumar R, et al. Use of the six-minute walk test poststroke: is there a practice effect? Arch Phys Med Rehabil. 2008;89(9):1686–1692.

[27] Edwards DF, Lang CE, Wagner JM, et al. An evaluation of the wolf motor function test in motor trials early after stroke. Arch Phys Med Rehabil. 2012;93(4):660–668.

[28] Morris DM, Uswatte G, Crago JE, et al. The reliability of the wolf motor function test for assessing upper extremity function after stroke. Arch Phys Med Rehabil. 2001;82(6): 750–755.

[29] Hiengkaew V, Jitaree K, Chaiyawat P. Minimal detectable changes of the berg balance scale, Fugl-Meyer Assessment scale, timed "up & go" test, gait speeds, and 2-minute walk test in individuals with chronic stroke with different degrees of ankle plantarflexor tone. Arch Phys Med Rehabil. 2012;93(7):1201–1208.

[30] Mak MK, Lau AL, Law FS, et al. Validation of the Chinese translated activities-specific balance confidence scale. Arch Phys Med Rehabil. 2007;88(4):496–503.

[31] Botner EM, Miller WC, Eng JJ. Measurement properties of the activities-specific balance confidence scale among individuals with stroke. Disabil Rehabil. 2005;27(4):156–163.

[32] Lachman ME, Howland J, Tennstedt S, et al. Fear of falling and activity restriction: the survey of activities and fear of falling in the elderly (safe). J Gerontol B Psychol Sci Soc Sci. 1998;53(1):P43–50.

[33] Chou KL, Yeung FK, Wong EC. Fear of falling and depressivesymptoms in Chinese elderly living in nursing homes: fall efficacy and activity level as mediator or moderator? Aging Ment Health. 2005;9(3):255–261.

[34] Hornyak V, Brach JS, Wert DM, et al. What is the relation between fear of falling and physical activity in older adults? Arch Phys Med Rehabil. 2013;94(12):2529–2534.

[35] Vellone E, Savini S, Fida R, et al. Psychometric evaluation of the Stroke Impact Scale 3.0. J Cardiovasc Nurs. 2015;30(3):229–241.

[36] Duncan PW, Wallace D, Lai SM, et al. The Stroke Impact Scale version 2.0. Evaluation of reliability, validity, and sensitivity to change. Stroke. 1999;30(10):2131–2140.

[37] Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. 1979;86(2):420–428.

[38] Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155–163.

[39] Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159–174.

[40] Portney LG, Watkins MP. Foundations of clinical research: applications to practice. London: Pearsons; 2013.

[41] Stratford PW. Estimating the standard error of measurement from reliability studies. Physiother Can. 2004;56(1): 27–30.

[42] Haley SM, Fragala-Pinkham MA. Interpreting change scores of tests and measures used in physical therapy. Phys Ther. 2006;86(5):735–743.

[43] Kline P. The handbook of psychological testing. 2nd ed. London: Routledge; 2000.

[44] Ng SSM, Liu TW, Tsoh J, et al. Psychometric properties of the trail walking test for people with stroke. Front Neurol. 2022;13:821670.

[45] Bouffioulx E, Arnould C, Thonnard JL. Satisfaction with activity and participation and its relationships with body functions, activities, or environmental factors in stroke patients. Arch Phys Med Rehabil. 2011;92(9):1404–1410.

[46] Berg K, Wood-Dauphine S, Williams J, et al. Measuring balance in the elderly: preliminary development of an instrument. Physiotherapy Canada. 1989;41(6):304–311.

[47] Liu TW, Ng SSM. The reliability and validity of the survey of activities and fear of falling in the elderly for assessing fear and activity avoidance among stroke survivors. PLoS One. 2019;14(4):e0214796.

[48] Mulder M, Nijland R. Stroke impact scale. J Physiother. 2016;62(2):117.):

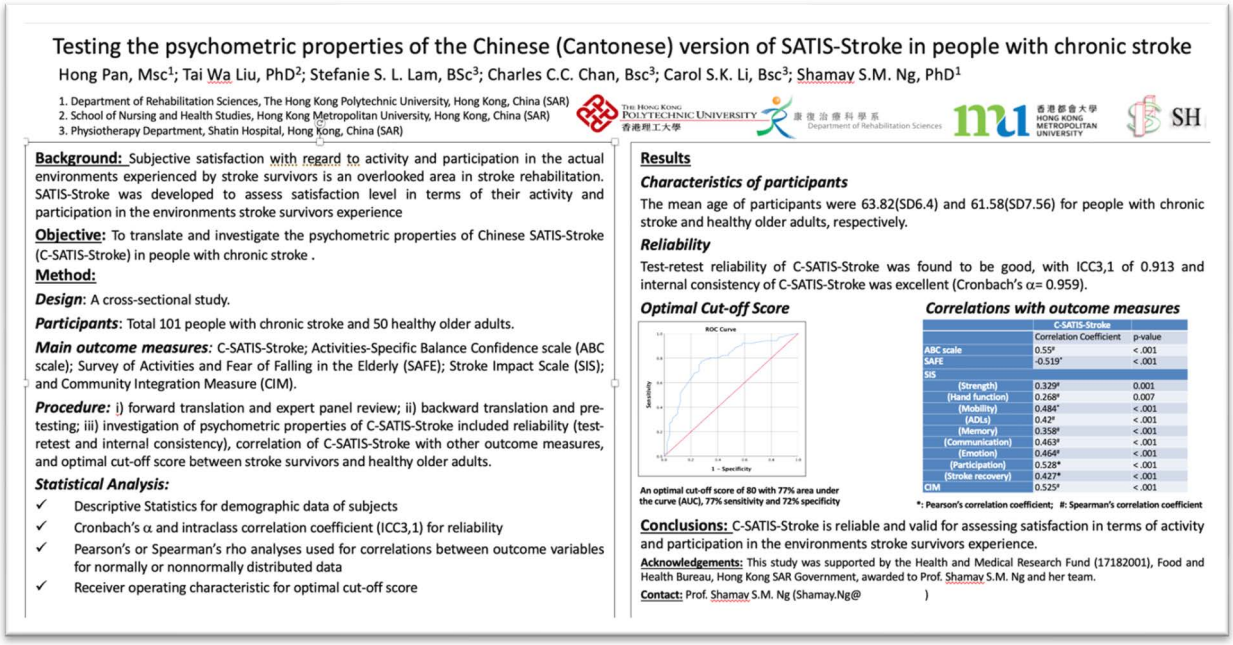
[49] Lin KC, Fu T, Wu CY, et al. Psychometric comparisons of the Stroke Impact Scale 3.0 and stroke-specific quality of life scale. Qual Life Res. 2010;19(3):435–443.

[50] Cohen JW, Ivanova TD, Brouwer B, et al. Do performance measures of strength, balance, and mobility predict quality of life and community reintegration after stroke? Arch Phys Med Rehabil. 2018;99(4):713–719.

[51] Faria-Fortini I, Basilio ML, Scianni AA, et al. Performance and capacity-based measures of locomotion, compared to impairment-based measures, best predicted participation in individuals with hemiparesis due to stroke. Disabil Rehabil. 2018;40(15):1791–1798.

[52] Adamit T, Maeir A, Ben Assayag E, et al. Impact of first-ever mild stroke on participation at 3 and 6 month post-event: the Tabasco study. Disabil Rehabil. 2015;37(8):667–673.

Appendix 5.3 The poster of "Testing the psychometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke" demonstrated in 10th World Congress for Neurorehabilitation.



Testing the psychometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke

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Background: Subjective satisfaction with regard to activity and participation in the actual environments experienced by stroke survivors is an overlooked area in stroke rehabilitation. SATIS-Stroke was developed to assess satisfaction level in terms of their activity and participation in the environments stroke survivors experience

Objective: To translate and investigate the psychometric properties of Chinese SATIS-Stroke (C-SATIS-Stroke) in people with chronic stroke .

Method:

Design: A cross-sectional study.

Participants: Total 101 people with chronic stroke and 50 healthy older adults.

Main outcome measures: C-SATIS-Stroke; Activities-Specific Balance Confidence scale (ABC scale); Survey of Activities and Fear of Falling in the Elderly (SAFE); Stroke Impact Scale (SIS); and Community Integration Measure (CIM).

Procedure: i) forward translation and expert panel review; ii) backward translation and pre-testing; iii) investigation of psychometric properties of C-SATIS-Stroke included reliability (test-retest and internal consistency), correlation of C-SATIS-Stroke with other outcome measures, and optimal cut-off score between stroke survivors and healthy older adults.

Statistical Analysis:

- ✓ Descriptive Statistics for demographic data of subjects
- ✓ Cronbach's α and intraclass correlation coefficient (ICC3,1) for reliability
- ✓ Pearson's or Spearman's rho analyses used for correlations between outcome variables for normally or nonnormally distributed data
- ✓ Receiver operating characteristic for optimal cut-off score

Results

Characteristics of participants

The mean age of participants were 63.82(SD6.4) and 61.58(SD7.56) for people with chronic stroke and healthy older adults, respectively.

Reliability

Test-retest reliability of C-SATIS-Stroke was found to be good, with ICC3,1 of 0.913 and internal consistency of C-SATIS-Stroke was excellent (Cronbach's α= 0.959).

Optimal Cut-off Score

An optimal cut-off score of 80 with 77% area under the curve (AUC), 77% sensitivity and 72% specificity

Correlations with outcome measures

	C-SATIS-Stroke	
	Correlation Coefficient	p-value
ABC scale	0.55*	< .001
SAFE	-0.519*	< .001
SIS		
(Strength)	0.329#	0.001
(Hand function)	0.268#	0.007
(Mobility)	0.484*	< .001
(ADLs)	0.42#	< .001
(Memory)	0.358#	< .001
(Communication)	0.463#	< .001
(Emotion)	0.464#	< .001
(Participation)	0.528*	< .001
(Stroke recovery)	0.427#	< .001
CIM	0.525#	< .001

*: Pearson's correlation coefficient; #: Spearman's correlation coefficient

Conclusions: C-SATIS-Stroke is reliable and valid for assessing satisfaction in terms of activity and participation in the environments stroke survivors experience.

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Contact: Prof. Shamay S.M. Ng (Shamay.Ng@)

Appendix 6.1 The consent form of the randomized control trial at Shatin Hospital

The Hong Kong Polytechnic University

Department of Rehabilitation Sciences

Project entitled: A randomized controlled trial of upper limb training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper limb motor functions in people with stroke having post-stroke duration from 3 weeks to 6 months

Investigator: Prof. Shamay S. M. Ng

Purpose:

To investigate whether mirror therapy (MT) combined with transcutaneous electrical nerve stimulation (TENS) would be superior to Sham-mirror therapy with TENS in improving upper limb motor functions in people with stroke having post-stroke duration from 3 weeks to 6 months.

Methods:

All eligible subjects will be randomly assigned into 2 groups: (1) mirror therapy combined with bilateral transcutaneous electrical nerve stimulation over both paretic and non-paretic upper limb (bilateral-TENS) and (2) Sham-mirror therapy combined with bilateral transcutaneous electrical nerve stimulation over both paretic and non-paretic upper limb (bilateral TENS) respectively for 8 weeks, 2 times a week (total 16 treatment sessions).

Subjects will be assessed on improvement of Fugl Meyer Assessment Upper Extremity Portion, Wolf Motor Function test, maximum paretic hand grip strength, Jacket Test, Upper Extremity Functional Index, Motor Activity Log, Stroke Impact Scale, Community Integration Measure, and SATIS-Stroke. Each assessment session will last for 45 minutes. The procedures of each assessment will be explained fully. The treatment venue will be in the Physiotherapy Department in the Geriatric Day Hospital at Shatin Hospital.

Potential Risks and Benefits:

The major benefit from participating in this study is that subjects may have the opportunity to know their own level of motor functions of their upper limbs. The results may also be beneficial for planning an intensive rehabilitation program for improving upper limb motor functions in patients with stroke. The mirror therapy, TENS, upper limb training, and testing procedures have been well proved to be safe and used with negligible side effects, both clinically and experimentally. A few subjects may feel some exhaustion during assessment and therefore rest will be allowed between assessment procedures.

Informed Consent:

I, _____, understand the details of this study. I voluntarily consent to participate in this study. I understand that I can withdraw from this study at any time without giving reasons, and my withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential risk in joining this study. I also understand that my personal information will not be disclosed to people who are not related to this study and my name will not appear on any publications resulted from this study.

I can contact the chief investigator, Prof. Shamay Ng at telephone 2766-4889 for any questions about this study. If I have complaints related to the investigators, I can contact Ms. Chung secretary of Departmental Research Committee, at 2766-4329. I know I will be given a signed copy of this consent form.

Signature (participant): _____ Date: _____

Signature (Witness): _____ Date: _____

香港理工大學康復治療科學系參加研究同意書

科研題目: 隨機對照臨床試驗: 上肢訓練配合鏡子治療及經皮神經電刺激對改善中風後 3 周至 6 個月病人的上肢功能之功效

科研人員: 伍尚美教授

科研目的及內容: 旨在研究鏡子治療配合經皮神經電刺激的治療，是否比偽鏡子治療配合經皮神經電刺激，更有效於改善中風後 3 周至 6 個月病人的上肢功能之功效

研究方法: 所有合資格參加者會被隨機分為兩組，第一組：鏡子治療配合經皮神經電刺激，第二組：偽鏡子治療配合經皮神經電刺激。參加者接受為期八星期，每星期兩次（共十六次治療）。參加者並於接受鏡子治療配合經皮神經電刺激或偽鏡子治療配合經皮神經電刺激期間，同時進行上肢訓練，每次治療需時約三十分鐘。參加者將會接受上肢的功能、日常生活運用、及社區融合等測試，以評估進展，每次檢查需時約四十五分鐘。研究人員將會向閣下詳細解釋測試的方法。參加治療地點拟設於沙田醫院老人日間醫院物理治療部.

潛在危險性及得益: 若參與此研究，參加者可以了解自己的上肢功能的表現，此外亦能提供重要數據幫助設計給中風患者改善上肢功能的康復治療。鏡子治療、經皮神經電刺激、上肢的控制訓練和整個檢查程序都經過驗證，證明過程十分安全，不論在臨床上或實驗上，其副作用都可以忽略，唯期間小部份參與人士可能會感到少許疲倦，參加者可按需要於測試期間作中段休息。

同意書：

本人_____已瞭解此次研究的具體情況。本人願意參加此次研究, 本人有權在任何時候、無任何原因的情況下放棄參與此次研究, 而此舉不會導致本人受到任何懲

罰或不公平的對待。本人明白參加此研究課題的潛在危險性以及本人的資料將不會洩露給與此研究無關的人員，我的名字或相片也不會出現在任何的出版物上。

本人可以用電話 2766 4889 來聯繫此次研究課題的負責人，伍尚美教授。若本人對研究人員有任何投訴，可以聯繫鍾女士（部門科研委員會秘書），電話：2766 4329。本人亦明白，參與此研究課題需要本人簽署一份同意書。

簽名（參與者）：_____ 日期：_____

簽名（證人）：_____ 日期：_____

Appendix 6.2 The ethic approved by The Chinese University of Hong Kong

香港中文大學醫學院
Faculty Of Medicine
The Chinese University Of Hong Kong

醫院管理局
新界東醫院聯網
Hospital Authority
New Territories East Cluster

Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee
香港中文大學-新界東醫院聯網 臨床研究倫理 聯席委員會

8/F, Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, Shatin, HK
Tel : (852) 3505 3935 / 2144 5926 Fax : (852) 2646 6653 Website : http://www.crec.cuhk.edu.hk

The Joint CUHK-NTEC CREC is an independent committee established by CUHK/NTEC and authorized to perform ethics and scientific review and oversight of clinical studies within the jurisdiction of CUHK/NTEC in accordance with its standard operating procedure and the principles of the Declaration of Helsinki and ICH Good Clinical Practice.

CREC Ref. No.: 2019.665-T

20 JAN '23

To: Ms. Stefanie So Ling LAM
Physiotherapy Department
Shatin Hospital

This notice is issued by the Joint CUHK-NTEC CREC with respect to the application/submission by you, being the principal investigator of the following study at your study site:

- **Study Protocol Title:** Randomized controlled trial of upper limb training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper limb functions in patients with sub-acute stroke
- **Investigator(s):** Stefanie So Ling LAM, Shamay Sheung Mei NG, Charles Wai Kin LAI, Raymond Chi Keung CHUNG, Winnie Wing Ling NG, Maria Wing Sze TANG, Elsie HUI, Jean WOO and Carol Suk Kuen LI

In accordance with our standard operating procedure, we have duly performed ethics and scientific review of your application/submission as detailed below:

- **Nature of Your Application/Submission:** ☐ Initial application ☐ Amendments/changes ☐ Others: ☒ Renewal
- **Mode of Review:** ☐ Full review ☒ Expedited review
- **Date of Initial/Renewal Approval:** 22 January 2023
- **Document(s) Reviewed:** See Schedule 1
- **Reviewer(s):** See Schedule 2

After due review by our reviewer(s), we hereby write to inform you of our decision on your application/submission as follows:

- **Decision:**
  - ☐ Application/Submission approved
  - ☐ Application/Submission approved with condition(s) (see condition(s) below)
  - ☒ Application/Submission approved with remark(s) (see remark(s) below)
  - ☐ Application/Submission approved with condition(s) and remark(s) (see condition(s) and remark(s) below)
- **Remark(s):** Certificate of Insurance dated 20 October 2021 covering period from 01 October 2021 to 30 September 2022

香港中文大學醫學院
Faculty Of Medicine
The Chinese University Of Hong Kong

醫院管理局
新界東醫院聯網
Hospital Authority
New Territories East Cluster

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香港中文大學-新界東醫院聯網 臨床研究倫理 聯席委員會

8/F, Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, Shatin, HK
Tel : (852) 3505 3935 / 2144 5926 Fax : (852) 2646 6653 Website : http://www.crec.cuhk.edu.hk

20 JAN '20

• **Regular Progress Report(s) Required:**	Every 12 months from the date of initial/renewal approval and during the period of the study if required

You, being the principal investigator of the study at your study site, are reminded to comply with our requirements and to maintain communication with us during the period of the study by undertaking the principal investigator's responsibilities including (but not limited to):

- if the study is an industry-sponsored clinical study, submitting to us a copy of the fully executed indemnity agreement satisfying the Hospital Authority's requirement prior to commencement of the study (if it has not been submitted yet);
- observing and complying with all applicable requirements under our standard operating procedure ("IRB/REC SOP"), the Declaration of Helsinki and the ICH GCP (if applicable);
- submitting regular progress report(s) at the required intervals (as specified above) in accordance with the requirements in the IRB/REC SOP;
- not implementing any amendment/change to any approved study document/material without our written approval, except where necessary to eliminate any immediate hazard to the subjects or if an amendment/change is only of an administrative or logistical nature;
- notifying us of any new information that may adversely affect the rights, safety or well-being of the subjects or the proper conduct of the study;
- reporting any deviation from the study protocol or compliance incident that has occurred during the study and may adversely affect the rights, safety or well-being of any subject in accordance with the requirements in the IRB/REC SOP;
- submitting safety reports on all SAEs observed at your study site or SUSARs reported from outside your study site in accordance with the requirements in the IRB/REC SOP; and
- submitting a final report in accordance with the requirements in the IRB/REC SOP upon completion or termination of the study at your study site.

In addition to the above, you are also reminded to observe and comply with other applicable regulatory and management requirements including (but not limited to):

- if required by Hong Kong laws or regulations, obtaining a certificate for clinical trial through the Hong Kong Department of Health and complying with the associated requirements;
- obtaining the necessary consent from the management of your institution/department in accordance with the requirements of your institution/department;
- if required by local laws or regulations at conducting site out of IRB/REC's jurisdiction, obtaining an approval and complying with associated requirements;
- not representing to any third party or in any way likely to mislead any third party forming the view that the approval from the IRB/REC has any extraterritorial effect; and
- with due diligence ensuring your teams, staff, agents or whosoever connected with you to comply with the preceding requirements.

Yours sincerely,

Envy Lee (Secretary)
for and on behalf of
The Joint CUHK-NTEC CREC

EL/al

Schedule 1
Documents Reviewed

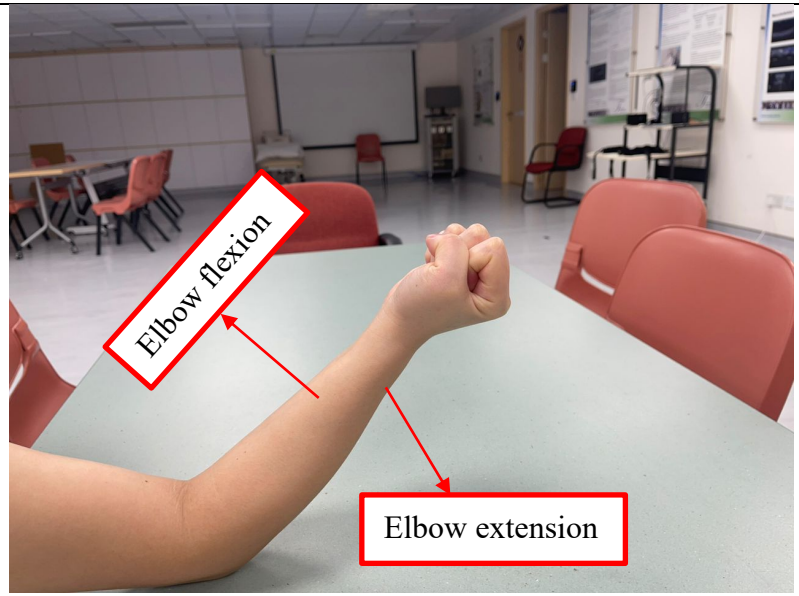
The documents reviewed by with respect to the said application/submission include:

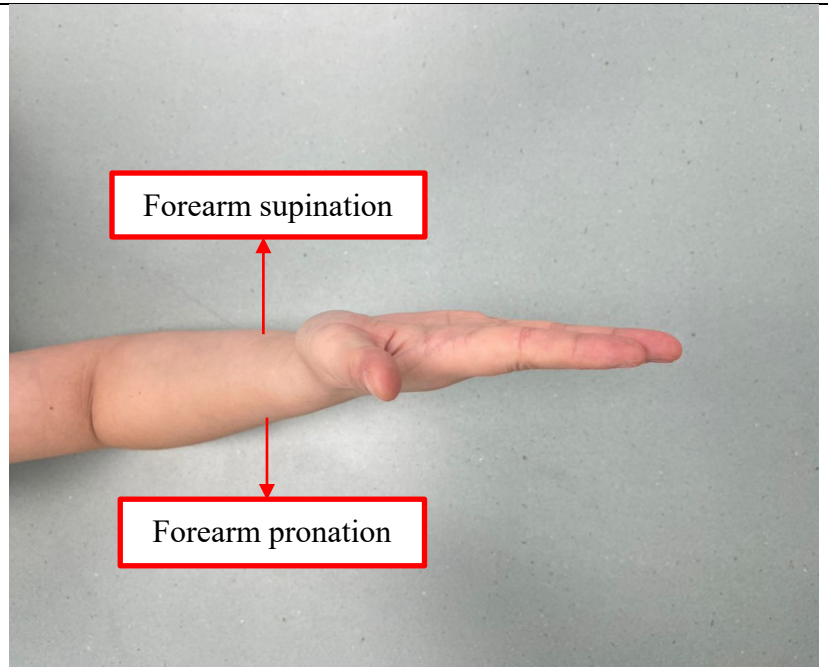
(Not Applicable)

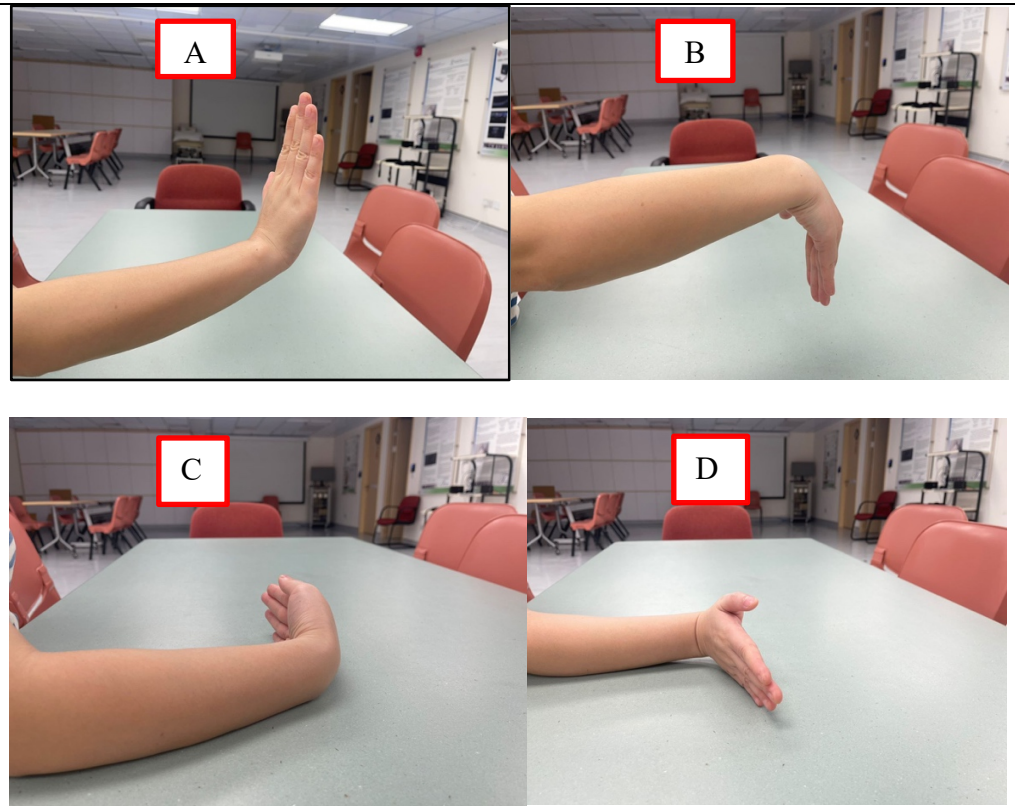
Schedule 2
Reviewers List
Joint CUHK-NTEC Clinical Research Ethics Committee

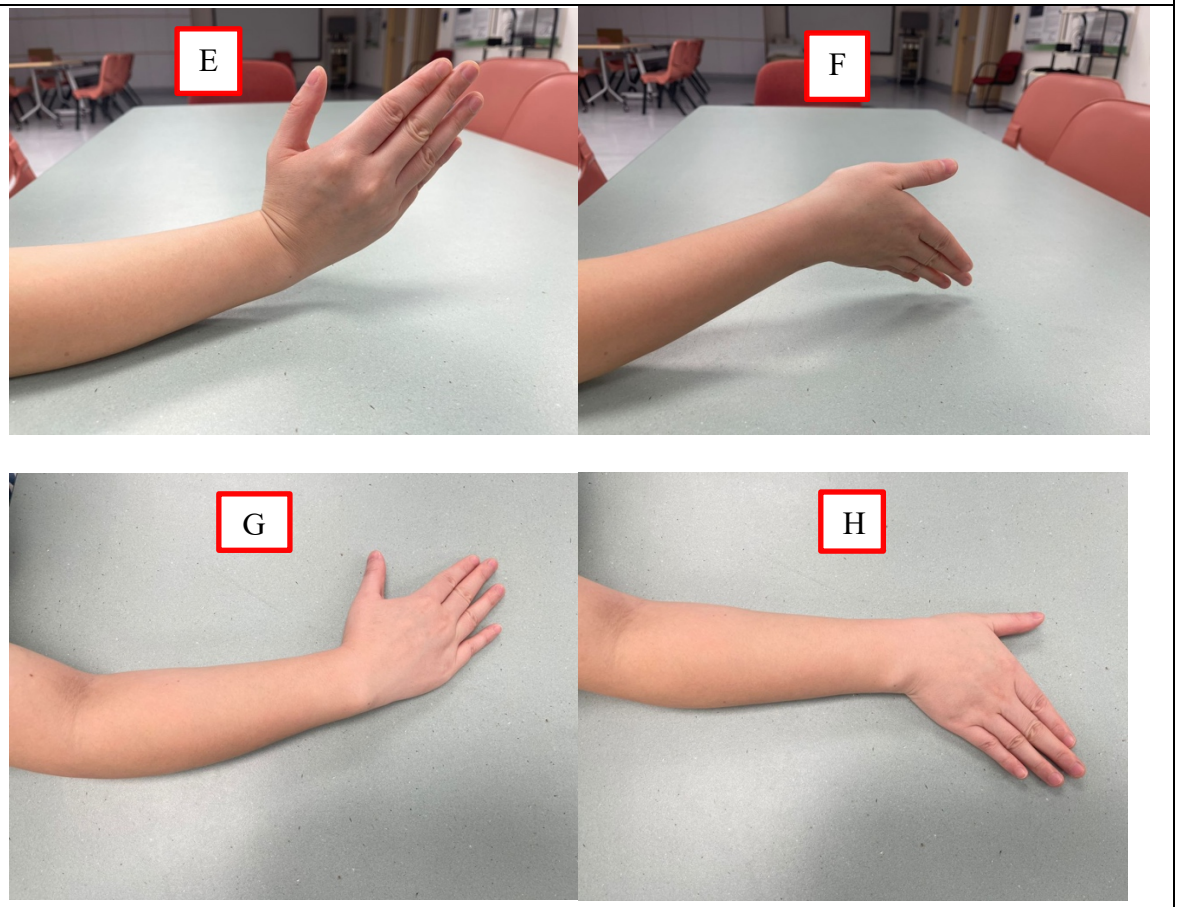
Title and Name	Occupation	Qualification	Male / Female (M/F)
Prof. Hoi Shan LO	Associate Professor,The Nethersole School of Nursing, CUHK	BN, MSc, PhD, RN, FHKAN (Education)	F
Dr. Eddy H. K. SIU	Manager, Physiotherapy Department, PWH	PhD (Physiotherapy), MSc (Manip Physiotherapy), MSc (Ex & Nutr Sci), BSc (Physiotherapy)	M

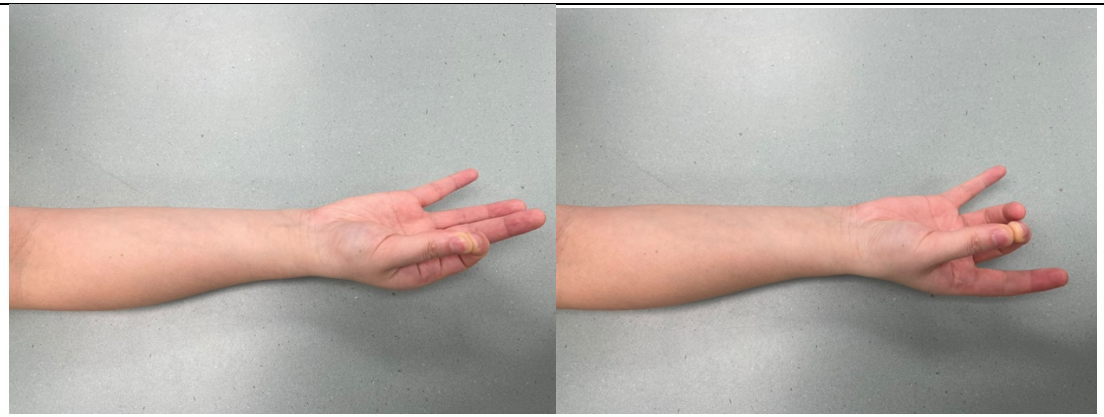
Appendix 6.3 The detailed protocol of bilateral upper extremity exercises

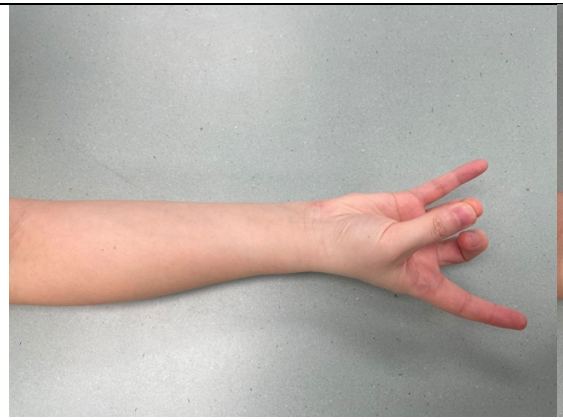
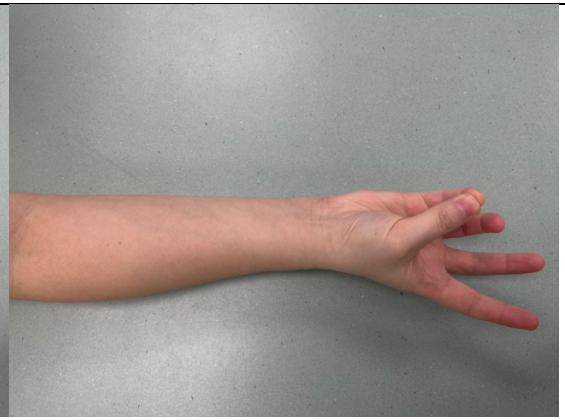
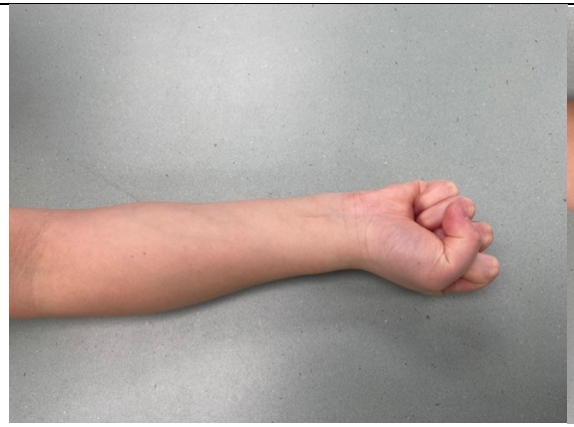
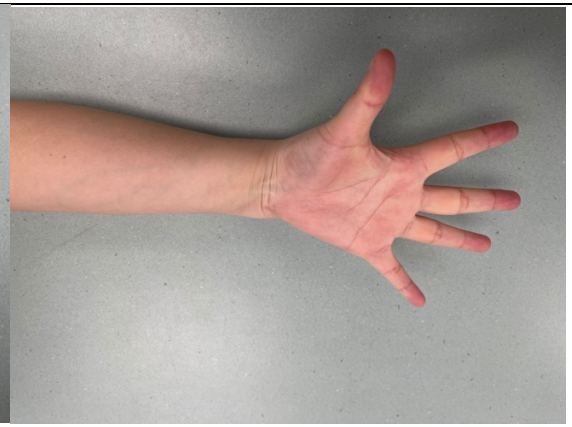
Item	Exercise component	Demonstration
Elbow flexion and extension	**Aim:** to instruct the paretic upper extremity to do exercise of elbow flexion and extension with the guidance of non-paretic upper extremity. **Details of exercises:** (1) the subject was asked to perform elbow flexion and extension alternately as much as they could until reach the end of active ROM. (2) the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes.	

Forearm supination and pronation	**Aim:** to instruct the paretic upper extremity to do exercise of forearm supination and pronation with the guidance of non-paretic upper extremity. **Details of exercises:** (1) the subject was asked to perform forearm supination and pronation alternately as much as they could until reach the end of active ROM. (2) the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes.	

Wrist flexion and extension	**Aim:** to instruct the paretic upper extremity to do exercise of wrist flexion and extension with the guidance of non-paretic upper extremity. **Details of exercises:** (1) the subject was asked to perform wrist flexion and extension alternately as much as they could until reach the end of active ROM with the influence of gravity and the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes (Figure A and B). (2) if the subject could not perform the wrist flexion and extension with gravity, subject was asked to perform wrist flexion and extension alternately as much as they could until reach the end of active ROM without the influence of gravity and the subject was asked to complete as many 10	

	repetitions/set as possible during 5 minutes (Figure C and D).	
Wrist radial and ulnar deviation	**Aim:** to instruct the paretic upper extremity to do exercise of wrist radial and ulnar deviation with the guidance of non-paretic upper extremity. **Details of exercises:** (1) the subject was asked to perform wrist radial and ulnar deviation alternately as much as they could until reach the end of active ROM with the influence of gravity and the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes (Figure E and F). (2) if the subject could not perform the wrist radial and ulnar deviation with gravity, subject was asked to perform radial and ulnar deviation alternately as much as they could until reach the end of active	

	ROM without the influence of gravity and the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes (Figure G and H).	
Finger opposition	**Aim:** to instruct the paretic upper extremity to do exercise of finger opposition with the guidance of non-paretic upper extremity. **Details of exercises:** (1) the subject was asked to perform finger opposition from Thumb to Pinky alternately as much as they could until perform fully finger opposition and fully strength. (2) the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes.	

		 
Gripping	**Aim:** to instruct the paretic upper extremity to do exercise of gripping with the guidance of non-paretic upper extremity. **Details of exercises:** (1) the subject was asked to perform hand gripping with fingers flexion and extension alternately as much as they could until reach the end of active ROM. (2) the subject was asked to complete as many 10 repetitions/set as possible during 5 minutes.	 

Appendix 6.4 Primary Outcome Measure: Fugl-Meyer Assessment-Upper Extremity (FMA-UE)

A. UPPER EXTREMITY, sitting position				
I. Reflex activity		**none**	**can be elicited**	
Flexors: biceps and finger flexors		0	2	
Extensors: triceps		0	2	
	Subtotal I (max 4)			
II. Volitional movement within synergies, without gravitational help		**none**	**partial**	**full**
Flexor synergy: Hand from contralateral knee to ipsilateral ear. From extensor synergy (shoulder adduction/internal rotation, elbow extension, forearm pronation) to flexor syngery (shoulder abduction/external rotation, elbow flexion, forearm supination)	Shoulder: retraction Shoulder: elevation Shoulder: abduction (90^0) Shoulder: external rotation Elbow: flexion Forearm: supination	0 0 0 0 0 0	1 1 1 1 1 1	2 2 2 2 2 2
Extensor synergy: Hand from ipsilateral ear to the contralateral knee.	Shoulder: adduction/internal rotation Elbow: extension Forearm: pronation	0 0 0	1 1 1	2 2 2
	Subtotal II (max 18)			
III. Volitional movement mixing synergies, without compensation		**none**	**partial**	**full**
Hand to lumbar spine	-Cannot be performed, hand in front of SIAS -Hand behind SIAS (without compensation -Hand to lumbar spine (without compensation)	0	1	2
Shoulder flexion 0^0 - 90^0 Elbow at 0^0 Pronation–supination 0^0	-immediate abduction or elbow flexion -abduction or elbow flexion during movement -complete flexion at 90^0, and maintains 0^0 in elbow	0	1	2
Pronation- supination Elbow at 90^0 Shoulder at 0^0	-no pronation / supination, starting position impossible -limited pronation / supination, maintains position -complete pronation / supination, maintains position	0	1	2
	Subtotal III (max 6)			
IV. Volitional movement with little or no synergy		**none**	**partial**	**full**
Shoulder abduction 0^0 - 90^0 Elbow at 0^0 Forearm pronated	-immediate supination or elbow flexion - supination or elbow flexion during movement	0	1	2

	-abduction 90^0, maintains extension and pronation			
Shoulder flexion 90^0 - 180^0 Elbow at 0^0 Pronation–supination 0^0	-immediate abduction or elbow flexion - abduction or elbow flexion during movement -complete flexion, maintains 0^0 in elbow	0	1	2
Pronation- supination Elbow at 0^0 Shoulder at 30^0-90^0 flexion	-no pronation / supination, starting position impossible -limited pronation / supination, maintains extension -full pronation / supination, maintains elbow extension	0	1	2
Subtotal IV (max 6)				
V. Normal reflex activity evaluated only if full score of 6 points achieved on part IV				
Biceps, triceps, finger flexors	-0 points on part IV or 2 of 3 reflexes markedly hyperactive -1 reflexor markedly hyperactive or at least 2 reflexes lively -Maximum of 1 reflex lively, none hyperactive	0	1	2
Subtotal V (max 2)				
TOTAL A (MAX 36)				

B. WRIST support may be provided at the elbow to take or hold the position, no support at wrist, check the passive range of motion prior testing		**none**	**partial**	**full**
Stability at 15^0 dorsiflexion Elbow at 90^0, Forearm pronated, shoulder at 0^0	-less than 15^0 active dorsiflexion - dorsiflexion 15^0, no resistance is taken -maintain s position against resistance	0	1	2
Repeated dorsiflexion/volar flexion Elbow at 90^0, Forearm pronated, shoulder at 0^0, slight finger flexion	-cannot perform volitionally -limited active range of motion -full active range of motion, smoothly	0	1	2
Stability at 15^0 dorsiflexion Elbow at 0^0, Forearm pronated, slight shoulder flexion/abduction	--less than 15^0 active dorsiflexion - dorsiflexion 15^0, no resistance is taken -maintain s position against resistance	0	1	2
Repeated dorsiflexion/volar flexion Elbow at 0^0, Forearm pronated, slight shoulder flexion/abduction	-cannot perform volitionally -limited active range of motion -full active range of motion, smoothly	0	1	2
Circumduction	-Cannot perform volitionally -jerky movement or incomplete	0	1	2

	-complete and smooth circumduction			
TOTAL B (MAX 10)				

C. HAND support may be provided at the elbow to keep 90^0 flexion, no support at wrist, compare with unaffected hand, the objects are interposed, active grasp		**none**	**partial**	**full**
Mass flexion From full active or passive extension		0	1	2
Mass extension From full active or passive flexion		0	1	2
GRASP				
A. flexion in PIP and DIP (digits II-V) **Extension in MCP II-V**	-cannot be performed -can hold position but weak -maintains position against resistance	0	1	2
B. thumb adduction 1-st CMC, MCP, IP at 0^0, scrap of paper between thumb and 2-nd MCP joint	-cannot be performed -can hold paper but not against tug - can hold paper against a tug	0	1	2
C. opposition pulpa of the thumb against the pulpa of 2-nd finger, pencil, tug upward	-cannot be performed -can hold pencil but not against tug - can hold pencil against a tug	0	1	2
D. cylinder grip Cylinder shaped object (small can), tug upward, opposite in digits I and II	-cannot be performed -can hold cylinder but not against tug - can hold cylinder against a tug	0	1	2
E. spherical grip Fingers in abduction/flexion, thumb opposed, tennis ball	-cannot be performed -can hold ball but not against tug - can hold ball against a tug	0	1	2
TOTAL C (MAX 14)				

D. COORDINATION / SPEED after one trial with both arms, blind-folded, tip of the index finger from knee to nose, 5 times as fast as possible		**marked**	**slight**	**none**
Tremor		0	1	2
Dysmetria	-Pronounced or unsystematic -slight and systematic -no dysmetria	0	1	2
		>5s	2-5s	<1s
Time	-more than 5 seconds slower than unaffected side -2-5 seconds slower than unaffected side -maximum differences of 1 second between sides	0	1	2
TOTAL D (MAX 6)				

TOTAL A-D (MAX 66)	

Appendix 6.5 Primary Outcome Measure: Wolf Motor Function Test (WMFT)

Arm tested:	More-affected: R /L		Less-affected: R / L
Task Comment	Time	Functional Ability	Time
1. Forearm to table (side)	_____	0 1 2 3 4 5	_____
2. Forearm to box (side)	_____	0 1 2 3 4 5	_____
3. Extend elbow (side)	_____	0 1 2 3 4 5	_____
4. Extend elbow (weight)	_____	0 1 2 3 4 5	_____
5. Hand to table (front)	_____	0 1 2 3 4 5	_____
6. Hand to box (front)	_____	0 1 2 3 4 5	_____
8. Reach and retrieve	_____	0 1 2 3 4 5	_____
9. Lift can	_____	0 1 2 3 4 5	_____
10. Lift pencil	_____	0 1 2 3 4 5	_____
11. Lift paper clip	_____	0 1 2 3 4 5	_____
12. Stack checkers	_____	0 1 2 3 4 5	_____
13. Flip cards	_____	0 1 2 3 4 5	_____
15. Turn key in lock	_____	0 1 2 3 4 5	_____
16. Fold towel	_____	0 1 2 3 4 5	_____
17. Lift basket	_____	0 1 2 3 4 5	_____

Appendix 6.6 Second Outcome Measure: The Jacket Test

1. The test was performed in the standing position.

2. On the command “Go”, the participant was required to put on completely a long-sleeved standardized lab coat from the affected arm to the unaffected arm so that it was straight on the participant’s shoulder and then to remove it completely from the unaffected arm to the affected arm.

3. Stopwatch was used to record the time from the command to when the lab coat had been completely removed in the standing position.

4. Two minutes rest was allowed between each trial to avoid fatigue during assessment.

5. Three trials of the Jacket Test time were collected and averaged of three-time test was used for data analysis.

Appendix 6.7 Second Outcome Measure: The Chinese version of Upper Extremity Functional Index (C-UEFI)

上肢活動能力指數

我們有興趣透過此問卷瞭解您現時所關注的上肢問題，會否對你進行以下活動造成苦難。請回答以下所有問題。

今天，你曾否在進行以下活動時遇上困難

(請於每行圈出一個數字)

	活動	非常困難或不能進行該活動	很困難	中等困難	少許困難	沒有困難
1	您的任何日常活動，家務或學校活動	0	1	2	3	4
2	提起一袋日用品至腰間位置	0	1	2	3	4
3	從高於頭部的置物架放置或取出物件	0	1	2	3	4
4	洗頭	0	1	2	3	4
5	以手撐起自己（例如從浴缸或椅子）	0	1	2	3	4
6	預備食材（例如去皮，且東西）	0	1	2	3	4
7	在商鋪內使用購物車選購商品	0	1	2	3	4
8	吸塵，掃地或打掃露台	0	1	2	3	4
9	扣鈕	0	1	1	2	3
10	使用工具或電器	0	1	2	3	4
11	開門	0	1	2	3	4
12	清潔	0	1	2	3	4
13	洗衣（例如清洗，熨衫，摺疊）	0	1	2	3	4
14	開瓶	0	1	2	3	4
15	以患肢提著小型行李	0	1	2	3	4
	總分:					

最小可偵測變化值（90%置信區間）：　　分數:—— /59

Appendix 6.8 Second Outcome Measure: The Motor Activity Log (MAL) (Chinese version)

家居活動紀錄表	使用程度 (甲) (AOU)	動作質素 (乙) (QOM)	如沒有進行此活動，請說明 (填代號)
1. 開關輕觸式的燈掣			
2. 開抽屜			
3. 從抽屜取出一件衣物			
4. 拿起電話聽筒			
5. 抹枱或廚櫃面			
6. 落車 (只包括當車門打開後，從坐到站之動作)			
7. 打開雪櫃			
8. 扭開門鎖並推開門			
9. 使用電視遙控器			
10. 洗手 (包括使用皂液及冲洗，但不包括開關水龍頭)			
11. 開關水龍頭			
12. 抹手			
13. 穿襪子			
14. 脫下襪子			
15. 穿鞋子 (包括綁鞋帶或貼魔術貼)			
16. 脫下鞋子 (包括解開鞋帶或解開魔術貼)			
17. 從有扶手的椅子站起來			
18. 坐下前把椅子從桌下拉開			
19. 坐下後把椅子拉近桌子			
20. 拿起杯子、水杯、水樽或罐頭 (不包括飲用)			
21. 刷牙 (不包括預備牙刷或洗刷除下來的假牙)			
22. 搽潤膚露 / 剃鬚膏 / 美容用品到臉上			
23. 用鎖匙開門			
24. 在紙上寫字 (如中風前使用健側手寫字，則可忽略此題)			
25. 手拿著物件 (不包括用手臂掛起物件)			
26. 使用义子或湯匙進食			
27. 梳頭			
28. 拿著杯柄拿杯			
29. 扣鈕			
30. 進食三文治或用手指拿小食			

患側上肢的使用程度的評分標準

0 分　　没有使用患側手；

0.5 分

1 分　　极少使用患側手；

1.5 分

2 分　　偶爾使用患側手，大部分時間使用健側手

2.5 分

3 分　　間中使用患側手，使用程度約為中風前之一半

3.5 分

4 分　　經常使用患側手，使用程度約為中風前之 7-8 成

4.5 分

5 分　常常使用患側手，使用程度與中風前一樣

患側上肢的使用程度的评分标准

0 分　　没有使用患側上肢來進行任何活動；

0.5 分

1 分　　患側手在進行活動時，患側手可輕微移動，但對該活動沒有幫助；

1.5 分

2 分　　患側手在進行活動時，患側需在健側手的幫助下才可以完成此活動或者使用患側手有困難

2.5 分

3 分　　使用患側手可以慢慢地或困難地把活動完成

3.5 分

4 分　用患側手可把活動完成，但比健側手慢一點或沒有這樣準確

4.5 分

5 分　用患側手可完成活動，並與健側手的表現一樣

Appendix 6.9 Second Outcome Measure: The Stroke Impact Scale (SIS) (Chinese version)

中風生存質量影響量(SIS)3.0 代理人版中文版本正文此問卷的目的是為了評價中風患者_____（患者性名）的健康和生活的影響情況。我們想從您的角度了解中風時他/她有哪些影響。我們將問您一些問題，這些問題有的是關於中風所致的殘疾和功能障礙，有的則是關於中風怎樣影響了他/她的生存質量。最後，我們將請您對他/她的康復情況做等級評定。

以下這些有關中風可能導致的軀體方面的問題。

1.在過去的一個星期裡，您怎樣分等級評價他/她的以下這些部位的力氣	很有力氣	相當有力	有一些力氣	有一點力氣	一點力氣都沒有
1)受中風影響最嚴重的那隻胳膊?	5	4	3	2	1
2)受中風影響最嚴重的那隻手的握力	5	4	3	2	1
3)受中風影響最嚴重的那條腿?	5	4	3	2	1
4)受中風影響最嚴重的那隻腳?	5	4	3	2	1

以下這些問題有關他/她的記憶力和思維。

2.在過去的一個星期裡，您怎樣評價他/她做以下這些事情的困難程度	一點都不困難	有一點困難	有一定困難	很困難	極度困難
1)記住別人剛告訴他/她的事情?	5	4	3	2	1
2)記住別人前一天發生的事情	5	4	3	2	1
3)記著去做一些事情(例如按時赴約或吃藥)	5	4	3	2	1

4)知道是星期幾?	5	4	3	2	1
5)集中注意力?	5	4	3	2	1
6)思維敏捷?	5	4	3	2	1
7)解決日常問題?	5	4	3	2	1

以下這些問題有關中風發生以來，他/她的感受、情緒變化和控制情緒的能力。

3.在過去的一個星期裡，他/她是不是經常	從來沒有	很少	有時	大部份時間	所有時間
1)覺得傷心?	5	4	3	2	1
2)覺得沒有親近的人?	5	4	3	2	1
3)覺得他/她是別人的負擔?	5	4	3	2	1
4)覺得沒有值得渴望的事?	5	4	3	2	1
5)對您做錯的事反而感到自責?	5	4	3	2	1
6)像平時一樣時事物感興趣?	5	4	3	2	1
7)感到十分緊張?	5	4	3	2	1
8)覺得人生有價值?	5	4	3	2	1
9)每天至少一次微笑和放聲大笑?	5	4	3	2	1

以下問題有關他/她同別人溝通的能力以及閱讀能力和聽懂對話的能力。

4. 在過去的一個星期裡，對他/她來說，有多大困難去	一點都不困難	有一點困難	有一定困難	很困難	極度困難
1)面對面說出別人的名字?	5	4	3	2	1
2)理解別人對他/她說的話?	5	4	3	2	1
3)回答問題?	5	4	3	2	1
4)准確命名物體?	5	4	3	2	1
5)參與一群人的談話?	5	4	3	2	1
6)在電話裡與人交談?	5	4	3	2	1
7)打電話給別人，包括選擇正確的電話號碼和正確撥號?	5	4	3	2	1

以下問題有關他/她平時的日常行為能力。

5. 在過去的兩個星期裡，您認為對他/她來說，有多大困難去	一點都不困難	有一點困難	有一定困難	很困難	極度困難
1)用筷子夾菜?	5	4	3	2	1
2)穿上身的衣服?	5	4	3	2	1
3)自己洗澡?	5	4	3	2	1
4)剪腳指甲?	5	4	3	2	1
5)定時上廁所?	5	4	3	2	1
6)控制小便（不失禁）?	5	4	3	2	1
7)控制大便（不失禁）?	5	4	3	2	1
8)做輕鬆的家務(擦拭灰塵、舖床、倒垃圾)?	5	4	3	2	1
9) 去商店購物?	5	4	3	2	1
10)做重體力家務(吸塵器吸塵、洗衣或庭院勞動)?	5	4	3	2	1

下列問題是有關他/她在家或在社區的行動能力。

6. 在過去的兩個星期裡，您認為對他/她來說，有多大困難去	一點都不困難	有一點困難	有一定困難	很困難	極度困難
1)保持坐姿而不會失去平衡?	5	4	3	2	1
2)保持站姿而不會失去平衡?	5	4	3	2	1
3)行走而不會失去平衡?	5	4	3	2	1
4)從床上轉移到椅子上?	5	4	3	2	1
5)走過一個路口?	5	4	3	2	1
6)快步走?	5	4	3	2	1
7)爬一層樓梯?	5	4	3	2	1
8)爬幾層樓梯?	5	4	3	2	1
9) 進（出）汽車?	5	4	3	2	1

以下問題有關他/她受中風影響最重的手的活動能力。

7. 在過去的兩個星期裡，您認為對他/她來說，有多大困難使用受中風影響最厲害的那隻手去	一點都不困難	有一點困難	有一定困難	很困難	極度困難
1)提重物（蔬菜水果袋）?	5	4	3	2	1

2)旋轉門把手?	5	4	3	2	1
3)開罐頭或果醬瓶?	5	4	3	2	1
4)繫鞋帶?	5	4	3	2	1
5)拾起硬幣?	5	4	3	2	1

以下問題有關中風如何影響了（患者姓名）去參加原本會常去的活動，這些活動對他/她來說很有意義，使他/她從中找到生活的目的。

8. 在過去的四個星期裡，他/她在多少情況在下面這些活動中受到限制	從來沒有	很少	有時	大部份時間	所有時間
1)他/她的工作（有酬的，義工，或其他形式的工作）?	5	4	3	2	1
2)他/她的社會活動?	5	4	3	2	1
3)靜態的娛樂活動（下棋、看電視）?	5	4	3	2	1
4)動態的娛樂活動?	5	4	3	2	1
5)他/她作為家庭成員和/或朋友所起的作用?	5	4	3	2	1
6)他/她求神或做禮拜?	5	4	3	2	1
7)他/按自己的意願去生活的能力?	5	4	3	2	1
8)他/她幫助別人的能力	5	4	3	2	1

中風康復程度

9. 下面是一個 0 - 100 的標尺，100 表示完全康復，0 表示完全沒有恢復，您認為_____（患者姓名）康復的程度如何?

標出合適的數字

100（完全康復）

90

80

70

60

50

40

30

20

10

0（沒有康復）

Appendix 6.10 Second Outcome Measure: Community Integration Measures (CIM)

(Chinese version)

社區整合量法

在下列的問題裡，請選擇同意或不同意:

1. 我覺得我是這個社會的一部分，我屬於這個社會
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

2. 我清楚我在這個社會的方向
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

3. 我知道在這個社會的規則，我可以適應它
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

4. 我覺得我被這個社會所接納的
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

5. 我可以在這個社區獨立
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

6. 我喜愛我現在居住的地方
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

7. 在這個社會裡有我相熟的人
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

8. 在這個社會裡我認識一了些朋友會跟我打招呼的
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

9. 在這個社會裡我可以在空餘時間做自己喜歡的事
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

10. 在這個社會裡，我每天都可以做到一些有用和有生產力的事
［　］經常同意
［　］有時同意
［　］中立
［　］有時不同意
［　］經常不同意

Appendix 6.11 Second Outcome Measure: SATIS-Stroke (Chinese version)

中風後社會參與的滿意度

在過去一個月，您對進行以下生活處境有多滿意？

0分-非常不滿意：患者在没有任何其他幫助的情况下無法執行活動；

1分-不滿意：患者能够在没有任何幫助的情况下進行活動，但遇到了一些困難；

2分-滿意：患者能够在没有任何幫助的情况下進行活動，也不會遇到任何困難；

3分-非常滿意；

問號：患者無法估計活動的滿意度，因為他從未在過去的一個月的時間裡做過該活動；

您對進行以下生活處境有多滿意？		非常不滿意	不滿意	滿意	非常滿意	？
01	在所有情況下參與準備食物及飲品	0	1	2	3	
02	在所有情況下使用刀，叉及羹	0	1	2	3	
03	參與和您夥伴的言語交流	0	1	2	3	
04	按您的需要洗頭	0	1	2	3	
05	能除下衣服使用家中或家居以外洗手間，然後穿回衣服	0	1	2	3	
06	按您的需要整理個人衛生	0	1	2	3	
07	在家中或家居以外都能控制小便	0	1	2	3	
08	參與藝術及文化活動（戲院，劇院等）	0	1	2	3	
09	與您的夥伴合作	0	1	2	3	
10	在所有情況下閱讀及理解文件	0	1	2	3	
11	在家中按您的需要使用電話	0	1	2	3	
12	按您的需要收聽電台和收看電視節目	0	1	2	3	
13	在所有情況下管理收入	0	1	2	3	
14	在所有情況下使用硬幣及紙幣	0	1	2	3	
15	在所有情況下按您的需要除下及穿上衣服	0	1	2	3	
16	確保您的權利受到尊重	0	1	2	3	
17	投入婚姻關係	0	1	2	3	
18	按您的需要浸浴或淋浴	0	1	2	3	
19	觸及在您就近的物件	0	1	2	3	
20	在衣櫥中取出衣服	0	1	2	3	
21	在所有情況下填寫行政文件	0	1	2	3	
22	在家中走動	0	1	2	3	

23	在所有情況下於家居以外的地方走動	0	1	2	3	
24	按您的需要在您住的地方上下樓梯	0	1	2	3	
25	按您的需要進出家門	0	1	2	3	
26	打開或關上您家中的門	0	1	2	3	
27	使用家中的儲物空間	0	1	2	3	
28	選取適當的衣服	0	1	2	3	
29	分享您的心情	0	1	2	3	
30	意識到您周圍的事物	0	1	2	3	
31	向他人表達自己	0	1	2	3	
32	參與典禮（婚禮，家庭聚會等）	0	1	2	3	
33	在緊急情況下求助	0	1	2	3	
34	在所有情況下管理您的疼痛	0	1	2	3	
35	享有情感生活	0	1	2	3	
36	擁有性生活	0	1	2	3	

Appendix 7.1 The consent form of the randomized control trial at Hong Kong Polytechnic University

The Hong Kong Polytechnic University

Department of Rehabilitation Sciences

Project entitled: A randomized controlled trial of upper limb training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper limb motor functions in people with stroke having post-stroke duration from 6 months to 10 years

Investigator: Prof. Shamay S. M. Ng

Purpose:

To investigate whether mirror therapy (MT) combined with transcutaneous electrical nerve stimulation (TENS) would be superior to Sham-MT with TENS in improving upper limb motor functions in people with stroke having post-stroke duration from 6 months to 10 years.

Methods:

All eligible subjects will be randomly assigned into 2 groups: (1) mirror therapy combined with bilateral transcutaneous electrical nerve stimulation (Bi-TENS) over both paretic and non-paretic upper limb and (2) Sham-MT combined with Bi-TENS over both paretic and non-paretic upper limb, respectively for 8 weeks, 2 times a week (total 16 treatment sessions). Subjects will be assessed on improvement of Fugl Meyer Assessment Upper Extremity Portion, Wolf Motor Function test, maximum paretic grip strength, Jacket Test,

Upper Extremity Functional Index, Motor Activity Log, Stroke Impact Scale, Community Integration Measure, and SATIS-Stroke. Each assessment session will last for 45 minutes. The procedures of each assessment will be explained fully. The treatment venue will be in the Neurorehabilitation Laboratory of the Hong Kong Polytechnic University (ST 010).

Potential Risks and Benefits:

The major benefit from participating in this study is that subjects may have the opportunity to know their own level of motor functions of their upper limbs. The results may also be beneficial for planning an intensive rehabilitation program for improving upper limb motor functions in patients with stroke. The mirror therapy, TENS, upper limb training, and testing procedures have been well proved to be safe and used with negligible side effects, both clinically and experimentally. A few subjects may feel some exhaustion during assessment and therefore rest will be allowed between assessment procedures.

Informed Consent:

I, _____, understand the details of this study. I voluntarily consent to participate in this study. I understand that I can withdraw from this study at any time without giving reasons, and my withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential risk in joining this study. I also understand that my personal information will not be disclosed to people who are not related to this study and my name will not appear on any publications resulted from this study.

I can contact the chief investigator, Prof. Shamay Ng at telephone 2766-4889 for any questions about this study. If I have complaints related to the investigators, I can contact Ms. Chung secretary of Departmental Research Committee, at 2766-4329. I know I will be given a signed copy of this consent form.

Signature (participant): _____ Date: _____

Signature (Witness): _____ Date: _____

香港理工大學康復治療科學系參加研究同意書

科研題目: 隨機對照臨床試驗: 上肢訓練配合鏡子治療及經皮神經電刺激對改善中風後 6 個月至 10 年病人的上肢功能之功效

科研人員: 伍尚美教授

科研目的及內容: 旨在研究鏡子治療配合經皮神經電刺激的治療，是否比偽鏡子治療配合經皮神經電刺激，更有效於改善上肢訓練配合鏡子治療及經皮神經電刺激對改善中風後 6 個月至 10 年病人的上肢功能之功效

研究方法: 所有合資格參加者會被隨機分為兩組，第一組：鏡子治療配合經皮神經電刺激，第二組：偽鏡子治療配合經皮神經電刺激。參加者接受為期八星期，每星期兩次（共十六次治療）。參加者並於接受鏡子治療配合經皮神經電刺激或偽鏡子治療配合經皮神經電刺激期間，同時進行上肢訓練，每次治療需時約三十分鐘。參加者將會接受上肢的功能、日常生活運用、及社區融合等測試，以評估進展，每次檢查需時約四十五分鐘。研究人員將會向閣下詳細解釋測試的方法。參加治療地點拟設於香港理工大學神經康復實驗室 (ST 010).

潛在危險性及得益: 若參與此研究，參加者可以了解自己的上肢功能的表現，此外亦能提供重要數據幫助設計給中風患者改善上肢功能的康復治療。鏡子治療、經皮神經電刺激、上肢的控制訓練和整個檢查程序都經過驗證，證明過程十分安全，不論在臨床上或實驗

上，其副作用都可以忽略，唯期間小部份參與人士可能會感到少許疲倦，參加者可按需要於測試期間作中段休息。

同意書：

本人_____已瞭解此次研究的具體情況。本人願意參加此次研究, 本人有權在任何時候、無任何原因的情況下放棄參與此次研究, 而此舉不會導致本人受到任何懲罰或不公平的對待。本人明白參加此研究課題的潛在危險性以及本人的資料將不會洩露給與此研究無關的人員，我的名字或相片也不會出現在任何的出版物上。

本人可以用電話 2766 4889 來聯繫此次研究課題的負責人，伍尚美教授。若本人對研究人員有任何投訴，可以聯繫鍾女士（部門科研委員會秘書），電話：2766 4329。本人亦明白，參與此研究課題需要本人簽署一份同意書。

簽名（參與者）：_____ 日期：_____

簽名（證人）：_____ 日期：_____

Appendix 7. 2 The ethic approved by The Hong Kong Polytechnic University

THE HONG KONG POLYTECHNIC UNIVERSITY
香港理工大學

To	Ng Sheung Mei Shamay (Department of Rehabilitation Sciences)		
From	Yee Kay Yan Benjamin, Delegate, Departmental Research Committee		
Email	benjamin.yee@	Date	11-Apr-2023

Application for Ethical Review for Teaching/Research Involving Human Subjects

I write to inform you that approval has been given to your application for human subjects ethics review of the following project for a period from 01-Mar-2018 to 28-Feb-2024:

Project Title:	Randomized controlled trial of upper limb training with mirror therapy and transcutaneous electrical nerve stimulation to improve upper limb functions in patients with sub-acute stroke
Department:	Department of Rehabilitation Sciences
Principal Investigator:	Ng Sheung Mei Shamay
Project Start Date:	01-Mar-2018
Reference Number:	HSEARS20180221001-04

You will be held responsible for the ethical approval granted for the project and the ethical conduct of the personnel involved in the project. In case the Co-PI, if any, has also obtained ethical approval for the project, the Co-PI will also assume the responsibility in respect of the ethical approval (in relation to the areas of expertise of respective Co-PI in accordance with the stipulations given by the approving authority).

You are responsible for informing the PolyU Institutional Review Board in advance of any changes in the proposal or procedures which may affect the validity of this ethical approval.

Yee Kay Yan Benjamin

Delegate

Departmental Research Committee (on behalf of PolyU Institutional Review Board)

REFERENCES

Abizanda, P., Navarro, J. L., García-Tomás, M. I., López-Jiménez, E., Martínez-Sánchez, E., & Paterna, G. (2012). Validity and usefulness of hand-held dynamometry for measuring muscle strength in community-dwelling older persons. *Arch Gerontol Geriatr*, *54* (1), 21-27.

Acerra, N., Souvlis, T., & Moseley, G. (2005). Does mirror-box therapy improve sensory and motor changes in the early post-stroke population? A randomised controlled trial. *J. Physiother*, 51(4-e Suppl.), S7.

Adams, R. W., Gandevia, S. C., & Skuse, N. F. (1990). The distribution of muscle weakness in upper motoneuron lesions affecting the lower limb. *Brain*, 113 (Pt 5), 1459-1476.

Ademoyegun, A. B., Mbada, C. E., Sonuga, O. A., Malomo, O. E., Fatai, W. A., & Aghedo, I. A. (2022). Does grip strength of the less-affected side of ischemic stroke survivors influences performance of self-care activities? *Bulletin Faculty Phys Ther (Online)*, *27* (1), 1-11.

Aderinto, N., AbdulBasit, M. O., Olatunji, G., & Adejumo, T. (2023). Exploring the transformative influence of neuroplasticity on stroke rehabilitation: a narrative review of current evidence. *Ann Med Surg (Lond)*, *85* (9), 4425-4432.

Aizu, N., Sudo, T., Oouchida, Y., & Izumi, S. I. (2023). Facilitation of imitative movement in patients with chronic hemiplegia triggered by illusory ownership. *Sci Rep*, *13* (1), 16143.

Albuquerque, F. C. (2013). Hemorrhagic stroke: the broad horizon of aneurysm treatment. *J Neurointerv Surg*, *5 Suppl 3*, iii1-2.

Aljathlani, M. F., Alshammari, M. O., Alsuwaygh, M. A., Al-Mutairi, M. S., Aljassir, F. F., Bindawas, S. M., & Alnahdi, A. H. (2022). Cross-cultural adaptation and validation of the Arabic version of the upper extremity functional index. *Disabil Rehabil*, *44* (19), 5656-5662.

Alnahdi, A. H., & Albarrati, A. (2021). The upper extremity functional index: reliability and validity in patients with chronic obstructive pulmonary disease. *Int J Environ Res Public Health*, *18* (20): 10608.

Alnahdi, A. H., Almutairi, M. S., & Alnamlah, O. S. (2024). Structural validity of the arabic upper extremity functional index using exploratory and confirmatory factor analysis. *J Disabil Res*, *3* (3), 20240037.

Alon, G., Levitt, A. F., & McCarthy, P. A. (2007). Functional electrical stimulation enhancement of upper extremity functional recovery during stroke rehabilitation: a pilot study. *Neurorehabil Neural Repair*, *21* (3), 207-215.

Alwhaibi, R. M., Mahmoud, N. F., Zakaria, H. M., Ragab, W. M., Al Awaji, N. N., Elzanaty, M. Y., & Elserougy, H. R. (2021). Therapeutic efficacy of transcutaneous electrical

nerve stimulation acupoints on motor and neural recovery of the affected upper extremity in chronic stroke: A sham-controlled randomized clinical trial. *Healthcare (Basel)*, *9* (5), 614.

Andersen, K. K., Olsen, T. S., Dehlendorff, C., & Kammersgaard, L. P. (2009). Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. *Stroke*, *40* (6), 2068-2072.

Andrews, A. W., & Bohannon, R. W. (2000). Distribution of muscle strength impairments following stroke. *Clin Rehabil*, *14* (1), 79-87.

Antoniotti, P., Veronelli, L., Caronni, A., Monti, A., Aristidou, E., Montesano, M., & Corbo, M. (2019). No evidence of effectiveness of mirror therapy early after stroke: an assessor-blinded randomized controlled trial. *Clin Rehabil*, *33* (5), 885-893.

Arafat, S., Chowdhury, H. R., Qusar, M., & Hafez, M. (2016). Cross-cultural adaptation and psychometric validation of research instruments: A methodological review. *Journal of Behavioral Health*, *5* (3), 129-136.

Arene, N., & Hidler, J. (2009). Understanding motor impairment in the paretic lower limb after a stroke: a review of the literature. *Top Stroke Rehabil*, *16* (5), 346-356.

Arya, K. N., Pandian, S., & Kumar, V. (2019). Effect of activity-based mirror therapy on lower limb motor-recovery and gait in stroke: A randomised controlled trial. *Neuropsychol Rehabil*, *29* (8), 1193-1210.

Au-Yeung, S. S., Ng, J. T., & Lo, S. K. (2003). Does balance or motor impairment of limbs discriminate the ambulatory status of stroke survivors? *Am J Phys Med Rehabil*, *82* (4), 279-283.

Aytar, A., Yuruk, Z. O., Tuzun, E. H., Baltaci, G., Karatas, M., & Eker, L. (2015). The upper extremity functional index (UEFI): cross-cultural adaptation, reliability, and validity of the Turkish version. *J Back Musculoskelet Rehabil*, *28* (3), 489-495.

Aziz-Zadeh, L., Maeda, F., Zaidel, E., Mazziotta, J., & Iacoboni, M. (2002). Lateralization in motor facilitation during action observation: a TMS study. *Exp Brain Res*, *144* (1), 127-131.

Bagg, S., Pombo, A. P., & Hopman, W. (2002). Effect of age on functional outcomes after stroke rehabilitation. *Stroke (1970)*, *33* (1), 179-185.

Bai, Z., Zhang, J., Zhang, Z., Shu, T., & Niu, W. (2019). Comparison between movement-based and task-based mirror therapies on improving upper limb functions in patients with stroke: a pilot randomized controlled trial. *Front Neurol*, *10*, 288.

Baier, B., Zu Eulenburg, P., Geber, C., Rohde, F., Rolke, R., Maihöfner, C., Birklein, F., & Dieterich, M. (2014). Insula and sensory insular cortex and somatosensory control in patients with insular stroke. *Eur J Pain*, *18* (10), 1385-1393.

Ballester, B. R., Maier, M., Duff, A., Cameirão, M., Bermúdez, S., Duarte, E., Cuxart, A., Rodríguez, S., San Segundo Mozo, R. M., & Verschure, P. (2019). A critical time window for recovery extends beyond one-year post-stroke. *J Neurophysiol*, *122*(1), 350-357.

Beese, S., Avşar, T. S., Price, M., Quinn, D., Lim, H. S., Dretzke, J., Ogwulu, C. O., Barton, P., Jackson, L., & Moore, D. (2024). Clinical and cost-effectiveness of left ventricular assist devices as destination therapy for advanced heart failure: systematic review and economic evaluation. *Health Technol Assess*, *28* (38), 1-237.

Bertrand, A. M., Fournier, K., Wick Brasey, M. G., Kaiser, M. L., Frischknecht, R., & Diserens, K. (2015). Reliability of maximal grip strength measurements and grip strength recovery following a stroke. *J Hand Ther*, *28* (4), 356-362.

Boissy, P., Bourbonnais, D., Carlotti, M. M., Gravel, D., & Arsenault, B. A. (1999). Maximal grip force in chronic stroke subjects and its relationship to global upper extremity function. *Clin Rehabil*, *13* (4), 354-362.

Bonett, D. G. (2003). Sample size requirements for comparing two alpha coefficients. *Applied Psychological Measurement*, *27* (1), 72-74.

Botner, E. M., Miller, W. C., & Eng, J. J. (2005). Measurement properties of the activities-specific balance confidence scale among individuals with stroke. *Disabil Rehabil*, *27* (4), 156-163.

Bouffioulx, E., Arnould, C., & Thonnard, J. L. (2008). SATIS-Stroke: a satisfaction measure of activities and participation in the actual environment experienced by patients with chronic stroke. *J Rehabil Med*, *40* (10), 836-843.

Bouffioulx, E., Arnould, C., Vandervelde, L., & Thonnard, J. L. (2010). Changes in satisfaction with activities and participitation between acute, post-acute and chronic stroke phases: a responsiveness study of the SATIS-Stroke questionnaire. *J Rehabil Med*, *42* (10), 944-948.

Brim, R. L., & Miller, F. G. (2013). The potential benefit of the placebo effect in sham-controlled trials: implications for risk-benefit assessments and informed consent. *J Med Ethics*, *39*(11), 703-707.

Broderick, P., Horgan, F., Blake, C., Ehrensberger, M., Simpson, D., & Monaghan, K. (2018). Mirror therapy for improving lower limb motor function and mobility after stroke: A systematic review and meta-analysis. *Gait Posture*, *63*, 208-220.

Bujang, M. A., Omar, E. D., & Baharum, N. A. (2018). A review on sample size determination for cronbach's alpha test: a simple guide for researchers. *Malays J Med Sci*, *25* (6), 85-99.

Buma, F., Kwakkel, G., & Ramsey, N. (2013). Understanding upper limb recovery after stroke. *Restor Neurol Neurosci*, *31* (6), 707-722.

Canning, C. G., Ada, L., & O'Dwyer, N. J. (2000). Abnormal muscle activation characteristics associated with loss of dexterity after stroke. *J Neurol Sci*, *176* (1), 45-56.

Carey, L., Macdonell, R., & Matyas, T. A. (2011). SENSe: Study of the effectiveness of neurorehabilitation on sensation: a randomized controlled trial. *Neurorehabil Neural Repair*, *25* (4), 304-313.

Carey, L. M., & Matyas, T. A. (2011). Frequency of discriminative sensory loss in the hand after stroke in a rehabilitation setting. *J Rehabil Med*, *43* (3), 257-263.

Celnik, P., Hummel, F., Harris-Love, M., Wolk, R., & Cohen, L. G. (2007). Somatosensory stimulation enhances the effects of training functional hand tasks in patients with chronic stroke. *Arch Phys Med Rehabil*, *88* (11), 1369-1376.

Celnik, P., Webster, B., Glasser, D. M., & Cohen, L. G. (2008). Effects of action observation on physical training after stroke. *Stroke*, *39* (6), 1814-1820.

Chan, W. C., & Au-Yeung, S. S. Y. (2018). Recovery in the severely impaired arm post-stroke after mirror therapy: A randomized controlled study. *Am J Phys Med Rehabil*, *97* (8), 572-577.

Chen, C. M., Tsai, C. C., Chung, C. Y., Chen, C. L., Wu, K. P., & Chen, H. C. (2015). Potential predictors for health-related quality of life in stroke patients undergoing inpatient rehabilitation. *Health Qual Life Outcomes*, *13*, 118.

Chen, J, Wu, J.S., Gu, M.X. (2015). Effects of mirror therapy combined with electromyographic biofeedback on hand function in patients with stroke. *J Neurosci Ment Health,* 15 (6):602–604.

Chen, K. K., Lee, S. Y., Pang, B. W. J., Lau, L. K., Jabbar, K. A., Seah, W. T., Tou, N. X., Yap, P. L. K., Ng, T. P., & Wee, S. L. (2022). Associations of low handgrip strength and hand laterality with cognitive function and functional mobility - the Yishun Study. *BMC Geriatr*, 22 (1), 677.

Chen, P., Lai, C. K. Y., Chung, R. C. K., & Ng, S. S. M. (2017). The jacket test for assessing people with chronic stroke. *Disabil Rehabil*, *39* (25), 2577-2583.

Chen, P., Liu, T. W., Kwong, P. W. H., Lai, C. K. Y., Chung, R. C. K., Tsoh, J., & Ng, S. S. M. (2022). Bilateral transcutaneous electrical nerve stimulation improves upper limb motor recovery in stroke: a randomized controlled trial. *Stroke*, *53* (4), 1134-1140.

Chen, S. C., Chen, Y. L., Chen, C. J., Lai, C. H., Chiang, W. H., & Chen, W. L. (2005). Effects of surface electrical stimulation on the muscle-tendon junction of spastic gastrocnemius in stroke patients. *Disabil Rehabil*, *27* (3), 105-110.

Chesworth, B. M., Hamilton, C. B., Walton, D. M., Benoit, M., Blake, T. A., Bredy, H., Burns, C., Chan, L., Frey, E., Gillies, G., Gravelle, T., Ho, R., Holmes, R., Lavallée, R. L., MacKinnon, M., Merchant, A. J., Sherman, T., Spears, K., & Yardley, D. (2014).

Reliability and validity of two versions of the upper extremity functional index. *Physiother Can*, *66* (3), 243-253.

Chipchase, L. S., Schabrun, S. M., & Hodges, P. W. (2011). Corticospinal excitability is dependent on the parameters of peripheral electric stimulation: a preliminary study. *Arch Phys Med Rehabil*, *92* (9), 1423-1430.

Cho, H.-Y., In, T. S., Cho, K. H., & Song, C. H. (2013). A single trial of transcutaneous electrical nerve stimulation (TENS) improves spasticity and balance in patients with chronic Stroke. *Tohoku J Exp Med, 229* (3), 187-193.

Cho, H. S., & Cha, H. G. (2015). Effect of mirror therapy with tDCS on functional recovery of the upper extremity of stroke patients. *J Phys Ther Sci*, *27*(4), 1045-1047.

Choi, H. S., Shin, W. S., & Bang, D. H. (2019). Mirror therapy using gesture recognition for upper limb function, neck discomfort, and quality of life after chronic stroke: a single-blind randomized controlled trial. *Med Sci Monit*, *25*, 3271-3278.

Chokroverty, S., Reyes, M. G., Rubino, F. A., & Barron, K. D. (1976). Hemiplegic amyotrophy. muscle and motor point biopsy study. *Arch Neurol*, *33* (2), 104-110.

Chou, K. L., Yeung, F. K., & Wong, E. C. (2005). Fear of falling and depressive symptoms in Chinese elderly living in nursing homes: fall efficacy and activity level as mediator or moderator? *Aging Ment Health*, *9* (3), 255-261.

Chuang, L. L., Chen, Y. L., Chen, C. C., Li, Y. C., Wong, A. M., Hsu, A. L., & Chang, Y. J. (2017). Effect of EMG-triggered neuromuscular electrical stimulation with bilateral arm training on hemiplegic shoulder pain and arm function after stroke: a randomized controlled trial. *J Neuroeng Rehabil*, *14* (1), 122.

Cicinelli, P., Traversa, R., & Rossini, P. M. (1997). Post-stroke reorganization of brain motor output to the hand: a 2-4 month follow-up with focal magnetic transcranial stimulation. *Electroencephalogr Clin Neurophysiol*, *105* (6), 438-450.

Colebatch, J. G., & Gandevia, S. C. (1989). The distribution of muscular weakness in upper motor neuron lesions affecting the arm. *Brain*, *112 (Pt 3)*, 749-763.

Colomer, C., Noé, E., & Llorens, R. (2016). Mirror therapy in chronic stroke survivors with severely impaired upper limb function: a randomized controlled trial. *Eur J Phys Rehabil Med*, *52* (3), 271-278.

Cunningham, D. A., Knutson, J. S., Sankarasubramanian, V., Potter-Baker, K. A., Machado, A. G., & Plow, E. B. (2019). Bilateral contralaterally controlled functional electrical stimulation reveals new insights into the interhemispheric competition model in chronic Stroke. *Neurorehabil Neural Repair*, *33* (9), 707-717.

Daskalakis, Z. J., Christensen, B. K., Fitzgerald, P. B., Roshan, L., & Chen, R. (2002). The mechanisms of interhemispheric inhibition in the human motor cortex. *J Physiol*, *543* (Pt1), 317-326.

Deconinck, F. J., Smorenburg, A. R., Benham, A., Ledebt, A., Feltham, M. G., & Savelsbergh, G. J. (2015). Reflections on mirror therapy: a systematic review of the effect of mirror visual feedback on the brain. *Neurorehabil Neural Repair*, *29* (4), 349-361.

Del Gratta, C., Della Penna, S., Tartaro, A., Ferretti, A., Torquati, K., Bonomo, L., Romani, G. L., & Rossini, P. M. (2000). Topographic organization of the human primary and secondary somatosensory areas: an fMRI study. *Neuroreport*, *11* (9), 2035-2043.

Department of Health HKSAR. (2022). HKUMed research shows 30% increase in 'young stroke' incidence in Hong Kong and calls for better control of vascular risk factors such as hypertension. Retrieved from https://www.med.hku.hk/en/news/press/20221027-increase-in-young-stroke.

Ding, L., Wang, X., Chen, S., Wang, H., Tian, J., Rong, J., Shao, P., Tong, S., Guo, X., & Jia, J. (2019). Camera-based mirror visual input for priming promotes motor recovery, daily function, and brain network segregation in subacute stroke patients. *Neurorehabil Neural Repair*, *33* (4), 307-318.

Dodd, K. C., Nair, V. A., & Prabhakaran, V. (2017). Role of the contralesional vs. ipsilesional hemisphere in stroke recovery. *Front Hum Neurosci*, *11*, 469.

Dohle, C., Püllen, J., Nakaten, A., Küst, J., Rietz, C., & Karbe, H. (2009). Mirror therapy promotes recovery from severe hemiparesis: a randomized controlled trial. *Neurorehabil Neural Repair*, *23* (3), 209-217.

Doyle, S., Bennett, S., Fasoli, S. E., & McKenna, K. T. (2010). Interventions for sensory impairment in the upper limb after stroke. *Cochrane Database Syst Rev*, *2010* (6), Cd006331.

Drevon, D., Fursa, S. R., & Malcolm, A. L. (2017). Intercoder reliability and validity of webPlotDigitizer in extracting graphed data. *Behav Modif*, *41* (2), 323-339.

Duncan, P. W., Bode, R. K., Min Lai, S., & Perera, S. (2003). Rasch analysis of a new stroke-specific outcome scale: the Stroke Impact Scale. *Arch Phys Med Rehabil*, *84* (7), 950-963.

Duncan, P. W., Goldstein, L. B., Matchar, D., Divine, G. W., & Feussner, J. (1992). Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. *Stroke*, *23* (8), 1084-1089.

Duncan, P. W., Propst, M., & Nelson, S. G. (1983). Reliability of the fugl-meyer assessment of sensorimotor recovery following cerebrovascular accident. *Phys Ther*, *63* (10), 1606-1610.

Duncan, P. W., Wallace, D., Lai, S. M., Johnson, D., Embretson, S., & Laster, L. J. (1999). The stroke impact scale version 2.0. Evaluation of reliability, validity, and sensitivity to change. *Stroke*, *30* (10), 2131-2140.

Edwards, D. F., Lang, C. E., Wagner, J. M., Birkenmeier, R., & Dromerick, A. W. (2012). An evaluation of the wolf motor function test in motor trials early after stroke. *Arch Phys Med Rehabil*, *93* (4), 660-668.

Ehrensberger, M., Simpson, D., Broderick, P., Blake, C., Horgan, F., Hickey, P., O'Reilly, J., & Monaghan, K. (2019). Unilateral strength training and mirror therapy in patients with chronic stroke: a pilot randomized trial. *Am J Phys Med Rehabil*, *98* (8), 657-665.

Eraifej, J., Clark, W., France, B., Desando, S., & Moore, D. (2017). Effectiveness of upper limb functional electrical stimulation after stroke for the improvement of activities of daily living and motor function: a systematic review and meta-analysis. *Syst Rev*, *6* (1), 40.

Essers, B., Van Gils, A., Lafosse, C., Michielsen, M., Beyens, H., Schillebeeckx, F., Veerbeek, J. M., Luft, A. R., Kos, D., & Verheyden, G. (2021). Evolution and prediction of mismatch between observed and perceived upper limb function after stroke: a prospective, longitudinal, observational cohort study. *BMC Neurol*, *21* (1), 488.

Fadiga, L., Fogassi, L., Pavesi, G., & Rizzolatti, G. (1995). Motor facilitation during action observation: a magnetic stimulation study. *J Neurophysiol*, *73* (6), 2608-2611.

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*, *39* (2), 175-191.

Feigin, V. L., Nguyen, G., Cercy, K., et al. (2018). Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. *N Engl J Med*, *379* (25), 2429-2437.

Fellows, S. J., Kaus, C., & Thilmann, A. F. (1994). Voluntary movement at the elbow in spastic hemiparesis. *Ann Neurol*, *36* (3), 397-407.

Feng, Q., Xu, H.Y., Zhou, Y.B., Jin, J., Zhang, J., Huang, C.Y. (2021). Application of transcutaneous electrical acupoint stimulation combined with mirror therapy in rehabilitation nursing of patients with upper limb spasticity after stroke. *Chin Nurs Res*, 35 (16):2879–2883.

Ferrarello, F., Baccini, M., Rinaldi, L. A., Cavallini, M. C., Mossello, E., Masotti, G., Marchionni, N., & Di Bari, M. (2011). Efficacy of physiotherapy interventions late after stroke: a meta-analysis. *J Neurol Neurosurg Psychiatry*, 82 (2), 136-143.

Feys, H., De Weerdt, W., Verbeke, G., Steck, G. C., Capiau, C., Kiekens, C., Dejaeger, E., Van Hoydonck, G., Vermeersch, G., & Cras, P. (2004). Early and repetitive stimulation of the arm can substantially improve the long-term outcome after stroke: a 5-year follow-up study of a randomized trial. *Stroke*, *35* (4), 924-929.

Field, A. (2009). Discovering statistics using SPSS, 3rd ed, Sage, Thousand Oaks,Calif, USA.

Fink, G. R., Marshall, J. C., Halligan, P. W., Frith, C. D., Driver, J., Frackowiak, R. S., & Dolan, R. J. (1999). The neural consequences of conflict between intention and the senses. *Brain*, *122 (Pt 3)*, 497-512.

Fletcher, G. F., Ades, P. A., Kligfield, P., Arena, R., Balady, G. J., Bittner, V. A., Coke, L. A., Fleg, J. L., Forman, D. E., Gerber, T. C., Gulati, M., Madan, K., Rhodes, J., Thompson, P. D., & Williams, M. A. (2013). Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation*, *128* (8), 873-934.

Fugl-Meyer, A. R., Jääskö, L., Leyman, I., Olsson, S., & Steglind, S. (1975). The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. *Scand J Rehabil Med*, *7* (1), 13-31.

Fukaguchi, K., Yamagami, H., Soeno, S., Hara, K., Shirakawa, T., Sonoo, T., Nakamura, K., & Goto, T. (2021). Association of initial potassium levels with the type of stroke in the emergency department. *J Stroke Cerebrovasc Dis*, *30* (8), 105875.

Garrison, K. A., Winstein, C. J., & Aziz-Zadeh, L. (2010). The mirror neuron system: a neural substrate for methods in stroke rehabilitation. *Neurorehabil Neural Repair*, *24* (5), 404-412.

Geller, D., Nilsen, D. M., Quinn, L., Van Lew, S., Bayona, C., & Gillen, G. (2022). Home mirror therapy: a randomized controlled pilot study comparing unimanual and bimanual mirror therapy for improved arm and hand function post-stroke. *Disabil Rehabil*, *44* (22), 6766-6774.

Ghaffari, A., Rostami, H. R., & Akbarfahimi, M. (2021). Predictors of instrumental activities of daily living performance in patients with stroke. *Occup Ther Int*, *2021*, 6675680.

Ghaziani, E., Couppé, C., Siersma, V., Søndergaard, M., Christensen, H., & Magnusson, S. P. (2018). Electrical somatosensory stimulation in early rehabilitation of arm paresis after stroke: a randomized controlled trial. *Neurorehabil Neural Repair*, *32* (10), 899-912.

Gibson, C. L. (2013). Cerebral ischemic stroke: is gender important? *J Cereb Blood Flow Metab*, *33*(9), 1355-1361.

Giebel, G. D. (2020). Use of mHealth devices to screen for atrial fibrillation: cost-effectiveness analysis. *JMIR Mhealth Uhealth*, *8* (10), e20496.

Gladstone, D. J., Danells, C. J., & Black, S. E. (2002). The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties. *Neurorehabil Neural Repair*, *16* (3), 232-240.

Goff, A. J., De Oliveira Silva, D., Merolli, M., Bell, E. C., Crossley, K. M., & Barton, C. J. (2021). Patient education improves pain and function in people with knee osteoarthritis with better effects when combined with exercise therapy: a systematic review. *J Physiother*, *67* (3), 177-189.

Graf, C. (2008). The lawton instrumental activities of daily living scale. *Am J Nurs*, *108* (4), 52-62.

Grefkes, C., & Fink, G. R. (2020). Recovery from stroke: current concepts and future perspectives. *Neurol Res Pract*, *2*, 17.

Grefkes, C., Nowak, D. A., Eickhoff, S. B., Dafotakis, M., Küst, J., Karbe, H., & Fink, G. R. (2008). Cortical connectivity after subcortical stroke assessed with functional magnetic resonance imaging. *Ann Neurol*, *63* (2), 236-246.

Guan, T., Alam, M. K., & Rao, M. B. (2023). Sample size calculations in simple linear regression: a new approach. *Entropy (Basel)*, *25* (4):611.

Guidetti, S., Ytterberg, C., Ekstam, L., Johansson, U., & Eriksson, G. (2014). Changes in the impact of stroke between 3 and 12 months post-stroke, assessed with the stroke impact scale. *J Rehabil Med*, *46* (10), 963-968.

Guo, C., Sui, Y., Xu, S., Zhuang, R., Zhang, M., Zhu, S., Wang, J., Zhang, Y., Kan, C., Shi, Y., Wang, T., & Shen, Y. (2022). Contralaterally controlled neuromuscular electrical stimulation-induced changes in functional connectivity in patients with stroke assessed using functional near-infrared spectroscopy. *Front Neural Circuits*, *16*, 955728.

Guyatt, G., Oxman, A. D., Akl, E. A., Kunz, R., Vist, G., Brozek, J., Norris, S., Falck-Ytter, Y., Glasziou, P., DeBeer, H., Jaeschke, R., Rind, D., Meerpohl, J., Dahm, P., & Schünemann, H. J. (2011). GRADE guidelines: 1. introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*, *64* (4), 383-394.

Gygax, M. J., Schneider, P., & Newman, C. J. (2011). Mirror therapy in children with hemiplegia: a pilot study. *Dev Med Child Neurol*, *53* (5), 473-476.

Hakon, J., Quattromani, M. J., Sjölund, C., Tomasevic, G., Carey, L., Lee, J. M., Ruscher, K., Wieloch, T., & Bauer, A. Q. (2018). Multisensory stimulation improves functional recovery and resting-state functional connectivity in the mouse brain after stroke. *Neuroimage Clin*, *17*, 717-730.

Haley, S. M., & Fragala-Pinkham, M. A. (2006). Interpreting change scores of tests and measures used in physical therapy. *Phys Ther*, *86* (5), 735-743.

Hamilton, C. B., & Chesworth, B. M. (2013). A rasch-validated version of the upper extremity functional index for interval-level measurement of upper extremity function. *Phys Ther*, 93 (11), 1507-1519.

Hamzei, F., Erath, G., Kücking, U., Weiller, C., & Rijntjes, M. (2020). Anatomy of brain lesions after stroke predicts effectiveness of mirror therapy. *Eur J Neurosci*, 52 (6), 3628-3641.

Hankey, G. J. (2017). Stroke. *Lancet*, *389*(10069), 641-654.

Hara, Y., Obayashi, S., Tsujiuchi, K., & Muraoka, Y. (2013). The effects of electromyography-controlled functional electrical stimulation on upper extremity function and cortical perfusion in stroke patients. *Clin Neurophysiol*, *124* (10), 2008-2015.

Hatem, S. M., Saussez, G., Della Faille, M., Prist, V., Zhang, X., Dispa, D., & Bleyenheuft, Y. (2016). Rehabilitation of Motor Function after Stroke: A Multiple Systematic Review

Focused on Techniques to Stimulate Upper Extremity Recovery. *Front Hum Neurosci*, *10*, 442.

Hiengkaew, V., Jitaree, K., & Chaiyawat, P. (2012). Minimal detectable changes of the Berg Balance Scale, Fugl-Meyer Assessment Scale, Timed "Up & Go" Test, gait speeds, and 2-minute walk test in individuals with chronic stroke with different degrees of ankle plantarflexor tone. *Arch Phys Med Rehabil*, *93* (7), 1201-1208.

Higgins, J.P.T., Green, A. (2011). Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration, Version 5.1.0 [updated March 2011].

Hobart, J. C., Cano, S. J., Warner, T. T., & Thompson, A. J. (2012). What sample sizes for reliability and validity studies in neurology? *J Neurol*, *259*, 2681-2694.

Hobart, J. C., Lamping, D. L., Freeman, J. A., Langdon, D. W., McLellan, D. L., Greenwood, R. J., & Thompson, A. J. (2001). Evidence-based measurement: which disability scale for neurologic rehabilitation? *Neurology*, *57* (4), 639-644.

Hodkinson, H. M. (1972). Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age Ageing*, *1* (4), 233-238.

Hoonhorst, M. H., Nijland, R. H., van den Berg, J. S., Emmelot, C. H., Kollen, B. J., & Kwakkel, G. (2015). How do fugl-meyer arm motor scores relate to dexterity according to the action research arm test at 6 months poststroke? *Arch Phys Med Rehabil*, *96* (10), 1845-1849.

Hsu, H. Y., Kuo, L. C., Lin, Y. C., Su, F. C., Yang, T. H., & Lin, C. W. (2022). Effects of a virtual reality-based mirror therapy program on improving sensorimotor function of hands in chronic stroke patients: a randomized controlled trial. *Neurorehabil Neural Repair*, *36* (6), 335-345.

Hu, X., Suresh, A. K., Li, X., Rymer, W. Z., & Suresh, N. L. (2012). Impaired motor unit control in paretic muscle post stroke assessed using surface electromyography: a preliminary report. *Annu Int Conf IEEE Eng Med Biol Soc*, *2012*, 4116-4119.

Huang, P. C., Hsieh, Y. W., Wang, C. M., Wu, C. Y., Huang, S. C., & Lin, K. C. (2014). Predictors of motor, daily function, and quality-of-life improvements after upper-extremity robot-assisted rehabilitation in stroke. *Am J Occup Ther*, *68*(3), 325-333.

Hui-Chan, C. W., & Levin, M. F. (1993). Stretch reflex latencies in spastic hemiparetic subjects are prolonged after transcutaneous electrical nerve stimulation. *Can J Neurol Sci*, *20* (2), 97-106.

Hunnicutt, J. L., & Gregory, C. M. (2017). Skeletal muscle changes following stroke: a systematic review and comparison to healthy individuals. *Top Stroke Rehabil*, *24* (6), 463-471.

Hunter, S., & Crome, P. (2002). Hand function and stroke. *Rev Clin Gerontol*, *12* (1), 68-81.

Iacoboni, M., & Dapretto, M. (2006). The mirror neuron system and the consequences of its dysfunction. *Nat Rev Neurosci*, *7* (12), 942-951.

Iacoboni, M., & Mazziotta, J. C. (2007). Mirror neuron system: basic findings and clinical applications. *Ann Neurol*, *62* (3), 213-218.

Iacoboni, M., Woods, R. P., Brass, M., Bekkering, H., Mazziotta, J. C., & Rizzolatti, G. (1999). Cortical mechanisms of human imitation. *Science*, *286* (5449), 2526-2528.

Innes, E. (1999). Handgrip strength testing: a review of the literature. *Aust Occup Ther J*, *46* (3), 120-140.

Invernizzi, M., Negrini, S., Carda, S., Lanzotti, L., Cisari, C., & Baricich, A. (2013). The value of adding mirror therapy for upper limb motor recovery of subacute stroke patients: a randomized controlled trial. *Eur J Phys Rehabil Med*, *49* (3), 311-317.

Jensen, C. V. (1991). A computer program for randomizing patients with near-even distribution of important parameters. *Comput Biomed Res*, *24* (5), 429-434.

Ji, S. G., & Kim, M. K. (2015). The effects of mirror therapy on the gait of subacute stroke patients: a randomized controlled trial. *Clin Rehabil*, *29* (4), 348-354.

Johansson, B. B., Haker, E., Von Arbin, M.,et al. (2001). Acupuncture and transcutaneous nerve stimulation in stroke rehabilitation: a randomized, controlled trial. *Stroke (1970)*, *32* (3), 707-713.

Johnson, M. (2007). Transcutaneous electrical nerve stimulation: mechanisms, clinical application and evidence. *Rev Pain*, *1* (1), 7-11.

Jørgensen, H. S., Nakayama, H., Raaschou, H. O., Vive-Larsen, J., Støier, M., & Olsen, T. S. (1995). Outcome and time course of recovery in stroke. Part II: Time course of recovery. The Copenhagen Stroke Study. *Arch Phys Med Rehabil*, *76* (5), 406-412.

Jung, K., Jung, J., In, T., Kim, T., & Cho, H. Y. (2017). The influence of task-related training combined with transcutaneous electrical nerve stimulation on paretic upper limb muscle activation in patients with chronic stroke. *NeuroRehabilitation*, *40* (3), 315-323.

Jung, K. S., In, T. S., & Cho, H. Y. (2017). Effects of sit-to-stand training combined with transcutaneous electrical stimulation on spasticity, muscle strength and balance ability in patients with stroke: A randomized controlled study. *Gait Posture*, *54*, 183-187.

Jung, K. S., Jung, J. H., In, T. S., & Cho, H. Y. (2020). Effectiveness of heel-raise-lower exercise after transcutaneous electrical nerve stimulation in patients with stroke: a randomized controlled study. *J Clin Med*, *9* (11), 1-8.

Juniper, A. R., & Connor, L. T. (2022). Self-Perceived ADL/IADL function is influenced by residual neurological impairment, aphasia, and anxiety. *Can J Occup Ther*, *89* (3), 307-314.

Kaiser, H. F. (1974). An index of factorial simplicity. *psychometrika*, *39* (1), 31-36.

Kalra, A., Urban, M. O., & Sluka, K. A. (2001). Blockade of opioid receptors in rostral ventral medulla prevents antihyperalgesia produced by transcutaneous electrical nerve stimulation (TENS). *J Pharmacol Exp Ther*, *298* (1), 257-263.

Khan, F., Abusharha, S., Alfuraidy, A., Nimatallah, K., Almalki, R., Basaffar, R., Mirdad, M., Chevidikunnan, M. F., & Basuodan, R. (2022). Prediction of factors affecting mobility in patients with stroke and finding the mediation effect of balance on mobility: a cross-sectional study. *Int J Environ Res Public Health*, *19* (24):16612.

Khan, M. A., Fares, H., Ghayvat, H., Brunner, I. C., Puthusserypady, S., Razavi, B., Lansberg, M., Poon, A., & Meador, K. J. (2023). A systematic review on functional electrical stimulation based rehabilitation systems for upper limb post-stroke recovery. *Front Neurol*, *14*, 1272992.

Khaslavskaia, S., Ladouceur, M., & Sinkjaer, T. (2002). Increase in tibialis anterior motor cortex excitability following repetitive electrical stimulation of the common peroneal nerve. *Exp Brain Res*, *145* (3), 309-315.

Kim, H., Lee, G., & Song, C. (2014). Effect of functional electrical stimulation with mirror therapy on upper extremity motor function in poststroke patients. *J Stroke Cerebrovasc Dis*, *23* (4), 655-661.

Kim, J. H., & Lee, B. H. (2015). Mirror therapy combined with biofeedback functional electrical stimulation for motor recovery of upper extremities after stroke: a pilot randomized controlled trial. *Occup Ther Int,* (2), 51-60.

Kim, T. H., In, T. S., & Cho, H. Y. (2013). Task-related training combined with transcutaneous electrical nerve stimulation promotes upper limb functions in patients with chronic stroke. *Tohoku J Exp Med*, *231*(2), 93-100.

Kim, Y. S., Song, J. Y., Park, S. H., & Lee, M. M. (2023). Effect of functional electrical stimulation-based mirror therapy using gesture recognition biofeedback on upper extremity function in patients with chronic stroke: a randomized controlled trial. *Medicine (Baltimore)*, *102* (52), e36546.

Kirton, A., Deveber, G., Gunraj, C., & Chen, R. (2010). Cortical excitability and interhemispheric inhibition after subcortical pediatric stroke: plastic organization and effects of rTMS. *Clin Neurophysiol*, *121* (11), 1922-1929.

Klaiput, A., & Kitisomprayoonkul, W. (2009). Increased pinch strength in acute and subacute stroke patients after simultaneous median and ulnar sensory stimulation. *Neurorehabil Neural Repair*, *23* (4), 351-356.

Klamroth-Marganska, V., Blanco, J., Campen, K., Curt, A., Dietz, V., Ettlin, T., Felder, M., Fellinghauer, B., Guidali, M., Kollmar, A., Luft, A., Nef, T., Schuster-Amft, C., Stahel, W., & Riener, R. (2014). Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial. *Lancet Neurol*, *13* (2), 159-166.

Koo, T. K., & Li, M. Y. (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med*, *15* (2), 155-163.

Kuo, C. L., & Hu, G. C. (2018). Post-stroke spasticity: a review of epidemiology, pathophysiology, and treatments. *Int J Gerontol*, *12* (4), 280-284.

Kwakkel, G., Kollen, B., & Lindeman, E. (2004). Understanding the pattern of functional recovery after stroke: facts and theories. *Restor Neurol Neurosci*, *22* (3-5), 281-299.

Kwakkel, G., Kollen, B. J., van der Grond, J., & Prevo, A. J. (2003). Probability of regaining dexterity in the flaccid upper limb: impact of severity of paresis and time since onset in acute stroke. *Stroke*, *34* (9), 2181-2186.

Kwong, P. W., Ng, G. Y., Chung, R. C., & Ng, S. S. (2018). Transcutaneous electrical nerve stimulation improves walking capacity and reduces spasticity in stroke survivors: a systematic review and meta-analysis. *Clin Rehabil*, *32* (9), 1203-1219.

Kwong, P. W. H., Ng, G. Y. F., Chung, R. C. K., & Ng, S. S. M. (2018). Bilateral transcutaneous electrical nerve stimulation improves lower-limb motor function in subjects with chronic stroke: a randomized controlled trial. *J Am Heart Assoc*, *7* (4):e007341.

Kwong, P. W. H., & Ng, S. S. M. (2019). Cutoff score of the lower-extremity motor subscale of fugl-meyer assessment in chronic stroke survivors: a cross-sectional study. *Arch Phys Med Rehabil*, *100* (9), 1782-1787.

Kwong, P. W. H., Ng, S. S. M., Chung, R. C. K., & Ng, G. Y. F. (2017). A structural equation model of the relationship between muscle strength, balance performance, walking endurance and community integration in stroke survivors. *PLoS One*, *12* (10), e0185807.

Lachman, M. E., Howland, J., Tennstedt, S., Jette, A., Assmann, S., & Peterson, E. W. (1998). Fear of falling and activity restriction: the survey of activities and fear of falling in the elderly (SAFE). *J Gerontol B Psychol Sci Soc Sci*, *53* (1), P43-50.

Lacroix, S., Havton, L. A., McKay, H., Yang, H., Brant, A., Roberts, J., & Tuszynski, M. H. (2004). Bilateral corticospinal projections arise from each motor cortex in the macaque monkey: a quantitative study. *J Comp Neurol*, *473* (2), 147-161.

Lai, M. I., Pan, L. L., Tsai, M. W., Shih, Y. F., Wei, S. H., & Chou, L. W. (2016). Investigating the effects of peripheral electrical stimulation on corticomuscular functional connectivity stroke survivors. *Top Stroke Rehabil*, *23* (3), 154-162.

Lam, S. C., Wong, Y.-y., & Woo, J. (2010). Reliability and validity of the abbreviated mental test (Hong Kong version) in residential care homes. *J Am Geriatr Soc*, *58* (11), 2255-2257.

Lamberti, N., Straudi, S., Malagoni, A. M., Argirò, M., Felisatti, M., Nardini, E., Zambon, C., Basaglia, N., & Manfredini, F. (2017). Effects of low-intensity endurance and

resistance training on mobility in chronic stroke survivors: a pilot randomized controlled study. *Eur J Phys Rehabil Med*, *53* (2), 228-239.

Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics*, *33* (1), 159-174.

Lang C.E., Edwards D. F., Birkenmeier R.L., Dromerick A.W. (2008). Estimating minimal clinically important differences of upper-extremity measures early after stroke. *Arch Phys Med Rehabil*, 89 (9):1693-700.

Läppchen, C. H., Ringer, T., Blessin, J., Seidel, G., Grieshammer, S., Lange, R., & Hamzei, F. (2012). Optical illusion alters M1 excitability after mirror therapy: a TMS study. *J Neurophysiol*, *108* (10), 2857-2861.

Larsen, L. H., Zibrandtsen, I. C., Wienecke, T., Kjaer, T. W., Christensen, M. S., Nielsen, J. B., & Langberg, H. (2017). Corticomuscular coherence in the acute and subacute phase after stroke. *Clin Neurophysiol*, *128* (11), 2217-2226.

Lee, K. B., Lim, S. H., Kim, K. H., Kim, K. J., Kim, Y. R., Chang, W. N., Yeom, J. W., Kim, Y. D., & Hwang, B. Y. (2015). Six-month functional recovery of stroke patients: a multi-time-point study. *Int J Rehabil Res*, *38*(2), 173-180.

Lee, M. M., Cho, H. Y., & Song, C. H. (2012). The mirror therapy program enhances upper-limb motor recovery and motor function in acute stroke patients. *Am J Phys Med Rehabil*, *91* (8), 689-696.

Lee, Y.Y., Lin, K.C., Wu, C.Y., Liao, C.H., Lin, J.C., & Chen, C. (2015). Combining afferent stimulation and mirror therapy for improving muscular, sensorimotor, and daily functions after chronic stroke: a randomized, placebo-controlled study. *Am J Phys Med Rehabil*, *94* (10S), 859-868.

Lemon, R. N. (2008). Descending pathways in motor control. *Annu Rev Neurosci*, *31*, 195-218.

Levin, M. F., & Hui-Chan, C. W. (1992). Relief of hemiparetic spasticity by TENS is associated with improvement in reflex and voluntary motor functions. *Electroencephalogr Clin Neurophysiol*, *85* (2), 131-142.

Levin, M. F., & Hui-Chan, C. W. (1993). Conventional and acupuncture-like transcutaneous electrical nerve stimulation excite similar afferent fibers. *Arch Phys Med Rehabil*, *74* (1), 54-60.

Li, Y., Wei, Q., Gou, W., & He, C. (2018). Effects of mirror therapy on walking ability, balance and lower limb motor recovery after stroke: a systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil*, *32* (8), 1007-1021.

Lieshout, E., van de Port, I. G., Dijkhuizen, R. M., & Visser-Meily, J. M. A. (2020). Does upper limb strength play a prominent role in health-related quality of life in stroke patients discharged from inpatient rehabilitation? *Top Stroke Rehabil*, *27* (7), 525-533.

Lin, K.C., Chen, Y.T., Huang, P. C., Wu, C.Y., Huang, W. L., Yang, H. W., Lai, H. T., & Lu, H. J. (2014). Effect of mirror therapy combined with somatosensory stimulation on motor recovery and daily function in stroke patients: A pilot study. *J Formos Med Assoc*, *113* (7), 422-428.

Lin, K. C., Huang, P. C., Chen, Y.T., Wu, C.Y., & Huang, W. L. (2014). Combining afferent stimulation and mirror therapy for rehabilitating motor function, motor control, ambulation, and daily functions after stroke. *Neurorehabil Neural Repair*, *28* (2), 153-162.

Lin, K. C., Huang, P. C., Chen, Y. T., Wu, C. Y., & Huang, W. L. (2014). Combining afferent stimulation and mirror therapy for rehabilitating motor function, motor control, ambulation, and daily functions after stroke. *Neurorehabil Neural Repair*, *28* (2), 153-162.

Lin, S., Sun, Q., Wang, H., & Xie, G. (2018). Influence of transcutaneous electrical nerve stimulation on spasticity, balance, and walking speed in stroke patients: A systematic review and meta-analysis. *J Rehabil Med*, *50* (1), 3-7.

Liu, J., Drutz, C., Kumar, R., McVicar, L., Weinberger, R., Brooks, D., & Salbach, N. M. (2008). Use of the six-minute walk test poststroke: is there a practice effect? *Arch Phys Med Rehabil*, *89* (9), 1686-1692.

Liu, J., Sheng, Y., Zeng, J., & Liu, H. (2019). Corticomuscular coherence for upper arm flexor and extensor muscles during isometric exercise and cyclically isokinetic movement. *Front Neurosci*, *13*, 522.

Liu, T. W., Ng, G. Y. F., Chung, R. C. K., & Ng, S. S. M. (2018). Cognitive behavioural therapy for fear of falling and balance among older people: a systematic review and meta-analysis. *Age Ageing*, *47* (4), 520-527.

Liu, T. W., Ng, S. S., & Ng, G. Y. (2014). Translation and initial validation of the Chinese (Cantonese) version of community integration measure for use in patients with chronic stroke. *Biomed Res Int*, *2014*, 623836.

Liu, T. W., & Ng, S. S. M. (2019). Assessing the fall risks of community-dwelling stroke survivors using the Short-form Physiological Profile Assessment (S-PPA). *PLoS One*, *14* (5), e0216769.

Lotze, M., Markert, J., Sauseng, P., Hoppe, J., Plewnia, C., & Gerloff, C. (2006). The role of multiple contralesional motor areas for complex hand movements after internal capsular lesion. *J Neurosci*, *26* (22), 6096-6102.

Louie, D. R., Lim, S. B., & Eng, J. J. (2019). The efficacy of lower extremity mirror therapy for improving balance, gait, and motor function poststroke: a systematic review and meta-analysis. *J Stroke Cerebrovasc Dis*, *28* (1), 107-120.

Lu, Z. (2018). Effect of mirror image therapy combined with contralateral controlled functional electrical stimulation on early upper limb function of stroke patients with hemiplegia. *J Nurs Rehabil*, 17 (10):60–62.

Luft, A. R., McCombe-Waller, S., Whitall, J., Forrester, L. W., Macko, R., Sorkin, J. D., Schulz, J. B., Goldberg, A. P., & Hanley, D. F. (2004). Repetitive bilateral arm training and motor cortex activation in chronic stroke: a randomized controlled trial. *JAMA*, *292* (15), 1853-1861.

Lundquist, C. B., & Maribo, T. (2017). The Fugl-Meyer assessment of the upper extremity: reliability, responsiveness and validity of the Danish version. *Disabil Rehabil*, *39* (9), 934-939.

Luo, Z., Zeng, L. L., Qin, J., Hou, C., Shen, H., & Hu, D. (2020). Functional Parcellation of Human Brain Precuneus Using Density-Based Clustering. *Cereb Cortex*, *30* (1), 269-282.

Luo, Z., Zhou, Y., He, H., Lin, S., Zhu, R., Liu, Z., Liu, J., Liu, X., Chen, S., Zou, J., & Zeng, Q. (2020). Synergistic effect of combined mirror therapy on upper extremity in patients with stroke: a systematic review and meta-analysis. *Front Neurol*, *11*, 155.

Lv, W., Wang, A., Wang, Q., Wang, R., Xu, Q., Wu, S., Han, Y., Jiang, Y., Lin, J., Jing, J., Li, H., Wang, Y., & Meng, X. (2023). One-year direct and indirect costs of ischaemic stroke in China. *Stroke Vasc Neurol*, 9 (4): 380-389.

Macchiavelli, A., Giffone, A., Ferrarello, F., & Paci, M. (2021). Reliability of the six-minute walk test in individuals with stroke: systematic review and meta-analysis. *Neurol Sci*, *42* (1), 81-87.

MacIsaac, R., Ali, M., Peters, M., English, C., Rodgers, H., Jenkinson, C., Lees, K. R., & Quinn, T. J. (2016). Derivation and Validation of a Modified Short Form of the Stroke Impact Scale. *J Am Heart Assoc*, *5* (5): e003108.

Madhoun, H. Y., Tan, B., Feng, Y., Zhou, Y., Zhou, C., & Yu, L. (2020). Task-based mirror therapy enhances the upper limb motor function in subacute stroke patients: a randomized control trial. *Eur J Phys Rehabil Med*, *56* (3), 265-271.

Mak, M. K., Lau, A. L., Law, F. S., Cheung, C. C., & Wong, I. S. (2007). Validation of the Chinese translated Activities-Specific Balance Confidence scale. *Arch Phys Med Rehabil*, *88* (4), 496-503.

Mariana de Aquino Miranda, J., Mendes Borges, V., Bazan, R., José Luvizutto, G., & Sabrysna Morais Shinosaki, J. (2023). Early mobilization in acute stroke phase: a systematic review. *Top Stroke Rehabil*, *30* (2), 157-168.

Marquez-Chin, C., & Popovic, M. R. (2020). Functional electrical stimulation therapy for restoration of motor function after spinal cord injury and stroke: a review. *Biomed Eng Online*, *19* (1), 34.

Mathias, S., Nayak, U. S., & Isaacs, B. (1986). Balance in elderly patients: the "get-up and go" test. *Arch Phys Med Rehabil*, *67* (6), 387-389.

Mathieson, S., Parsons, J., Kaplan, M., & Parsons, M. (2018). Combining functional electrical stimulation and mirror therapy for upper limb motor recovery following stroke: a randomised trial. *Eur J Physiother*, *20* (4), 244-249.

Melzack, R., & Wall, P. D. (1965). Pain mechanisms: a new theory. *Science*, *150* (3699), 971-979.

Meng, X., Wang, A., Wang, R., Xu, Q., Wu, S., & Han, Y. (2022). EE208 direct cost and indirect cost of ischemic stroke in China. *Value Health*, *25* (12), S93-S94.

Michielsen, M. E., Selles, R. W., van der Geest, J. N., Eckhardt, M., Yavuzer, G., Stam, H. J., Smits, M., Ribbers, G. M., & Bussmann, J. B. (2011). Motor recovery and cortical reorganization after mirror therapy in chronic stroke patients: a phase II randomized controlled trial. *Neurorehabil Neural Repair*, *25* (3), 223-233.

Michielsen, M. E., Smits, M., Ribbers, G. M., Stam, H. J., van der Geest, J. N., Bussmann, J. B., & Selles, R. W. (2011). The neuronal correlates of mirror therapy: an fMRI study on mirror induced visual illusions in patients with stroke. *J Neurol Neurosurg Psychiatry*, *82* (4), 393-398.

Mohan, U., Babu, S. K., Kumar, K. V., Suresh, B. V., Misri, Z. K., & Chakrapani, M. (2013). Effectiveness of mirror therapy on lower extremity motor recovery, balance and mobility in patients with acute stroke: A randomized sham-controlled pilot trial. *Ann Indian Acad Neurol*, *16* (4), 634-639.

Moloney, J., Regan, J., & Walshe, M. (2023). Patient reported outcome measures in dysphagia research following stroke: a scoping review and qualitative analysis. *Dysphagia*, *38* (1), 181-190.

Mong, Y., Teo, T. W., & Ng, S. S. (2010). 5-repetition sit-to-stand test in subjects with chronic stroke: reliability and validity. *Arch Phys Med Rehabil*, *91* (3), 407-413.

Monte-Silva, K., Piscitelli, D., Norouzi-Gheidari, N., Batalla, M. A. P., Archambault, P., & Levin, M. F. (2019). Electromyogram-related neuromuscular electrical stimulation for restoring wrist and hand movement in poststroke hemiplegia: a systematic review and meta-analysis. *Neurorehabil Neural Repair*, *33* (2), 96-111.

Morris, D. M., Uswatte, G., Crago, J. E., Cook, E. W., 3rd, & Taub, E. (2001). The reliability of the wolf motor function test for assessing upper extremity function after stroke. *Arch Phys Med Rehabil*, *82* (6), 750-755.

Morris, J. H., van Wijck, F., Joice, S., & Donaghy, M. (2013). Predicting health related quality of life 6 months after stroke: the role of anxiety and upper limb dysfunction. *Disabil Rehabil*, *35* (4), 291-299.

Mulder, M., & Nijland, R. (2016). Stroke Impact Scale. *J Physiother*, *62* (2), 117.

Murase, N., Duque, J., Mazzocchio, R., & Cohen, L. G. (2004). Influence of interhemispheric interactions on motor function in chronic stroke. *Ann Neurol*, *55* (3), 400-409.

Nagapattinam, S., Babu, V. K., Kumar, S. N., & Ayyappan, V. (2015). Effect of task specific mirror therapy with functional electrical stimulation on upper limb function for subacute hemiplegia. *Int J Physiother*, *2* (5), 840-849.

Nakayama, H., Jørgensen, H. S., Raaschou, H. O., & Olsen, T. S. (1994). Recovery of upper extremity function in stroke patients: the Copenhagen Stroke Study. *Arch Phys Med Rehabil*, *75* (4), 394-398.

Nardone, A., & Schieppati, M. (2005). Reflex contribution of spindle group Ia and II afferent input to leg muscle spasticity as revealed by tendon vibration in hemiparesis. *Clin Neurophysiol*, *116* (6), 1370-1381.

Naz, F., Hussain, D., Ali, H., Raza, Q., & Siddique, F. (2024). Effectiveness of functional electrical stimulation machine in managing neurological diseases -a retrospective study. *Pak J Med Sci*, 40 (2ICON Suppl), S53-s57.

Ng, S. S., & Hui-Chan, C. W. (2005). The timed up & go test: its reliability and association with lower-limb impairments and locomotor capacities in people with chronic stroke. *Arch Phys Med Rehabil*, *86* (8), 1641-1647.

Ng, S. S., & Hui-Chan, C. W. (2007). Transcutaneous electrical nerve stimulation combined with task-related training improves lower limb functions in subjects with chronic stroke. *Stroke*, *38* (11), 2953-2959.

Ng, S. S. M., & Hui-Chan, C. W. Y. (2009). Does the use of TENS increase the effectiveness of exercise for improving walking after stroke? A randomized controlled clinical trial. *Clin Rehabil*, *23* (12), 1093-1103.

Ng, S. S. M., Liu, T. W., Chan, C. Y., Chan, C. W., Chu, C. L., Poon, C. H., Poon, L. Y., Lai, C. Y. Y., & Tse, M. M. Y. (2020). Reliability and validity of the long-distance corridor walk among stroke survivors. *J Rehabil Med*, *52* (5), jrm00062.

Ng, S. S. M., Liu, T. W., Tsoh, J., Chen, P., Cheng, T. S., Cheung, M. C. H., Leung, A. H. H., Ng, L. L. Y., So, K. Y. K., & Tse, M. M. Y. (2022). Psychometric properties of the trail walking test for people With stroke. *Front Neurol*, *13*, 821670.

Ni, Z., & Chen, R. (2008). Short-interval intracortical inhibition: a complex measure. *Clin Neurophysiol*, *119* (10), 2175-2176.

Norouzi-Gheidari, N., Hernandez, A., Archambault, P. S., Higgins, J., Poissant, L., & Kairy, D. (2019). Feasibility, safety and efficacy of a virtual reality exergame system to supplement upper extremity rehabilitation post-stroke: a pilot randomized clinical trial and proof of principle. *Int J Environ Res Public Health*, *17* (1):113.

Onose, G., Anghelescu, A., Blendea, D., Ciobanu, V., Daia, C., Firan, F. C., Oprea, M., Spinu, A., Popescu, C., Ionescu, A., Busnatu, Ș., & Munteanu, C. (2022). Cellular and molecular targets for non-invasive, non-pharmacological therapeutic/rehabilitative interventions in acute ischemic stroke. *Int J Mol Sci*, *23* (2):907.

Opheim, A., Danielsson, A., Alt Murphy, M., Persson, H. C., & Sunnerhagen, K. S. (2014). Upper-limb spasticity during the first year after stroke: stroke arm longitudinal study at the University of Gothenburg. *Am J Phys Med Rehabil*, *93* (10), 884-896.

Ostelo, R. W., De Vet, H. C., Knol, D. L., & Van Den Brandt, P. A. (2004). 24-item Roland-Morris Disability Questionnaire was preferred out of six functional status questionnaires for post-lumbar disc surgery. *J Clin Epidemiol*, *57* (3), 268-276.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., Stewart, L. A., Thomas, J., Tricco, A. C., Welch, V. A., Whiting, P., & Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*, *372*, n71.

Page, S. J., Fulk, G. D., & Boyne, P. (2012). Clinically important differences for the upper-extremity Fugl-Meyer Scale in people with minimal to moderate impairment due to chronic stroke. *Phys Ther*, *92* (6), 791-798.

Palmer, J. A., Wheaton, L. A., Gray, W. A., Saltão da Silva, M. A., Wolf, S. L., & Borich, M. R. (2019). Role of interhemispheric cortical interactions in poststroke motor function. *Neurorehabil Neural Repair*, *33* (9), 762-774.

Pan, H., Liu, T. W., Ng, S. S. M., Chen, P. M., Chung, R. C. K., Lam, S. S. L., Li, C. S. K., Chan, C. C. C., Lai, C. W. K., Ng, W. W. L., Tang, M. W. S., Hui, E., & Woo, J. (2024). Effects of mirror therapy with electrical stimulation for upper limb recovery in people with stroke: a systematic review and meta-analysis. *Disabil Rehabil*, 1-16.

Pan, H., Liu, T. W., Ng, S. S. M., Tsoh, J., Wong, T. W. L., Lam, S. S. L., Li, C. S. K., Chan, C. C. C., & Lai, C. Y. Y. (2024). Testing the psychometric properties of the Chinese (Cantonese) version of SATIS-Stroke in people with chronic stroke. *Disabil Rehabil*, *46* (1), 159-169.

Pan, H., Ng, S. S. M., Liu, T. W., Tsoh, J., & Wong, T. W. L. (2023). Psychometric properties of the Chinese (Cantonese) version of the Upper Extremity Functional Index in people with chronic stroke. *Front Neurol*, *14*, 989403.

Pan, L. H., Yang, W. W., Kao, C. L., Tsai, M. W., Wei, S. H., Fregni, F., Chen, V. C., & Chou, L. W. (2018). Effects of 8-week sensory electrical stimulation combined with motor training on EEG-EMG coherence and motor function in individuals with stroke. *Sci Rep*, *8* (1), 9217.

Park, J., Seo, D., Choi, W., & Lee, S. W. (2014). The effects of exercise with TENS on spasticity, balance, and gait in patients with chronic stroke: A randomized controlled trial. *Med Sci Monit*, *20*, 1890-1896.

Park, J. Y., Chang, M., Kim, K. M., & Kim, H. J. (2015). The effect of mirror therapy on upper-extremity function and activities of daily living in stroke patients. *J Phys Ther Sci*, *27* (6), 1681-1683.

Parry, R., Macias Soria, S., Pradat-Diehl, P., Marchand-Pauvert, V., Jarrassé, N., & Roby-Brami, A. (2019). Effects of Hand Configuration on the Grasping, Holding, and Placement of an Instrumented Object in Patients With Hemiparesis. *Front Neurol*, 10, 240.

Pereira, G. S., Corrêa, F. I., Júlio, C. E., Thonnard, J. L., Bouffioulx, E., Corrêa, J. C. F., & Silva, S. M. (2021). Clinimetric properties of the SATIS-Stroke questionnaire in the Brazilian population: A satisfaction assessment measure addressing activities and participation after a stroke. *Braz J Phys Ther*, *25* (6), 719-726.

Pereira, G. S., Silva, S. M., Júlio, C. E., Thonnard, J. L., Bouffioulx, E., Corrêa, J. C. F., & Corrêa, F. I. (2019). Translation and Cross-Cultural Adaptation of SATIS-Stroke for Use in Brazil: A Satisfaction Measure of Activities and Participation in Stroke Survivors. *Biomed Res Int*, *2019*, 8054640.

Pineda, J. A. (2008). Sensorimotor cortex as a critical component of an 'extended' mirror neuron system: Does it solve the development, correspondence, and control problems in mirroring? *Behav Brain Funct*, *4*, 47.

Pollock, A., Farmer, S. E., Brady, M. C., Langhorne, P., Mead, G. E., Mehrholz, J., & van Wijck, F. (2014). Interventions for improving upper limb function after stroke. *Cochrane Database Syst Rev*, *2014* (11), Cd010820.

Poon, M. T., Fonville, A. F., & Al-Shahi Salman, R. (2014). Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*, *85* (6), 660-667.

Postalian, A. (2023). Sham: A Trick That Deludes∗. *JACC: Cardiovascular Interventions*, *16*(20), 2555-2557.

Potempa, K., Lopez, M., Braun, L. T., Szidon, J. P., Fogg, L., & Tincknell, T. (1995). Physiological outcomes of aerobic exercise training in hemiparetic stroke patients. *Stroke*, *26*(1), 101-105.

Portney LG, Watkins MP. *Foundations of Clinical Research: Applications to Practice*. London: Pearsons (2013).

Preusser, S., Thiel, S. D., Rook, C., Roggenhofer, E., Kosatschek, A., Draganski, B., Blankenburg, F., Driver, J., Villringer, A., & Pleger, B. (2015). The perception of touch and the ventral somatosensory pathway. *Brain*, *138* (3), 540-548.

Prust, M. L., Forman, R., & Ovbiagele, B. (2024). Addressing disparities in the global epidemiology of stroke. *Nat Rev Neurol*, *20* (4), 207-221.

PW, S. (2004). Estimating the standard error of measurement from reliability studies. *Physiother Can*, *56* (1), 27-30.

Radajewska, A., Opara, J. A., Kucio, C., Błaszczyszyn, M., Mehlich, K., & Szczygiel, J. (2013). The effects of mirror therapy on arm and hand function in subacute stroke in patients. *Int J Rehabil Res*, *36* (3), 268-274.

Rajashekaran, P., Pai, K., Thunga, R., & Unnikrishnan, B. (2013). Post-stroke depression and lesion location: A hospital based cross-sectional study. *Indian J Psychiatry*, *55* (4), 343-348.

Ramachandran, V. S., Rogers-Ramachandran, D., & Cobb, S. (1995). Touching the phantom limb. *Nature*, *377* (6549), 489-490.

Rand, D., & Eng, J. J. (2015). Predicting daily use of the affected upper extremity 1 year after stroke. *J Stroke Cerebrovasc Dis*, *24* (2), 274-283.

Reeves, M., Lisabeth, L., Williams, L., Katzan, I., Kapral, M., Deutsch, A., & Prvu-Bettger, J. (2018). Patient-Reported Outcome Measures (PROMs) for Acute Stroke: Rationale, Methods and Future Directions. *Stroke*, *49* (6), 1549-1556.

Ring, H., & Rosenthal, N. (2005). Controlled study of neuroprosthetic functional electrical stimulation in sub-acute post-stroke rehabilitation. *J Rehabil Med*, 37 (1), 32-36.

Rivelis, Y., Zafar, N., & Morice, K. (2024). Spasticity. In StatPearls. StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC.

Rossini, P. M., Calautti, C., Pauri, F., & Baron, J. C. (2003). Post-stroke plastic reorganisation in the adult brain. *Lancet Neurol*, *2* (8), 493-502.

Roy-O'Reilly, M., & McCullough, L. D. (2018). Age and Sex Are Critical Factors in Ischemic Stroke Pathology. *Endocrinology*, *159* (8), 3120-3131.

Saavedra-García, A., Moral-Munoz, J. A., & Lucena-Anton, D. (2021). Mirror therapy simultaneously combined with electrical stimulation for upper limb motor function recovery after stroke: a systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil*, *35* (1), 39-50.

Sacco, R. L., Kasner, S. E., Broderick, J. P., Caplan, L. R., Connors, J. J., Culebras, A., Elkind, M. S., George, M. G., Hamdan, A. D., Higashida, R. T., Hoh, B. L., Janis, L. S., Kase, C. S., Kleindorfer, D. O., Lee, J. M., Moseley, M. E., Peterson, E. D., Turan, T. N., Valderrama, A. L., & Vinters, H. V. (2013). An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, *44* (7), 2064-2089.

Sach, M., Winkler, G., Glauche, V., Liepert, J., Heimbach, B., Koch, M. A., Büchel, C., & Weiller, C. (2004). Diffusion tensor MRI of early upper motor neuron involvement in amyotrophic lateral sclerosis. *Brain*, *127* (Pt 2), 340-350.

Samuelkamaleshkumar, S., Reethajanetsureka, S., Pauljebaraj, P., Benshamir, B., Padankatti, S. M., & David, J. A. (2014). Mirror therapy enhances motor performance in the paretic upper limb after stroke: a pilot randomized controlled trial. *Arch Phys Med Rehabil*, *95* (11), 2000-2005.

Sartor, M. M., Grau-Sánchez, J., Guillén-Solà, A., Boza, R., Puig, J., Stinear, C., Morgado-Perez, A., & Duarte, E. (2021). Intensive rehabilitation programme for patients with subacute stroke in an inpatient rehabilitation facility: describing a protocol of a prospective cohort study. *BMJ Open*, *11* (10), e046346.

Schaechter, J. D., & Perdue, K. L. (2008). Enhanced cortical activation in the contralesional hemisphere of chronic stroke patients in response to motor skill challenge. *Cereb Cortex*, *18* (3), 638-647.

Schick, T., Schlake, H. P., Kallusky, J., Hohlfeld, G., Steinmetz, M., Tripp, F., Krakow, K., Pinter, M., & Dohle, C. (2017). Synergy effects of combined multichannel EMG-triggered electrical stimulation and mirror therapy in subacute stroke patients with severe or very severe arm/hand paresis. *Restor Neurol Neurosci*, *35* (3), 319-332.

Seiffge, D. J., Werring, D. J., Paciaroni, M., Dawson, J., Warach, S., Milling, T. J., Engelter, S. T., Fischer, U., & Norrving, B. (2019). Timing of anticoagulation after recent ischaemic stroke in patients with atrial fibrillation. *Lancet Neurol*, *18* (1), 117-126.

Selles, R. W., Michielsen, M. E., Bussmann, J. B., Stam, H. J., Hurkmans, H. L., Heijnen, I., de Groot, D., & Ribbers, G. M. (2014). Effects of a mirror-induced visual illusion on a reaching task in stroke patients: implications for mirror therapy training. *Neurorehabil Neural Repair*, *28* (7), 652-659.

Sennfält, S., Norrving, B., Petersson, J., & Ullberg, T. (2019). Long-Term Survival and Function After Stroke: A Longitudinal Observational Study From the Swedish Stroke Register. *Stroke*, *50* (1), 53-61.

Shen, Y., Yin, Z., Fan, Y., Chen, C. F., Dai, W., Yi, W., Li, Y., Zhang, W., Zhang, Y., Bian, R., Huang, Y., Machado, S., Yuan, T. F., & Shan, C. (2015). Comparison of the Effects of Contralaterally Controlled Functional Electrical Stimulation and Neuromuscular Electrical Stimulation on Upper Extremity Functions in Patients with Stroke. *CNS Neurol Disord Drug Targets*, *14* (10), 1260-1266.

Shin, H., Suresh, N. L., Rymer, W. Z., & Hu, X. (2018). Relative contribution of different altered motor unit control to muscle weakness in stroke: a simulation study. *J Neural Eng*, *15* (1), 016014.

Siemionow, V., Sahgal, V., & Yue, G. H. (2010). Single-Trial EEG-EMG coherence analysis reveals muscle fatigue-related progressive alterations in corticomuscular coupling. *IEEE Trans Neural Syst Rehabil Eng*, *18* (2), 97-106.

Simpson, D., Ehrensberger, M., Horgan, F., Blake, C., Roberts, D., Broderick, P., & Monaghan, K. (2019). Unilateral dorsiflexor strengthening with mirror therapy to improve motor function after stroke: a pilot randomized study. *Physiother Res Int*, *24* (4), e1792.

Son, S. M., Kwon, J. W., Nam, S. H., Lee, N. K., Kim, K., & Kim, C. S. (2012). Adverse effects of motor-related symptoms on the ipsilateral upper limb according to long-term cane usage. *NeuroRehabilitation (Reading, Mass.)*, *31* (2), 137-141.

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H. Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A.,

Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., McAleenan, A., Reeves, B. C., Shepperd, S., Shrier, I., Stewart, L. A., Tilling, K., White, I. R., Whiting, P. F., & Higgins, J. P. T. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*, *366*, l4898.

Stewart, J. C., & Cramer, S. C. (2013). Patient-reported measures provide unique insights into motor function after stroke. *Stroke*, *44* (4), 1111-1116.

Stinear, C. M., Petoe, M. A., Anwar, S., Barber, P. A., & Byblow, W. D. (2014). Bilateral priming accelerates recovery of upper limb function after stroke: a randomized controlled trial. *Stroke*, *45* (1), 205-210.

Stoykov, M. E., & Madhavan, S. (2015). Motor priming in neurorehabilitation. *J Neurol Phys Ther*, *39* (1), 33-42.

Strens, L. H., Fogelson, N., Shanahan, P., Rothwell, J. C., & Brown, P. (2003). The ipsilateral human motor cortex can functionally compensate for acute contralateral motor cortex dysfunction. *Curr Biol*, *13* (14), 1201-1205.

Sturm, J. W., Donnan, G. A., Dewey, H. M., Macdonell, R. A. L., Gilligan, A. K., Srikanth, V., & Thrift, A. G. (2004). Quality of life after stroke: The North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke (1970)*, *35* (10), 2340-2345.

Su, F., & Xu, W. (2020). Enhancing Brain Plasticity to Promote Stroke Recovery. *Front Neurol*, *11*, 554089.

Suresh, N., Li, X., Zhou, P., & Rymer, W. Z. (2011). Examination of motor unit control properties in stroke survivors using surface EMG decomposition: a preliminary report. *Annu Int Conf IEEE Eng Med Biol Soc*, *2011*, 8243-8246.

Takahashi, Y., Kawakami, M., Mikami, R., Nakajima, T., Nagumo, T., Yamaguchi, T., Honaga, K., Kondo, K., Ishii, R., Fujiwara, T., & Liu, M. (2022). Relationship between spinal reflexes and leg motor function in sub-acute and chronic stroke patients. *Clin Neurophysiol*, *138*, 74-83.

Teasell, R., Mehta, S., Pereira, S., McIntyre, A., Janzen, S., Allen, L., Lobo, L., & Viana, R. (2012). Time to rethink long-term rehabilitation management of stroke patients. *Top Stroke Rehabil*, *19* (6), 457-462.

Tecchio, F., Rossini, P. M., Pizzella, V., Cassetta, E., & Romani, G. L. (1997). Spatial properties and interhemispheric differences of the sensory hand cortical representation: a neuromagnetic study. *Brain Res*, *767* (1), 100-108.

Tekeolu, Y. b., Adak, B., & Göksoy, T. (1998). Effect of transcutaneous electrical nerve stimulation (TENS) on Barthel Activities of Daily Living (ADL) Index score following stroke. *Clin Rehabil*, *12* (4), 277-280.

Terwee, C. B., Bot, S. D., de Boer, M. R., van der Windt, D. A., Knol, D. L., Dekker, J., Bouter, L. M., & de Vet, H. C. (2007). Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol*, *60* (1), 34-42.

Thieme, H., Bayn, M., Wurg, M., Zange, C., Pohl, M., & Behrens, J. (2013). Mirror therapy for patients with severe arm paresis after stroke--a randomized controlled trial. *Clin Rehabil*, *27* (4), 314-324.

Tyson, S. F., Hanley, M., Chillala, J., Selley, A. B., & Tallis, R. C. (2008). Sensory loss in hospital-admitted people with stroke: characteristics, associated factors, and relationship with function. *Neurorehabil Neural Repair*, *22* (2), 166-172.

Uswatte, G., Taub, E., Morris, D., Light, K., & Thompson, P. A. (2006). The Motor Activity Log-28: assessing daily use of the hemiparetic arm after stroke. *Neurology*, *67* (7), 1189-1194.

van der Knaap, L. J., & van der Ham, I. J. (2011). How does the corpus callosum mediate interhemispheric transfer? A review. *Behav Brain Res*, *223* (1), 211-221.

van der Lee, J. H., Beckerman, H., Knol, D. L., de Vet, H. C., & Bouter, L. M. (2004). Clinimetric properties of the motor activity log for the assessment of arm use in hemiparetic patients. *Stroke*, *35* (6), 1410-1414.

van Dijk, K. R., Scherder, E. J., Scheltens, P., & Sergeant, J. A. (2002). Effects of transcutaneous electrical nerve stimulation (TENS) on non-pain related cognitive and behavioural functioning. *Rev Neurosci*, *13* (3), 257-270.

Virani, S. S., Alonso, A., Aparicio, H. J., et al. (2021). Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. *Circulation*, *143* (8), e254-e743.

Vive, S., Bunketorp-Käll, L., & Carlsson, G. (2022). Experience of enriched rehabilitation in the chronic phase of stroke. *Disabil Rehabil*, *44* (3), 412-419.

W, D. (1959). Author's Choice. *Science*, *129* (3358), 1247.

Wang, L.J., Chen, L.Z., Ou,Y. (2015). Effects of mirror visual feedback and electromyographic biofeedback on upper extremity function in hemiplegics after stroke. *Chin J Rehabil Theory Pract*, 21 (2):202-205.

Wang, W., Jiang, B., Sun, H., Ru, X., Sun, D., Wang, L., Wang, L., Jiang, Y., Li, Y., Wang, Y., Chen, Z., Wu, S., Zhang, Y., Wang, D., Wang, Y., & Feigin, V. L. (2017). Prevalence, Incidence, and Mortality of Stroke in China: Results from a Nationwide Population-Based Survey of 480 687 Adults. *Circulation*, *135* (8), 759-771.

Wasaka, T., & Kakigi, R. (2012). Conflict caused by visual feedback modulates activation in somatosensory areas during movement execution. *Neuroimage*, *59* (2), 1501-1507.

Wattchow, K. A., McDonnell, M. N., & Hillier, S. L. (2018). Rehabilitation Interventions for Upper Limb Function in the First Four Weeks Following Stroke: A Systematic Review and Meta-Analysis of the Evidence. *Arch Phys Med Rehabil*, *99* (2), 367-382.

Weavil, J. C., & Amann, M. (2018). Corticospinal excitability during fatiguing whole body exercise. *Prog Brain Res*, *240*, 219-246.

Weidner, N., Ner, A., Salimi, N., & Tuszynski, M. H. (2001). Spontaneous corticospinal axonal plasticity and functional recovery after adult central nervous system injury. *Proc Natl Acad Sci U S A*, *98* (6), 3513-3518.

Wieloch, T., & Nikolich, K. (2006). Mechanisms of neural plasticity following brain injury. *Curr Opinion Neurobiol*, *16* (3), 258-264.

Wingfield, M., Fini, N. A., Brodtmann, A., Williams, G., Churilov, L., & Hayward, K. S. (2022). Upper-Limb Motor Intervention Elements That Drive Improvement in Biomarkers and Clinical Measures Post-Stroke: A Systematic Review in a Systems Paradigm. *Neurorehabil Neural Repair*, *36*(10-11), 726-739.

Wolf, S. L., Thompson, P. A., Morris, D. M., Rose, D. K., Winstein, C. J., Taub, E., Giuliani, C., & Pearson, S. L. (2005). The EXCITE trial: attributes of the Wolf Motor Function Test in patients with subacute stroke. *Neurorehabil Neural Repair*, *19* (3), 194-205.

Wolpert, D. M., Diedrichsen, J., & Flanagan, J. R. (2011). Principles of sensorimotor learning. *Nat Rev Neurosci*, *12* (12), 739-751.

Woodbury, M. L., Velozo, C. A., Richards, L. G., & Duncan, P. W. (2013). Rasch analysis staging methodology to classify upper extremity movement impairment after stroke. *Arch Phys Med Rehabil*, *94* (8), 1527-1533.

World Economic Forum (2023). Strokes could cause 10 million deaths by 2050, and other health stories you need to read this week. Retrieved from https://www.weforum.org/stories/2023/10/strokes-could-cause-10-million-deaths-by-2050-and-other-health-stories-you-need-to-read-this week/#:~:text=1.,are%20insufficient%2C%20the%20report%20warns.

World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. (2013). *JAMA*, *310* (20), 2191-2194.

World Stroke Organization (2022).Impact of Stroke. Retrieved from https://www.world-stroke.org/world-stroke-day-campaign/about-stroke/impact-of-stroke.

World Stroke Organization (2024). Retrieved from https://www.world-stroke.org/world-stroke-day-campaign

Wu, C. W., van Gelderen, P., Hanakawa, T., Yaseen, Z., & Cohen, L. G. (2005). Enduring representational plasticity after somatosensory stimulation. *Neuroimage*, *27* (4), 872-884.

Wu, C. Y., Huang, P. C., Chen, Y. T., Lin, K. C., & Yang, H. W. (2013). Effects of mirror therapy on motor and sensory recovery in chronic stroke: a randomized controlled trial. *Arch Phys Med Rehabil*, *94* (6), 1023-1030.

Wu, L. C., Weng, P. W., Chen, C. H., Huang, Y. Y., Tsuang, Y. H., & Chiang, C. J. (2018). Literature Review and Meta-Analysis of Transcutaneous Electrical Nerve Stimulation in Treating Chronic Back Pain. *Reg Anesth Pain Med*, *43* (4), 425-433.

Xie, S., Zhang, Y., Li, J., Wu, Z., & Bai, Y. (2024). Contralaterally Controlled Functional Electrical Stimulation for Improving Motor Function After Acquired Brain Injury: A Systematic Review and Meta-analysis. *Arch Phys Med Rehabil*, S0003-9993 (24)00882-7.

Xu, R., Zhang, H., Shi, X., Liang, J., Wan, C., & Ming, D. (2023). Lower-Limb Motor Assessment With Corticomuscular Coherence of Multiple Muscles During Ankle Dorsiflexion After Stroke. *IEEE Trans Neural Syst Rehabil Eng*, *31*, 160-168.

Xu, S., Li W.T., Ji, P.P.(2020). Effect of mirror therapy combined with power-assisted electric stimulation on upper extremity motor function and activities of daily living in patients with early stroke. *Pract J Card Cereb Pneumal Vascular Dis*, 28 (8):89–93.

Yang, F., & Butler, A. J. (2020). Efficacy of Controlled Whole-Body Vibration Training on Improving Fall Risk Factors in Stroke Survivors: A Meta-analysis. *Neurorehabil Neural Repair*, *34* (4), 275-288.

Yang, J. D., Liao, C. D., Huang, S. W., Tam, K. W., Liou, T. H., Lee, Y. H., Lin, C. Y., & Chen, H. C. (2019). Effectiveness of electrical stimulation therapy in improving arm function after stroke: a systematic review and a meta-analysis of randomised controlled trials. *Clin Rehabil*, *33* (8), 1286-1297.

Yang, Y., Zhao, Q., Zhang, Y., Wu, Q., Jiang, X., & Cheng, G. (2018). Effect of mirror therapy on recovery of stroke survivors: a systematic review and network meta-analysis. *Neuroscience*, *390*, 318-336.

Yao, S.Z., Lou, L.J., Liu, X.D., Wang, F.(2016). Clinical observation of mirror image therapy combined with electromyographic biofeedback therapy in promoting upper limb functional reconstruction of stroke patients with hemiplegia. *Chin J Phys Med Rehabil*. 2016;38 (10):746–749.

Yap, C., Solovyeva, O., de Bono, J., Rekowski, J., Patel, D., Jaki, T., Mander, A., Evans, T. R. J., Peck, R., Hayward, K. S., Hopewell, S., Ursino, M., Rantell, K. R., Calvert, M., Lee, S., Kightley, A., Ashby, D., Chan, A. W., Garrett-Mayer, E., Isaacs, J. D., Golub, R., Kholmanskikh, O., Richards, D., Boix, O., Matcham, J., Seymour, L., Ivy, S. P., Marshall, L. V., Hommais, A., Liu, R., Tanaka, Y., Berlin, J., Espinasse, A., Dimairo, M., & Weir, C. J. (2023). Enhancing reporting quality and impact of early phase dose-finding clinical trials: CONSORT Dose-finding Extension (CONSORT-DEFINE) guidance. *Bmj*, 383, e076387.

Yavuzer, G., Selles, R., Sezer, N., Sütbeyaz, S., Bussmann, J. B., Köseoğlu, F., Atay, M. B., & Stam, H. J. (2008). Mirror therapy improves hand function in subacute stroke: a randomized controlled trial. *Arch Phys Med Rehabil*, *89* (3), 393-398.

Yun, G. J., Chun, M. H., Park, J. Y., & Kim, B. R. (2011). The synergic effects of mirror therapy and neuromuscular electrical stimulation for hand function in stroke patients. *Ann Rehabil Med*, *35* (3), 316-321.

Zarahn, E., Alon, L., Ryan, S. L., Lazar, R. M., Vry, M. S., Weiller, C., Marshall, R. S., & Krakauer, J. W. (2011). Prediction of motor recovery using initial impairment and fMRI 48 h poststroke. *Cereb Cortex*, *21* (12), 2712-2721.

Zeng, W., Guo, Y., Wu, G., Liu, X., & Fang, Q. (2018). Mirror therapy for motor function of the upper extremity in patients with stroke: A meta-analysis. *J Rehabil Med*, *50* (1), 8-15.

Zhang, K., Ding, L., Wang, X., Zhuang, J., Tong, S., Jia, J., & Guo, X. (2024). Evidence of mirror therapy for recruitment of ipsilateral motor pathways in stroke recovery: A resting fMRI study. *Neurotherapeutics*, *21* (2), e00320.

Zhang, Y., Qu, B., Lun, S. S., Guo, Y., & Liu, J. (2012). The 36-item short form health survey: reliability and validity in Chinese medical students. *Int J Med Sci*, *9* (7), 521-526.

Zhang, Y., Zhang, X., Cheng, C., Huang, S., Hua, Y., Hu, J., Wang, Y., Zhang, W., Yang, Y., Liu, Y., Jia, J., Gou, P., Zhang, P., Zhou, F., Wei, X., & Bai, Y. (2024). Mirror therapy combined with contralaterally controlled functional electrical stimulation for the upper limb motor function after stroke: a randomized controlled trial. *Disabil Rehabil*, 46 (12):2528-2534.

Zhao, Y., Hua, X., Ren, X., Ouyang, M., Chen, C., Li, Y., Yin, X., Song, P., Chen, X., Wu, S., Song, L., & Anderson, C. S. (2023). Increasing burden of stroke in China: A systematic review and meta-analysis of prevalence, incidence, mortality, and case fatality. *Int J Stroke*, *18* (3), 259-267.

Zhou, Y.F., Chen, Q.Z., Hu, S.H., Li, Y.Y., Yu, L., Jin, J.R. (2021). Effect of mirror feedback therapy of contralaterally controlled functional electrical stimulation on hand function of apoplectic hemiplegic patients. *Rehabil Med*, 31 (1):63–68.

Zhuang, J.Y., Ding, L., Shu, B.B., Chen, D., & Jia, J. (2021). Associated Mirror Therapy Enhances Motor Recovery of the Upper Extremity and Daily Function after Stroke: A Randomized Control Study. *Neural plasticity*, *2021*, 7266263-7266269.