ASSESSMENT AND TREATMENT OF BIOMECHANICAL PROPERTIES OF FOOT AND MOBILITY DISORDER IN ELDERLY WITH TYPE 2 DIABETES

THOMAS KA WAI NG

M.Phil

The Hong Kong Polytechnic University

2014

The Hong Kong Polytechnic University

Department of Rehabilitation Sciences

Assessment and treatment of biomechanical properties of foot and mobility disorder in elderly with type 2 diabetes

THOMAS KA WAI NG

A thesis submitted in partial fulfillment for the requirements for the degree of Master of Philosophy

April 2014

CERTIFICATE OF ORIGINALITY

I hereby declare that this thesis is my own work and that, to the best of my knowledge and my 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 acknowledgements had been made in the text.

_________________________ (Signed)

NG KA WAI (Name of student)

Abstract of thesis entitled "Assessment of biomechanical properties of foot and management of mobility disorder in elderly with type 2 diabetes" submitted by Thomas Ka Wai Ng for the degree of Master of Philosophy at the Hong Kong Polytechnic University in 2014.

ABSTRACT

The prevalence of people suffering from diabetes mellitus is rising. This disease causes impairment in the blood glucose regulation and peripheral circulation, which may lead to complications that begin at the most distal part of the lower limbs. Subsequently, the disease may end up in diabetic peripheral neuropathy or foot ulceration. Concerning diabetic foot ulceration, there are various predisposing factors. Apart from the decrease in the sensation over the sole of foot, an increase in plantar pressure is one of the factors contributing to the development of foot ulcer. People with diabetes are prone to have increased plantar pressure due to the non-enzymatic glycosylation of collagen which increases the stiffness of the soft tissue of the sole. With such an increase in stiffness, the shock absorption ability is reduced during weight bearing activities and wear and tear of the soft tissue due to microtrauma might occur in this group of people. Besides, dehydration of soft tissue due to aging would reduce the thickness of plantar soft tissue and increases the likelihood of skin

breakdown. This explains why foot ulceration is more commonly observed in elderly with diabetes.

As the thickness and stiffness of plantar soft tissue are found to be related to plantar pressure, various devices have been recently developed to assess the thickness and stiffness of the plantar soft tissue. Such device can be useful in predicting the risk of foot ulcer. However, there is a lack of a reliable and standardized assessment on this aspect.

Apart from the change in biomechanical properties of foot, elderly with diabetes were found to have higher chance to fall and present in deteriorated mobility performance as compared with healthy age-matched control. Some studies suggested that the higher risk of fall might be contributed by the impairment over the ankles, including a decrease in ankle joint proprioception and muscles strength, and an increase in the stiffness in ankle dorsiflexion. However, no previous study has examined the influence of the abovementioned ankle characteristics on the risk of fall and mobility deterioration in diabetic population. Besides, no previous studies have examined the effects of targeted exercise training to improve the balance performance specifically to people with diabetes.

In order to fill up the above research gaps, three inter-related studies with specific objectives for each study were carried out. The objectives of the three studies are: (I) To investigate the test-retest reliability of the innovative Ultrasound Foot Scanner System in measuring the thickness and stiffness of plantar soft tissue of healthy subjects in sitting and standing positions; (II) To investigate the correlation between the ankle muscle strength, range of motion of ankle dorsiflexion, ankle joint proprioception and the mobility performance as measured by Timed Up and Go test in elderly with type 2 diabetes; (III) To investigate the effectiveness of a 10-week exercise program with specific regimen designed, based on findings obtained in study II, that aims at improving the balance and mobility performance in elderly with type 2 diabetes. The summary of the methodology and the results of the three studies are shown as below.

Study I:

Method and results: Fifteen healthy subjects were recruited in this study. Thickness and stiffness of the plantar soft tissue over the pulp of big toes, 1st metatarsal head, 2nd metatarsal heads, and 5th metatarsal heads and heel pads were measured by an innovative Ultrasound Foot Scanner System. The measurements were performed in both sitting and standing positions respectively. Same procedures were repeated again after one week-time for the retest assessment. The results obtained in sitting and standing in the first assessment day was compared. Our results showed a significant and excellent test-retest reliability (all Intraclass Correlation Coefficient (3,2) >0.90) (all $p<0.001$); paired t-test showed that the plantar soft tissue became significantly thinner (with percentage decrease ranged from 10% to 14% at various sties) and stiffer (with percentage increase ranged from 123% to 164% at various sites) when changed from a sitting to standing position (all $p<0.05$).

Study II:

Method and results: Eighty-five community dwelling elderly who had been diagnosed with type 2 diabetes were recruited. Timed Up and Go test was used to assess their mobility performance; active ankle joint repositioning test was used to assess for ankle joint proprioception sense; weight-bearing lunge test was used for assessing the stiffness of ankle dorsiflexion and Cybex Norm dynamometer was used to assess the ankle muscle strength (peak dorsiflexors and plantar flexors torque). Pearson correlation coefficient was used to analyze the relationship between Timed Up and Go test and the following independent variables: gender, age, history of diabetes, body mass index (BMI), glycated hemoglobin (HbA1c), normalized peak torque of ankle dorsiflexors, normalized peak torque of ankle plantar flexors, weight-bearing lunge test distance and active ankle joint repositioning error. Multiple regressions were used to examine the degree of association between the aforementioned independent variables and Timed Up and Go test. Our results showed that age, body mass index, normalized peak torque of plantar flexors and dorsiflexors, active ankle joint repositioning test errors and the weight-bearing lunge test distance were significantly associated with the Timed Up and Go test (all $p<0.05$). These physical characteristics, together with the demographic data of the subjects contributed to 59.9% of the variance in the findings of the Timed Up and Go test.

Study III:

Method and results: Ninety-eight community dwelling elderly diagnosed with type 2 diabetes were recruited in community centers and divided into exercise group and control group. A 10-week exercise program was implemented in order to improve the mobility performance, postural control and reduction in the stiffness of plantar soft tissue. Based on the findings obtained in study II, a specially designed exercise program was adopted targeting on the ankle characteristics that we identified in this group of client. In addition, home exercise was emphasized in the training period. Subjects in the control group did not receive any exercise training during the study period. Outcome measures included Timed Up and Go test for mobility performance;

Sensory Organization Test for postural stability; single leg stance test for unipedal balance. Two-way repeated measures ANCOVA with HbA1c entered as co-variate was used for interaction analysis. Our results showed that there were time x group interaction in the Sensory Organization Test composite score, visual ratio and vestibular ratio. Pair t-test showed significant within-group differences in the abovementioned variables in the exercise group. Trends of improvement were found in Timed Up and Go test and single leg stance test in exercise group.

PUBLICATION ARISING FROM THE THESIS

(A) Peer Review Journal

Thomas KW Ng, YP Zheng, Rachel LC Kwan, Gladys LY Cheing. An Innovative Ultrasound Foot Scanner System for Measuring the Change in Biomechanical Properties of Plantar Tissue from Sitting to Standing. Diabetic Technology and Therapeutics. Under Review.

Thomas KW Ng, SK Lo, Gladys LY Cheing. (2014) The Association Between Physical Characteristics of the Ankle Joint and the Mobility Performance in Elderly with Type 2 Diabetes Mellitus. Archives of Gerontology and Geriatrics. 59: 346-352 DOI information: 10.1016/j.archger.2014.07.001

Thomas KW Ng, Rachel LC Kwan, SK Lo, Gladys, LY Cheing. Effectiveness of Exercise Program with Specific Regimen on Improving Postural Control and Mobility Performance in Elderly with Type 2 Diabetes. Journal of Geriatric Physical Therapy. (submitted).

(B) Conference Papers

Thomas KW Ng, Yong-Ping Zheng, Rachel Lai Chu Kwan, Gladys LY Cheing. The Change of Plantar Soft Tissue Biomechanical Properties in Different Weight Bearing Positions. *13th Hong Kong Diabetes and Cardiovascular Risk Factors- East Meets West Symposium*; Hong Kong. 1st-2nd October 2011.

Thomas KW Ng, Gladys LY Cheing. Physical Characteristics Over the Ankle Joint Predict the Mobility Performance for Elderly with Type 2 Diabetes. *13th Hong Kong Diabetes and Cardiovascular Risk Factors- East Meets West Symposium;* Hong Kong, 1st-2nd October 2011.

Thomas KW Ng, Gladys LY Cheing. Effectiveness of exercise on balance and mobility performance in people with type 2 diabetes. *Diabetic Foot Global Conference*; Los Angeles, USA, 15th-17th March, 2012.

Ng KW, Cheing GLY, Lo SK. Association between ankle muscle strength, joint proprioception, dorsiflexion stiffness and the mobility performance in elderly with type 2 diabetes. 9th Pan-Pacific Conference on Rehabilitation cum 21st Annual Congress of Gerontology., Hong Kong, China, 29th-30th November 2014.

ACKNOWLEDGEMENTS

First of all, I would like to show my deepest gratitude to my chief supervisor, Prof. Gladys Cheing who has provided me with continuous support and encouragement throughout the years. Prof. Cheing supported me with her passion and patience to me whenever I faced difficulties and frustrations in the study. She also demonstrated her care to me as a mentor and a friend. In addition, I would like to thank my co-supervisor, Prof. Yong-Ping Zheng, who provided me with valuable advices in all the technical issues that I encountered during my study. I am heartily thankful to Dr. Rosanna Chau, who has offered me with unfailing support and opinions. Her knowledge, wisdom, experience and encouragement inspired me to overcome all the hurdles. My thanks also go Prof. Sing-Kai Lo for his expert opinion in the systematic review and the statistical analysis of my studies. His sense of humor provided an enjoyable learning experience to me during the study. I would also like to thank Dr. Polly Lau for her continuous encouragement to me to pursue a higher academic degree. Also, I appreciate the support from my research teammates, this study could not be accomplished without them. They are Ms Rachel Kwan, Ms Sinfia Vong, Mr. Eddy Cheung, Ms Evelyn Leung and Ms Tailsy Chow.

I would like to thank my family for their patience and spiritual support to me in these years, especially my mother for her preparation of dinner whenever I came home late due to work in school. Last but not least, thank you my Lord, Jesus Christ for his love and guidance to me and each prayer from my church mates which encouraged me to carry on my study when I was down.

Table of Contents

CHAPTER 3

INSTRUMENTATION

CHAPTER 5

RELATIONSHIP BETWEEN THE ANKLE CHARACTERISTICS AND THE POSTURAL CONTROL IN ELDERLY WITH TYPE 2 DIABETES

CHAPTER 6

EFFECTS OF EXERCISE ON MOBILITY PERFORMANCE AND BALANCE STATUS IN PEOPLE WITH TYPE 2 DIABETES: A SYSTEMATIC REVIEW

CHAPTER 7

EFFECTIVENESS OF EXERCISE PROGRAM WITH SPECIFIC REGIMEN ON IMPROVING POSTURAL CONTROL AND MOBILITY PERFORMANCE IN ELDERLY WITH TYPE 2 DIABETES

CHAPTER 8

APPENDICS

REFERENCES

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICS

LIST OF ABBREVIATIONS

6MWT	6-minute Walk Test
DM	Diabetes Mellitus
DPN	Diabetic peripheral neuropathy
HbA1c	Glycated Hemoglobin
MRI	Magnetic Resonance Imaging
SOT	Sensory Organization Test
TUPS	Tissue Ultrasound Palpation System
WBLT	Weight Bearing Lunge Test
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

According to the report from World Health Organization (WHO) in year 2011, there were more than 300 million people suffered from diabetes mellitus (DM). The mortality rate was also alarming with 3.4 million people worldwide died due to diabetes associated complications in 2004 and majority of them were from countries with low and middle-income. It was estimated that the number of people suffer from DM would keep increasing and become the 7th leading cause of death by the year 2030. Therefore, the necessary of implementing preventive measures on various complications brought by this disease should never be underestimated (*Diabetes Mellitus. Fact Sheet number 312, 2011*).

Foot ulceration is one of the various complications brought by DM. Around 15% of all people with diabetes had experienced foot ulceration during their life time and 25% of the hospital costs of diabetic care had been used to treat foot ulcer (Abouaesha, van Schie, Griffths, Young, & Boulton, 2001). If foot ulcer is not handled properly the wound would further deteriorate and might result in lower limb amputation. It was reported that 85% of amputation of lower limbs was preceded by foot ulcers (Reiber et al., 1999) and history of foot ulceration would increase the mortality rate in people with diabetes (Iversen et al., 2009).

Foot ulcerations are common in people with diabetes because the disease affects the peripheral sensation over the sole, which makes people unaware on the minor injury. On the other hand, hyperglycemia would cause delay of wound healing. However, beside these two well-known factors, the increase in plantar pressure was found to be another contributing factor that caused foot ulceration in people with diabetes (Murray, Young, Hollis, & Boulton, 1996). The increase in the plantar pressure can be caused by visible foot deformities such as hallus valgus. But for people with diabetes, the non-enzymatic glycosylation of collagen increases the stiffness of plantar soft tissue (Merza & Tesfaye, 2003), while dehydration of skin due to aging would decrease the thickness of the sole of foot. These two factors together explain why people with diabetes are prone to develop foot ulceration, especially in elderly population.

In order to reduce the risk of developing diabetic foot ulcers, a reliable and valid assessment tool is needed to assess the stiffness and thickness of the plantar soft tissue for early detection. However, there is lack of a reliable device for predicting the risk of having foot ulcers by measuring the thickness and stiffness of plantar soft tissue. A reliable assessment tool might be able to reduce the occurrence of foot ulceration in high risk population, including people with diabetes.

Apart from foot ulcerations, increase in risk of fall is another great concern among people with diabetes, especially for the elderly population. It was estimated that more than one-third of elderly at age 65 or above would experience fall every year, which makes it the leading cause of injury deaths among elderly (Lehtola, Koistinen, & Luukinen, 2006; Sleet, Moffett, & Stevens, 2008; Tinetti, Speechley, & Ginter, 1988). But it is worth to note that the risk of fall among elderly who have diabetes was found to be higher as compared with healthy elderly (Miller, Lui, Perry, Kaiser, & Morley, 1999; Schwartz et al., 2002). Since diabetes affects the peripheral circulation, it is logical to deduce that the physical changes associated with this disease usually begin from the most distal part of the limbs. Indeed, previous studies did found various factors which might contribute to the increase in risk of fall, including a decrease in ankle muscle strength (Andersen, Nielsen, Mogensen, & Jakobsen, 2004); an increase in stiffness of ankle joint (Mueller, Diamond, Delitto, & Sinacore, 1989) and a decrease in the ankle proprioceptive sense (van Deursen & Simoneau, 1999). However, previous studies did not examine the relationship between the aforementioned physical characteristics over the ankles and postural control or mobility performance for this group of client. If there is such relationship, then, we shall design an exercise training program with specific regimen targeting at the ankle impairments in order to improve their mobility performance.

1.2 OBJECTIVES

In order to answer those research questions, three inter-related studies were carried out in this thesis with the following objectives:

i) To investigate the test-retest reliability of the innovated Ultrasound Foot Scanner System in assessing the thickness and stiffness of plantar soft tissue in sitting and standing respectively in young healthy subjects. The thickness and stiffness of plantar soft tissue measured in sitting and standing were compared to investigate the effect of postural change to these biomechanical properties of plantar soft tissue.

ii) To investigate the relationship between the ankle stiffness in dorsiflexion, ankle muscle strength, ankle proprioception and the mobility performance assessed by Timed Up and Go test. Multiple regression analysis was used to investigate the contribution by each component to the performance in mobility among elderly people with diabetes.

iii) To investigate the effectiveness of a 10-week exercise program with specific regimen based on the findings obtained in study II in the improvement on postural control and mobility performance in elderly with type 2 diabetes.

In the following chapters, diabetes mellitus and its diagnostic criteria will be introduced (Chapter 2). In the same chapter, we will also discuss the biomechanical changes on plantar soft tissue and its contribution to the development of foot ulcers. Chapter 3 will be focused on the assessments that we had used for data collection, including the use of the innovative Ultrasound Foot Scanner System in measuring the thickness and stiffness of the plantar soft tissue and the investigation on the reliability of this device will be discussed in chapter 4. As mentioned, the risk of mobility deterioration is one of the complications found in elderly with diabetes. The study on the relationship between the ankle characteristics and mobility performance in elderly with type 2 DM will be discussed in chapter 5. Based on the result we obtained in chapter 5, an exercise program was designed aiming at improving the mobility performance. We also investigated if the balance and postural control performance would be improved after the program. But before discussing the exercise program, a systematic review on the effectiveness of exercise on mobility and balance performance in people with type 2 DM was conducted to review current clinical trials on this aspect (chapter 6) and the result of the exercise program designed by our team will be discussed in chapter 7.

1.3 ETHICAL CONSIDERATION

Ethical approval was obtained from The Hong Kong Polytechnic University for all the studies in the thesis during subject recruitment. Infomred consent was also obtained from each subject before the start of the start of each study Project ID was the ethical approval was: HSEARS20080328001.

CHAPTER 2

LITERATURE REVIEW

In this chapter, I will introduce the diabetes mellitus, including the diagnostic criteria and complications brought by the disease. Some complications brought by this disease will be discussed. Since there are many complications caused by DM, the focus of this chapter is on the musculoskeletal complications that are related to the present thesis, including the stiffness and thickness of plantar soft tissue, decline in ankle muscle strength, ankle joint proprioception sense and increase in stiffness in ankle dosiflexion range.

2.1 DIABETES MELLITUS

Diabetes mellitus (DM) is a chronic metabolic disease characterized by the defect in the insulin production by the pancreas. Insulin is a kind of peptide hormone produced by pancreatic beta cells which is responsible for regulating the carbohydrate and fat metabolism. Due to the deficit in insulin production, people with diabetes suffer from an increase in blood sugar level which may lead to various complications. DM can be sub-divided into different types, namely type 1, type 2, gestational diabetes and other types (*2011 National Diabetes Fact Sheet*, 2011). Type 1 diabetes are usually diagnosed at young age in which the pancreatic beta cells were found to be destroyed by the patients' own immune system and the pancreas of people with this type of DM can not produce insulin. In order to maintain the blood glucose level within normal range, this type of patients need to receive injection of insulin regularly; people with type 2 diabetes are usually diagnosed in adult age and it accounts for up to 90% of all diagnosed cases of diabetes (*Definition, diagnosis and classification of diabetes mellitus*, 1999). Unlike type 1 DM, people suffering from type 2 diabetes usually have problem in effective production of insulin by the pancreas. This group of people usually has milder symptoms as compared with those who have type 1 DM. Therefore, most people with type 2 diabetes are under diagnosed until complications appear. Gestational diabetes occurs in pregnant women, it is a kind of glucose intolerance that happens during pregnancy. If this is not treated properly, complications may happen to the infants. On top of these three types of diabetes, DM can be caused by other reasons such as medications or infections, it account for up to 5% of all diagnosed cases (*2011 National Diabetes Fact Sheet*, 2011)

2.1.1 DIAGNOISTIC CRITERIA

As diabetes is a chronic metabolic disorder characterized by an increase in the blood sugar level, the measurement of blood sugar level is the standardized method to confirm the diagnose. WHO has adopted the guidelines for diagnosing diabetes since 1965 (*Diabetes mellitus. Report of a WHO Expert Committee*, 1965). In 1986, WHO started to explore the applicability of glycated hemoglobin (HbA1c) as one of the diagnostic criteria (*Diabetes Mellitus: Report of a WHO Study Group. Technical Report Series 727*, 1985). HbA1c is formed in a non-enzymatic glycation pathway due to the exposure of hemoglobin in blood plasma glucose (Goulle, Larcorix, & Bouige, 2002). The level of HbA1c increases as the level of plasma glucose increases. The advantages of using HbA1c is it can reflect the average control of blood glucose level in the past eight to twelve weeks and no fasting is required before the blood sample taking. According to the latest publication of WHO on the diagnosis of diabetes, it is recommended that HbA1c of 6.5% as the cut off point for diagnosis diabetes (*Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus*, 2011).

2.1.2 PERIPHERAL NEUROPATHY

Diabetic neuropathy is one of the common complications brought by the disease which may result in foot ulcer. Studies showed that 15% of all diabetic patients would develop foot ulcer (Gordois, Scuffham, Shearer, Oglesby, & Tobian, 2003) and diabetic neuropathy is the leading cause of non-traumatic related lower limb amputation (Thomas, 1999). The primary cause of peripheral neuropathy in people with diabetes is hyperglycemia which causes damage to the nerve cells and decreases the blood flow to the nerve causing neuronal ischemia (Edwards, Vincent, Cheng, & Feldman, 2008).

There are different manifestations of diabetic neuropathy depending on what kind of nerve is being affected and many of them are related to foot ulceration: when the motor nerve is affected, it would lead to muscle atrophy in intrinsic muscle on the foot (Bus et al., 2002), which might deform the sole of foot and increase the likelihood of developing pressure point during weight bearing activities and increase the risk of causing foot ulcer; when autonomic nervous system (especially the sudomotor nerve) is affected, there might be drying of skin which might make the skin more brittle and shear and tear of the skin over the sole would again increase the risk of developing foot ulcer (Edwards et al., 2008). As the onset of diabetic peripheral neuropathy (DPN) is gradual, the symptoms are sub-clinical in the early stage which makes the patients unaware of the symptoms (American Diabetes Association, 1996).

The common diagnostic criteria of DPN include subjective symptoms reported by patients, ankle reflexes, and vibration perception thresholds of the lower limbs (Japanese

Study Group on Diabetic Neuropathy, 2001). In the present thesis, the target population was diabetic elderly without peripheral neuropathy. Therefore, the assessments of peripheral neuropathy mentioned above were used to exclude those who have neuropathy (Chapter 5 and Chapter 7).

2.2 BIOMECHNICAL CHANGES IN PLANTAR SOFT TISSUES

2.2.1 BIOMECHANICAL CHANGES IN PLANTAR SOFT TISSUES IN ELDERLY

Aging is a degenerating process involving multiple systems including the musculoskeletal system. In human foot, aging would cause the collagen and elastic fibers in the cell matrix become less soluble and the skin can break down more easily (Edelstein, 1992). This problem would bring negative influence on the shock absorbing properties of the foot at the weight bearing sites, ie metatarsals head and heel pads (Cavanagh, 1999) and these points would become more prone to develop ulcers after repetitive wearing and tearing by ground reaction force during walking or other weight bearing activities. Our research team found a positive linear relationship between age and stiffness over metatarsal heads and heel pads in human being (Kwan, Zheng, & Cheing, 2010). Besides, dehydration of the skins due to aging would make the skin more brittle. These factors are account for the increase in pressure over the sole of foot during weight bearing activities.

2.2.2 BIOMECHANICAL CHANGES IN PLANTAR SOFT TISSUES IN PEOPLE WITH DIABETES MELLITUS

Elevated plantar pressure is another common predisposing factors of foot ulcers (Mueller, Zou, & Lott, 2005). An increase in plantar soft tissue pressure can be caused by visible deformity such as hammer toes or hallus valgus, which may cause an increase in pressure over particular sites on the sole during weight bearing activities. Besides, the increase in stiffness over the plantar soft tissue is another cause of the increase in plantar soft tissue pressure. It was found that the plantar soft tissue stiffness in people with diabetes was higher than that found in healthy control subjects and it is supported by a positive relationship between the plantar soft tissue stiffness and plantar tissue pressures reported by a previous study (Chao, Zheng, & Cheing, 2011; Cheung, Zhang, Leung, & Fan, 2005). The increase in the stiffness of plantar soft tissue might subsequently increase the stress concentration and impair the pressure distribution during loading (Merza & Tesfaye, 2003).

Beside stiffness, thickness of plantar soft tissue would increase in likelihood of skin breakdown over the sole. Chao et al. (2011) found that the plantar soft tissue in people with diabetic neuropathy was thinner than that found in healthy control, and another study reported that there was an inverse relationship between the thickness of the plantar soft tissue and the plantar pressure (Abouaesha et al., 2001). Both thinning and stiffening of plantar soft tissue decreased the shock absorption ability of the weight bearing points of the sole (ie. metatarsal heads and heels) during weight bearing activities, which increased the likelihood of skin break down by repetitive micro-trauma, together with the impaired distal circulation it would eventually develop into ulcers. These factors explain why elderly with diabetes are prone to have foot ulcer.

2.2.3 MEASUREMENT TOOLS IN ASSESSING THE BIOMECHANICAL PROPERTIES OF THE PLANTAR SOFT TISSUE

As the biomechanical properties of plantar soft tissue (thickness and stiffness) are correlated to the plantar pressure (Abouaesha et al., 2001; Cheung et al., 2005), clinicians have been working hard to develop a reliable and accurate assessment tools to assess biomechanical properties of plantar soft tissue but there are various drawbacks for using these devices. Back to year 1987, Krouskop and colleagues developed an ultrasound doppler system to measure the stiffness of soft tissue based on the comparison of signals acquired before and after the displacement of the soft tissue (Krouskop, Dougherty, & Vinson, 1987). Later on, this technique was modified and commonly used for diagnosis of breast and prostate lesions. But this system was suggested to have limitation due to the difficulty in finding the magnitude and direction of the force during measurement of stiffness of soft tissue (Garra et al., 1997; Ginat et al., 2009).

A pipette aspiration system was developed in order to measure the stiffness of the plantar soft tissue (Aoki, Ohashi, Matsumoto, & Sato, 1997). It was done by applying a negative pressure over the soft tissue so that the tissue was aspirated into the pipette and the stiffness of the tissue over the particular site was calculated by measuring the displacement of the soft tissue at the center of the pipette and the pressure required. However, this system might not be applicable for measurement in plantar soft tissue due to the uneven surface of the foot which would cause loosening of the pipette during aspiration and the plantar soft tissue might not be soft enough to be aspirated by the pipette. Most importantly, this system could not simulate the pressure exerted on the plantar tissue during weight bearing activities, which is a positive pressure instead of negative pressure.

Different kinds of indentation systems have been developed to measure the plantar soft tissue. The use of indentation systems can simulate the positive pressure exerted on the tissue as what the subjects encounter during daily activities. Magnetic Resonance Imaging (MRI) developed by Gefen and colleagues consisted of an indentation system to deform the plantar soft tissue and a 0.5T MRI scanner was used to scan the image of the soft tissue. The stiffness of the plantar soft tissue was calculated by measuring the loading force and the displacement of the plantar tissue (Gefen, Megido-Ravid, Azariah, Itzchak, & Arcan, 2001). This system gave a clear image of the soft tissue for accurate measurement. But its feasibility to be put in clinical settings is questionable as MRI imaging is expensive. Another indentation system developed by Klaesner and colleagues used a load cell connected to a stylus to measure the stiffness of the plantar soft tissue. This was done by measuring the distance that the probe moved in reference to the first contact point of the skin, together with the force required to move the tissue collected by the load cell. However, the movement of the plantar soft tissue or the metatarsal head during the measurement would overestimated the thickness of the tissue (Klaesner, Commean, Hastings, Zou, & Mueller, 2001). The portable hand-held indentation system developed by Rome and colleagues for measuring the stiffness of heel pad in runners with plantar heel pain consisted of an indentor connected to a load cell for measuring the force to deform the soft tissue. The indentor passed through a hole in the testing surface made from Perspex, which was displaced during the indentation (Rome, Webb, Unsworth, & Haslock, 2001). This measurement method is considered to be indirect and the measurement is considered to be inaccurate as the movement of the plate depends on the force applied by the investigator. Besides, the reliability was not mentioned in the previous study.

2.2.4 TISSUE ULTRASOUND PALPATION SYSTEM

Among various imaging technologies, ultrasound is considered to be accurate and relatively inexpensive. Tissue Ultrasound Palpation System (TUPS) developed by Zheng and Mak (1996) comprised of a pen-sized hand held probe which contained an ultrasound transducer and a load cell (Zheng & Mak, 1996). The thickness of the plantar tissue was calculated by measuring the echo reflected by the soft tissue-bone interface and the skin. During the assessment of the stiffness, the subjects were required to lie in supine or prone position, or in long sitting position. The measurement was done when the assessor applied a manual force perpendicular to the tested body part and deformed the soft tissue. Stiffness of the soft tissue was expressed as Young's modulus that was calculated by an in-house software with specific equation installed in the personal computer.

(Mak, Lie, & Lee, 1994, Zheng, Choi, Wong, Chan, & Mak, 2000). TUPS was found to be a valid tool in assessing biomechanical properties of soft tissue (Zheng & Mak, 1996) and it had been widely used in assessing soft tissue, including plantar soft tissue (Lau, Li-

Tsang, & Zheng, 2005; Zheng et al., 2000; Zheng, Li, Choi, Lu, & Huang, 2006; Zheng, Mak, & Lue, 1999).

It is no doubt that weight bearing positions are more relevant in predicting the risk of developing foot ulcers since foot ulcers are caused during weight bearing activities. However, TUPS measured the thickness and stiffness of plantar soft tissue only in non-weight bearing position which is considered to be a limitation to investigate the risk of developing foot ulcerations. Human foot is composed of various soft tissues including ligaments and muscles which make the whole structure flexible that is ideal for shock absorption and maintaining balance during weight bearing activities. There is change in the shape of the foot and also the alteration of pressure points when a subject changes from a non-weight bearing position to weight bearing position. On the other hand, TUPS is a hand-held device in which a skillful and experienced assessor is required to provide reliable results. These factors limit TUPS's applicability in clinical usage. In order to tackle its drawbacks, an innovative Ultrasound Foot Scanner System was developed as advancement from TUPS.

The development of the Ultrasound Foot Scanner System was based on the technology used in TUPS with specific design and adjustments in both software and hardware so as to increase the reliability in assessing the thickness and stiffness of plantar soft tissue in weight bearing positions. The details of the device and the assessment on its reliability will be discussed in chapter 3.

2.3 DETERIORATION OF ANKLE MUSCLE STRENGTH

Muscle strength decline is a common problem of aging through sarcopenia. It was found that the muscle strength of lower extremities declined more rapidly in elderly with diabetes as compared with healthy control. In particular, studies showed that the ankle dorsiflexion and plantarflexion muscles strength of people with type 2 diabetes were significantly lower as compared with age-matched healthy elderly (Andersen et al., 2004; Park et al., 2006; Park et al., 2007). Andreassen et al. (2006) found that the annual decline percentage of ankle muscle strength in elderly with diabetes with neuropathy is higher than those who have asymptomatic neuropathy, followed by normal control (Andreassen, Jakobsen, & Andersen, 2006). In fact, the decline of muscle power is not solely caused by the reduction of muscle mass, but also a decline in muscle quality as reflected by the maximal muscle strength per unit mass (Park et al., 2007). One of the possible mechanisms behind the muscle decline is the metabolic consequence of poor glycemic control which causes increase in inflammatory cytokines level in the blood such as interleukin 6. Increase in inflammatory cytokines further breakdown the muscle protein and reduce the muscle strength (Cesari et al., 2004; Gokulakrishnan, Monhanavalli, Monickaraj, Mohan, & Balasubramanyam, 2009; Visser et al., 2002). Apart from that, it was found that there was more than 2 fold of excessive adipose tissue infiltration inside the ankle muscle in people with diabetes as compared with control group even though the leg muscles and volumes were comparable between the two groups (Hilton, Tuttle, Bohnert, Mueller, & Sinacore, 2008). However, the reason behind the excessive adipose infiltration was not addressed in that study and need to be further investigated.

2.4 DETERIORATION OF ANKLE JOINT PROPRIOCEPTION

Patients with diabetic peripheral neuropathy were shown to have impaired tactile and proprioception over the foot and ankle which affect the balance (Menz, Lord, & Fotzpatrick, 2004; van Deursen & Simoneau, 1999). In fact, diabetic patients without neuropathy were found to have certain degree of proprioception deficit in lower limbs, particularly over the ankles, just that the patients do not notice during their daily activity. One previous study found that diabetic patients with mild neuropathy showed significant deficit in ankle joint proprioceoptive sense as they showed a significant decrease in the ability to recover by ankle inversion from a lateral lean and also the time to generate a inversion torque for recovery was slower as compared with normal subjects, even though the ankle muscular strength was comparable (Gutierrez, Helber, Dealva, Ashton-Miller, & Richardson, 2001). The authors suggest that this deficit was probably caused by the impairment of proprioceptive threshold as the muscle power was comparable between the two groups. This result was supported by another study in which the authors found significant somatosensory deficit over the ankles in diabetic patients without peripheral neuropathy (Deshpande, Metter, & Ferrucci, 2010). Diabetic patients without neuropathy were found to have altered walking gait pattern when crossing an obstacle as compared with normal subjects. Gait analysis showed that subjects presented with a wrong estimation of ankle joint movement when they walked across the obstacles (Liu, Hsu, Lu, Chen, & Liu, 2010). This result implied that ankle proprioception deficit had already occurred before the typical signs of peripheral neuropathy are shown which might affect the mobility performance.

2.5 INCREASES IN ANKLE JOINT STIFFNESS

A decrease in ankle joint mobility in dorsiflexion range is another impairment found in elderly with diabetes (Giacomozzi, D' Ambrogi, Cesinaro, Macellari, & Uccioli, 2008; Hajrasouliha, Tavakoli, Esteki, Nafisi, & Noorolahi-Moghaddam, 2005; Salsich, Mueller, & Sahrmann, 2000; Simmons, Richardson, & Deutsch, 1997). The decrease in ankle joint mobility was firstly hypothesized to be caused by the thickening of periarticular connective tissue due to repeated unnoticed microtrauma of the foot in the late 80s (Mueller et al., 1989). Until late 90s, electronic microscope was used to investigate the Achilles tendon of people with diabetes and found that there is an increase in collagen fiber density and formation of abnormal fiber morphology as compared with control subjects (Grant et al., 1997). They also noted there was disorganization of collagen fiber and adhesion of collagen fibrils in the Achilles tendon. These findings explain why the ankle gets stiffer upon passive dorsiflexion. The reason behind these interesting phenomenon was due to hyperglycaemia which promotes nonenzymatic glycosylation of collagen, resulting in glycation end-products formation causing the increase of collagen cross links and stiffening of the soft tissue, including tendons, ligaments and joint capsules(Abate, Schiavone, Pelotti, & Salini, 2011). It was found that the biomechanical change of ankle soft tissue would alter the stretch distribution of Achilles tendon in diabetic subjects during normal walking (Cronin et al., 2010). Therefore, walking efficiency is reduced and abnormal gait is developed.

To summarize, diabetes mellitus does not only cause impairment in blood glucose regulation. The increase in blood glucose level itself also causes much physical impairment around the ankle. It is essential to have assessment in each of the impairment in order to quantify the changes for monitoring purpose. In the next chapter, the details of assessment tools and the assessment procedures adopted in the present thesis will be discussed.

CHAPTER 3

INSTUMENTATION

In this chapter, different assessment instruments that have been used in the studies will be discussed. Ultrasound Foot Scanner System was used to investigate the thickness and stiffness of the plantar soft tissue; the muscle strength of the ankle dorsiflexors and plantarflexors were measured by a dynamometer; ankle proprioceptive sense was measured by active ankle joint repositioning test by the same dynamometer; the stiffness of ankle joint in dorsiflexion was measured by the weight bearing lunge test (WBLT). For balance and mobility performance, Sensory Organization Test (SOT) was used to measure the postural control; Timed Up and Go (TUG) test was used for assessing the mobility performance and lastly, single leg stance test (SLST) was used to measure the single leg balance.

3.1 ASSESSMENT OF THICKNESS AND STIFFNESS OF PLANTAR SOFT TISSUE

The Ultrasound Foot Scanner System was developed by the Department of Health Technology and Informatics at The Hong Kong Polytechnic University. The entire system consists of a platform which was made of polyvinylchloride (PVC) collected to a personal computer (PC) (Figure 3.1). Inside the platform, there was an ultrasound transducer with a frequency of 3MHz and a diameter of 9mm which was connected in series to a motor and a load cell with 50N range (Figure 3.2). The levels of the platform and the transducer were the same (Figure 3.3). Thickness of the plantar soft tissue was measured by calculating the two echoes reflected by the skin and the soft tissue-bone interface. According to Zheng and Mak (1999) the speed of the ultrasound in the soft tissue is 1540m/sec (Zheng & Mak, 1999). With reference to Figure 3.3, there were two echoes on the screen. The first echo on the left side was reflected by the skin and the second echo was reflected by the soft tissue-bone interface. Thickness of the soft tissue was calculated by measuring the distance between the first peak of the first echo and the first peak of the second echo on the panel (Figure 3.4).

Figure 3.1 The Ultrasound Foot Scanner System

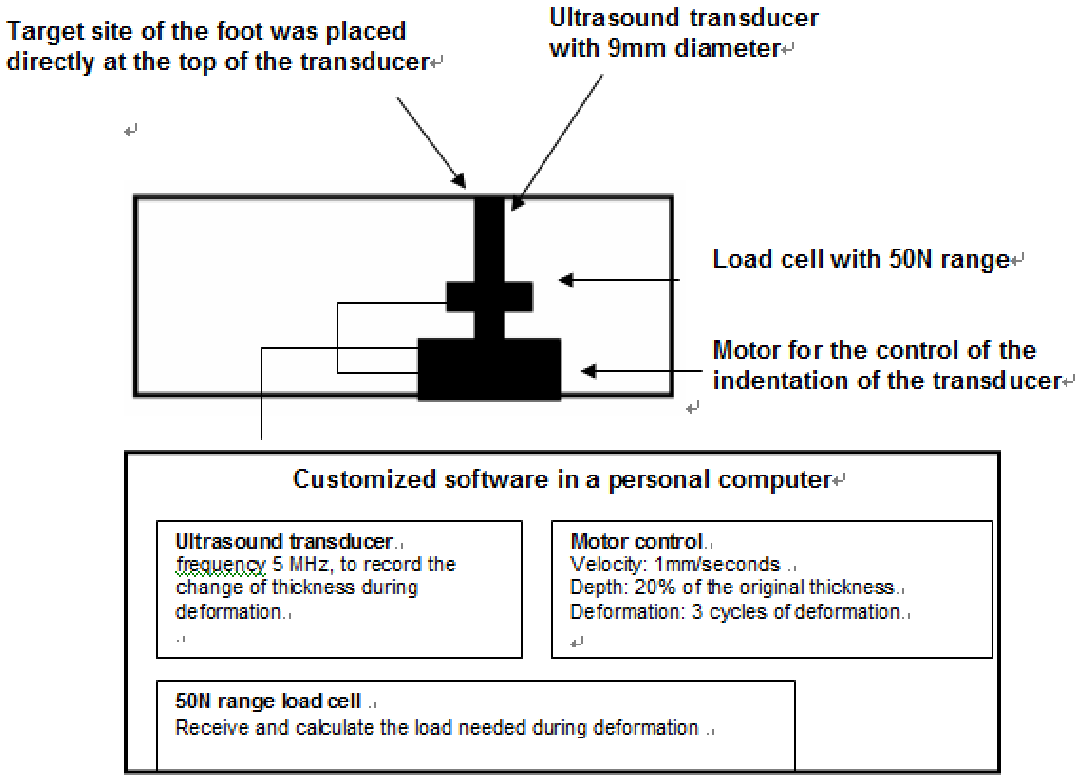


Figure 3.2 Schematic diagram of the Ultrasound Foot Scanner System

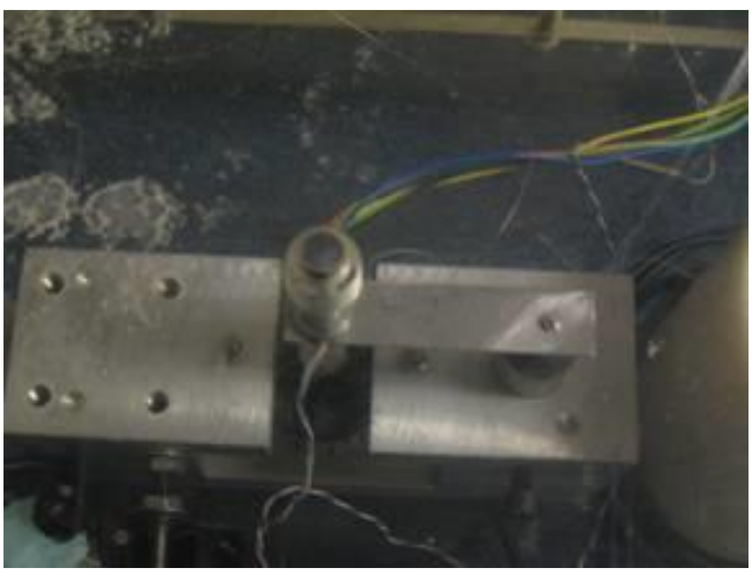


Figure 3.3 The platform and the ultrasound transducer embedded in the Ultrasound Foot Scanner System

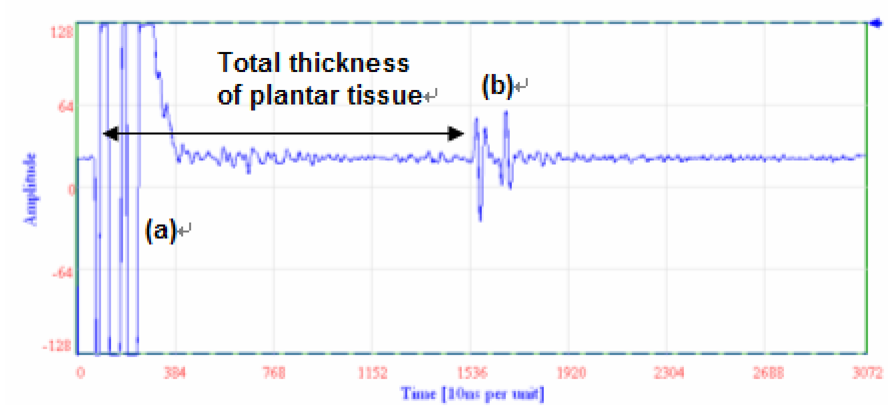


Figure 3.4 Measurement of the thickness of the plantar soft tissue Measurement of the thickness of plantar soft tissue at the first metatarsal head was conducted in standing by the Ultrasound Foot Scanner System. Wave (a) is the ultrasound echo reflected by the skin of the first metatarsal head while wave (b) is the echo reflected by the soft tissue-bone interface. The thickness of the plantar soft tissue was calculated by the distance measured between the two ultrasound echoes.

Inside the platform, the motor and the load cell connected in series with the ultrasound transducer were used to measure the stiffness of the soft tissue. The motor was used to drive the transducer to deform the soft tissue while the force added on the plantar soft tissue during the indentation was calculated by the load cell. With reference to Figure 3.5, the displacement of the soft tissue and the force required for the deformation were calculated and the correlation was plotted as the graph shown in Figure 3.6. The force/displacement value was obtained by finding the slope of the line of best fit and the value was considered to be significant with coefficient of determination of linear regression $R^2 \geq 0.9$. Stiffness of the soft tissue was expressed as Young’s modulus and it was calculated by an in-house software in the personal computer with the following equation.

$$E=P(1-v2)/2awk(a/h,v) \qquad ---------(1)$$

In this equation, E is the Young's modulus, P is the applied force on the load cell, w is the indentation depth, a is the radius of the indenter, v is the Poisson's ratio, h is the tissue thickness and k is a scaling factor which depends on both a/h and Poisson's ration v (Mak et al., 1994). In the present study, the Poisson's ratio was set at 0.45 which assumed that the soft tissue was nearly incompressible (Zheng et al., 2000). The equation (1) was firstly used in the study of articular cartilage and was later used to measure the Young's modulus of soft tissue (Zheng et al., 2000). In this measurement of the stiffness of plantar soft tissue in present study, three cycles of deformation were carried out with 400 frames of measurement for measuring the change in thickness. The driving velocity was set at 1 mm/ sec and the indentation depth was 20% of the original thickness of the tissue before indentation (Zheng et al., 1999).

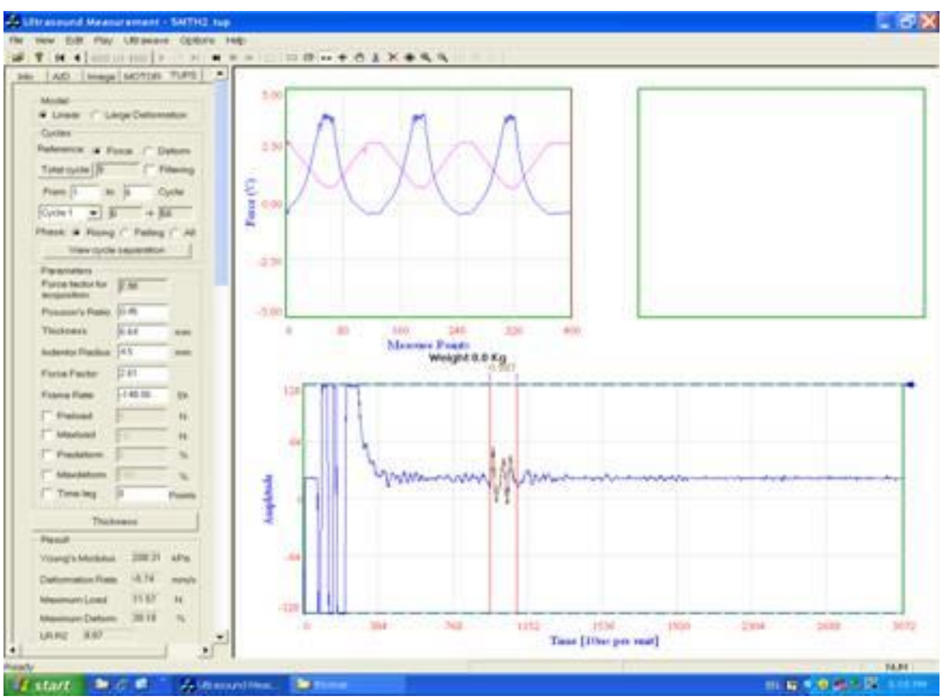


Figure 3.5 Measurement of the stiffness of the plantar soft tissue

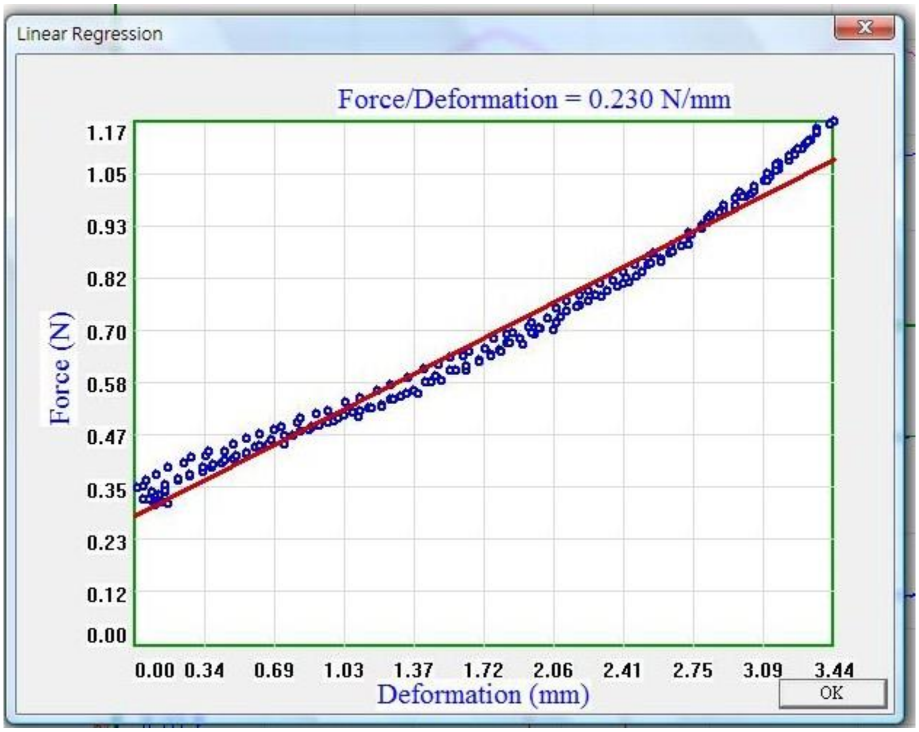


Figure 3.6 Correlation between force and the deformation of the plantar soft tissue

3.2 ASSESSMENT OF ANKLE MUSCLE STRENGTH

The strength of ankle plantarflexors and dorsiflexors was tested by the Cybex Norm dynamometer (Cybex International Inc, Ronkonkomam NY) using the protocol of assessing isokinetic strength of ankle with the angular velocity set at 60º/seconds (Figure 3.7). Subjects were required to lie in prone position. The foot was strapped on the foot plate of the dynamometer while the knee was kept in an extended position. During the test, the subjects were instructed to push the ankles away from themselves and then pull the ankles towards themselves as hard as they could. A total of three trials with three repetitions in each trial were done for each leg and the average peak torque normalized by their weight in newton meter per kilogram was calculated for analysis (Li, Xu, & Hong, 2009).

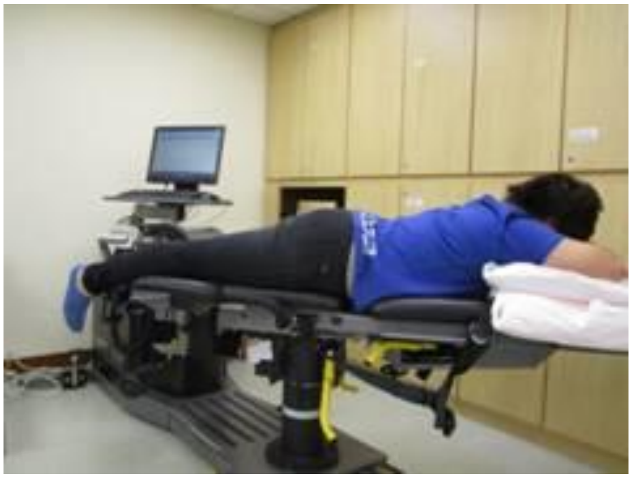


Figure 3.7 Measurement of muscle strength by Cybex Norm dynamometer (Cybex International Inc, Ronkonkomam NY)

3.3 ASSESSMENT OF ANKLE PROPRIOCEPTIVE SENSE

The proprioception of ankle joint was measured by the active joint repositioning test. Joint repositioning test is a test on joint proprioception sense by asking the subjects to actively or passively locate the target joint position after memorizing the same location within a given time. This test is commonly used for testing the joint proprioception sense in lower limbs (Deshpande, Connelly, Culham, & Costigan, 2003; Fu & Hui-Chan, 2007; Sekir, Yildiz, Hazneci, Ors, & Aydin, 2007; Westlake, Wu, & Culham, 2007). In the present study, the Cybex Norm dynamometer (Cybex International Inc, Ronkonkomam NY) was used with the subjects lied in prone position to avoid any visual feedback from the subjects. The foot was strapped on the foot plate of the dynamometer while the knee was kept in an extended position. The testing ankle of the subjects was then positioned to 10 degrees plantarflexion and 5-second time was given for memorizing the position. After 5 seconds of memorization, the ankle was then passively moved back to a neutral position and subjects were instructed to actively move the ankle back to the target position. A total of 3 trials were performed and in each trial the absolute error between the target angle and the reproduced angle was measured in degree, the mean values of 3 trials were calculated for analysis (Sefton et al., 2009). In a previous study, this test was done passively in which the ankles of the subjects (basketball players) were moved passively by the dynamometer and subjects indicated the target location by pressing a button with their thumbs making the audio signal (Fu and Hui-Chan 2005). However, the present study adopted the active repositioning test instead because our target subjects were elder people with diabetes. Elderly were known to have an increase in reaction time and they were likely to have delay in pressing the button when the ankle passed through the target location might produce random error that affected the accuracy of the test (Makishita & Matsunaga, 2008).

3.4 ASSESSMENT OF STIFFNESS IN ANKLE DORSIFLEXION

The stiffness of ankle joint in dorsiflexion was assessed by the weight bearing lunge test (WBLT) based on the knee-to-wall principle (Hoch, Staton, & McKeon, 2011). Subjects were instructed to stand in front of a wall with the toes of the tested leg pointing towards the wall and the heel touching the ground so that the second toe, the center of heel and the knee were kept in a plane which was perpendicular to the wall (Vicenzino, Branjerdporn, Teys, & Jordan, 2006). In order to prevent falling, another leg was placed at about 1 foot behind the tested leg. Subjects were allowed to have six trials to lunge forward into talocrural dorsiflexion with the knee touching the wall. To increase the talocrural dorsiflexion, subjects were allowed to position the tested feet backward within these six trials until the maximal distance between the big toe and the wall was reached with the knee touching the wall while the heel was kept in contact with the ground (Collins, Teys, & Vicenzino, 2004). The distance between the big toe and the wall was measured to the nearest 0.1 centimeter by tape measure secured on the floor for analysis. Excellence inter-tester and intra-tester reliability of WBLT was reported by Bennell and colleagues (Bennell, Talbot, Wajswelner, & Kelly, 1998).

3.5 ASSESSMENT OF POSTURAL CONTORL

In order to assess the ability of subjects in using visual, vestibular and somatosensory information to maintain postural stability, Sensory Organization Test (SOT) by using a computerized posturography machine (Smart EquiTest®, NeuroCom International, Inc) was used (Figure 3.8). This device contains a platform and a visual surround that can be sway-referenced. SOT was shown to have good test-retest reliability among community dwelling elderly (Ford-Smith, Wyman, Jr, Fernandex, & Newton, 1995).

Figure 3.8 Sensory Organization Test by computerized posturography machine (Smart EquiTest®, NeuroCom International, Inc)

During the test, subjects were required to stand on the platform with arms by the sides and look forward. To prevent falling, subjects wore a harness before the start of the test. Subjects were exposed to 6 testing conditions on the platform: (1) normal vision, fixed support; (2) eyes closed, fixed support; (3) vision sway-referenced, fixed support; (4) normal vision, support surface sway-referenced; (5) eyes closed, support surface sway-referenced and (6) vision and support surface sway-referenced. These six conditions assess the ability of the subjects in utilizing the three sensory systems in maintaining upright posture; they are visual, vestibular and somatosensory systems. In each condition, three 20-second trials were provided. During the assessment in each condition, the real-time center of pressure of the subject was captured by the machine and the machine recorded and calculated the sway of the center of pressure of the individual and compare it with his/her limit of stability (maximum peak-to-peak 12.5º), which depends on the body build of the subject (Fong, Tsang, & Ng, 2012).

In each of the 6 conditions, an equilibrium quotient out of 100 was generated. The score '100' represents 'no sway' during the assessment and the score '0'represents the center of pressure of the subject fall out of his/her limit of stability. The equilibrium quotient in each condition was examined to compare the performance in each specific condition; the composite score which indicates the overall performance of the individual. The findings obtained in the sensory score of visual, somatosensory and vestibular systems were recorded. Somatosensory ratio compares the results obtained in condition 2 to that of condition 1 that represents the ability of the subject to use somatosensory information to maintain balance when the visual information was blocked by closing their eyes. Visual ratio was calculated by comparing the results obtained in condition 4 to that in condition 1 to assess the ability of an individual to maintain balance with the somatosensory information altered by sway-referenced platform; vestibular ratio was calculated by comparing the results obtained in condition 5 to that of condition 1 to assess the ability of an individual to maintain balance with the somatosensory information altered and the visual information removed (Rosengren et al., 2007; Tsang, Wong, Fu, & Hui-Chan, 2004).

3.6 ASSESSMENT OF MOBILITY PERFORMANCE

Mobility performance of our subjects was assessed by Timed Up and Go test (TUG). TUG was done by requesting the subject to sit on a chair resting at the back rest and arms relaxed on arm rest. Subjects were then instructed to stand up, walk as quickly and safely as possible for 3 meters, turn around the mark on the ground then walk back to the chair again then sit down with their back touching the back rest of the chair at the end. Time to complete the task was measured by a stop watch. The stop watch was started once the back of the subject leave the back rest until the back of the subject touch the back rest again after walking (Shumway-Cook, Brauer, & Woollacott, 2000). Three trials were performed on each subject and the average time measured in the nearest second was calculated for analysis. This test was firstly described as a clinical test for elderly with balance impairment with a score from 1 to 5 based on the observers' perception (Mathias, Nayak, & Isaacs, 1986) and later this test was modified to assess the mobility status of elderly (Podsiadlo & Richardson, 1991). This test is commonly used in assessing the general mobility status of elderly and high test retest reliability has been shown (Steffen, Hacker, & Mollinger, 2002).

3.7 ASSESSMENT OF SINGLE LEG BALANCE

The assessment of single leg balance was done by single leg stance test (SLST). It was performed by asking the subjects to stand with one leg in an upright position with arms by the sides. The timer was started once the non-testing leg lifted up until either one of the following conditions occur: (1) the foot of the lifted leg touched the floor; (2) the stance foot displaced or (2) the subject used the lifted foot to support the stance leg (Hurvitz , Richardson, Werner, Ruhl, & Dixon, 2000). Subjects were considered to reach the maximum time if they manage to stand for 45 seconds. 3 trials were taken in each leg and the time to the nearest second was recorded. The mean was calculated for subsequent analysis. Although it has been suggested that 30 seconds in SLST should be considered as the maximal performance (Jonsson, Seiger, & Hirschfeld, 2004), Briggs et al. recommended to use 45 seconds as the cut off in order to reduce the ceiling effect (Briggs, Gossman, Birch, Drews, & Shaddeau, 1989). SLST is considered to be a functional balance assessment in elderly since many activities required human to stand with one leg such as climbing upstairs, turning or putting on trousers in a standing position.

In this chapter, the Ultrasound Foot Scanner System was an innovative device for measuring the stiffness and thickness of plantar soft tissue. The investigation of its reliability will be discussed in the next chapter.

CHAPTER 4

RELIABILITY OF AN INNOVATIVE ULTRASOUND FOOT SCANNER SYSTEM IN MEASURING THE BIOMECHANICAL PROPERTIES OF PLANTAR SOFT TISSUE

4.1 INTRODUCTION

Human foot is composed of a complex structure that contributes to shock absorption during weight bearing activities. The prevalence of foot complication in people with diabetes has been increasing that causes a huge burden to the society (*Diabetes Mellitus. Fact Sheet number 312*, 2011; Frykberg, 1998; Wild, Roglic, Greenm, Sicree, & King, 2004). The decrease in distal sensation and an increase in plantar pressure may lead to diabetic foot ulcer (Edwards et al., 2008), particularly for people with visible structural changes of the foot such as hammer toes or hallus valgus (Murray et al., 1996). However, for people with diabetes, hyperglycemia may lead to non-enzymatic glycosylation of collagen in plantar soft tissue that subsequently increases the collagen cross link and stiffen the plantar tissue (Abate et al., 2011; Reihsner, Melling, Pfeiler, & Menzel, 2000). The increase in stiffness of the plantar soft tissue may further decrease the shock absorption properties of the foot during weight bearing activities (Crawford, Inkster, Kleijnen, & Fahey, 2007).

Since previous studies found that plantar pressure is associated with the thickness and stiffness of the plantar foot (Abouaesha et al., 2001; Cheung et al., 2005). Therefore, clinicians are keen to develop a device to assess the biomechanical properties (i.e., thickness and stiffness) of plantar soft tissue so as to predict the risk of developing foot ulcers in people with diabetes. Several systems have been adopted to assess plantar pressure using different imaging technologies such as ultrasound (Gooding et al., 1986); computer tomography (Smith et al., 2000) and magnetic resonance imaging (Petre, Erdemir, & Cavanagh, 2008). Tissue Ultrasound Palpation System (TUPS) is a hand-held system with an ultrasound transducer and load cell installed at the head of the probe for measurement of the real time thickness of the tissue and the force needed to deform the tissue. The TUPS was shown to have high reliability and validity in measuring the biomechanical properties of soft tissues in humans in terms of thickness and stiffness (Zheng & Mak, 1996; Zheng et al., 1999). The details of TUPS can be referred to chapter 2 (section 2.2.4). Previous studies adopted TUPS in assessing the biomechanical properties of various type of soft tissue including plantar tissue (Kwan et al., 2010; Zheng et al., 2000). However, TUPS can be used in measuring the thickness and stiffness of the plantar tissue only in non-weight bearing positions including lying or half sitting which only provides limited information about the risk of developing foot ulcer because the most common functional activities that lead to foot ulcers are usually performed in weight-bearing positions such as walking with barefeet (Boulton, 2000).

An innovative Ultrasound Foot Scanner System was developed to overcome the shortcomings of TUPS. Measurements can be taken when the subject is in weight bearing position. Unlike TUPS that is a hand held device, the operator of the Ultrasound Foot Scanner System can pre-set the speed and depth of the indentation, and then the automatic indentation process can be controlled by a computer program. A pilot study showed that this device was feasible to assess the thickness and stiffness of plantar soft tissue in human subject but its reliability was left unknown and the change of biomechanical properties of the plantar soft tissue in different weight-bearing positions was not investigated by using the present device (Zheng et al., 2012). Therefore, the aims of the present study were to determine the reliability of the use of Ultrasound Foot

Scanner System in measuring the thickness and stiffness of the plantar soft tissue, and the measurement made in sitting and standing positions were compared.

4.2 METHOD

4.2.1 MATERIALS

The Ultrasound Foot Scanner System consists of a platform made of polyvinylchloride. Installed under the platform is an ultrasound transducer. The thickness of the plantar soft tissue was measured by calculating the distance between the echoes reflected by the skin and that reflected by the soft tissue-bone interface. The thickness of the soft tissue was calculated by measuring the distance between the first peak of the first echo and the first peak of the second echo. They represent the ultrasound echo reflected from the skin and the soft tissue-bone interface respectively. The detailed description of the scanner can be referred to chapter 3 (section 3.1).

In order to measure the stiffness of the plantar soft tissue, the ultrasound transducer was connected in series to a motor and a load cell. The motor was used to drive the transducer to deform the soft tissue perpendicularly to the surface of the skin, while the force used to deform the plantar soft tissue during the indentation process was recorded by the load cell. The stiffness of the soft tissue was expressed as an effective Young's modulus and the calculation was performed by the in-house software installed in the personal computer, using the following equation:

$$E = P(1-\nu^2)/2aw\kappa(a/h, \nu) \qquad \text{---------(1)}$$

In this equation, E is the Young's modulus, P is the force applied by the load cell, w is the indentation depth, a is the radius of the indenter, ν is the Poisson's ratio of the tissue, h is the tissue thickness, and κ is a scaling factor that depends on both a/h and Poisson's ratio ν (Mak et al., 1994). The Poisson's ratio was set at 0.45, based on the assumption that the soft tissue was nearly incompressible and this value had been widely adopted in previous studies using equation (1) for calculation (Kwan et al., 2010; Zheng et al., 2000) made for human soft tissue. The driving velocity of the motor for the deformation of the plantar tissue was set at 1 mm/sec and the indentation depth was 20% of the original thickness of the tissue before the indentation (Zheng & Mak, 1999). In each measurement, the probe was moved vertically up and down for 3 cycles to deform the plantar soft tissues for three times and 400 frames of measurement were made for measuring the change in thickness.

4.2.2 SUBJECTS

Fifteen healthy young subjects were recruited (7 males and 8 females, age ranged from 20 to 28). Exclusion criteria were people with a recent foot lesion, foot deformity, peripheral neuropathy, or a history of foot surgery. Any presence of callus was recorded. Ethical approval was obtained from a local university and written informed consent was obtained from each subject prior to the study. The demographic characteristics of the subjects are shown in Table 4.1.

Table 4.1

Demographic characteristics of the subjects (mean ± standard deviation)

Demographics	**All subjects (*n* = 15)**
Age (year)	22.5 ± 2.2
Male (%)	46.7
Height (cm)	164.5 ± 8.9
Weight (kg)	56.8 ± 14.0

4.2.3 EXPERIMENTAL SETUP

The humidity and the temperature of the assessment room were controlled during the whole study period. The test-retest reliability of the Ultrasound Foot Scanner System was performed by the same assessor at all measuring sites at the same time of two assessment sessions with one week apart. Five assessment sites on the foot were chosen, namely the pulp of the big toe, the first metatarsal head, second metatarsal head, fifth metatarsal head, and heel. These sites were selected because they are the weight-bearing points on the sole during walking (Menz & Morrison, 2006). The details on how to locate the measuring site on the scanner was described in a previous study (Zheng et al., 2012). After finishing the assessment in a sitting position, the subjects were asked to stand up and perform the assessment in a standing position. To avoid slipping while transferring from a sitting to standing position, a non-slip mattress was placed on the surface of the foot scanner and there was a wall bar for the subject to grasp for safety. An electronic balance scale was installed on the platform to ensure that the weight distribution on both legs was equal for the subject. Two trials of measurements were done on each testing foot site in sitting and standing positions. The mean scores of the thickness and stiffness of the plantar soft tissue were calculated for subsequent analysis. A 5-minute rest was provided between the measurements of each site. The data obtained on the first assessment session was used for comparing the thickness and stiffness of the tissue in sitting and standing.

4.2.4 STATISTICAL ANALYSIS

SPSS 17.0 was used to analyze the data. Intraclass correlation coefficient (ICC(3,2)) was used to analyze the test-retest reliability of the Ultrasound Foot Scanner System. In the ICC analysis, since only one rater participated in all data collection, model 3 was used; and as the mean value of each measurement was obtained by averaging the two scores, therefore form 2 was chosen. Paired t-test was used to compare the result obtained in the sitting and standing positions made by the Ultrasound Foot Scanner System. The level of significance was set at $p<0.05$. Because no significant difference was found in the data collected from the two legs, the data obtained from the two legs were averaged for subsequent analyses.

4.3 RESULTS

4.3.1 TEST-RETEST RELIABILITY OF THE ULTRASOUND FOOT SCANNER SYSTEM

The thickness and stiffness over big toes, first metatarsal heads, second metatarsal heads, fifth metatarsal heads and heels in day 1 and day 2 are listed in Table 4.2. Intraclass correlation coefficient reported excellent test-retest reliability of the Ultrasound Foot

Scanner System with all ICC (3,2) >0.9 (all *p* <0.001) at all five measurement sites taken one week apart.

Table 4.2

Test-retest reliability of the Ultrasound Foot Scanner System in measuring thickness and stiffness of plantar soft tissue

All data were the average data obtained from the left and right legs

Position	**Site**	**Day 1**	**Day 2**	**ICC (3,2)**	***p*-Value**
Thickness (mm)					
Sitting	Big toe	9.03 ± 1.34	8.94 ± 1.30	0.988	<0.001**
	First metatarsal head	11.19 ± 1.05	11.02 ± 1.12	0.973	<0.001**
	Second metatarsal head	10.64 ± 1.53	10.67 ± 1.50	0.989	<0.001**
	Fifth metatarsal head	8.43 ± 1.44	8.29 ± 1.46	0.993	<0.001**
	Heel	15.27 ± 3.99	15.23 ± 3.92	0.997	<0.001**
Standing	Big toe	8.11 ± 1.20	8.16 ± 1.13	0.988	<0.001**
	First metatarsal head	9.79 ± 1.24	9.70 ± 1.29	0.989	<0.001**
	Second metatarsal head	9.18 ± 1.33	9.15 ± 1.22	0.986	<0.001**
	Fifth metatarsal head	7.47 ± 1.27	7.44 ± 1.31	0.991	<0.001**
	Heel	13.30 ± 3.65	13.14 ± 3.57	0.997	<0.001**
Stiffness (kPa)					
Sitting	Big toe	66.50 ± 33.35	64.83 ± 32.35	0.997	<0.001**
	First metatarsal head	73.59 ± 60.44	75.83 ± 62.13	0.995	<0.001**
	Second metatarsal head	57.15 ± 28.81	56.24 ± 27.33	0.997	<0.001**

	Fifth metatarsal head	108.38 ± 99.90	111.86 ± 112.51	0.996	<0.001**
	Heel	143.59 ± 46.29	144.07 ± 47.32	0.994	<0.001**
Standing	Big toe	150.69 ± 75.03	150.33 ± 76.60	0.998	<0.001**
	First metatarsal head	238.25 ± 278.34	239.75 ± 280.24	1.000	<0.001**
	Second metatarsal head	149.48 ± 108.75	146.00 ± 103.07	0.998	<0.001**
	Fifth metatarsal head	351.87 ± 440.69	346.77 ± 425.69	0.998	<0.001**
	Heel	379.63 ± 87.72	384.07 ± 87.93	0.993	<0.001**

** $p \leq 0.001$

4.3.2 COMPARISONS OF THE THICKNESS AND STIFFNESS OF THE PLANTAR SOFT TISSUE MEASURED IN SITTING AND STANDING POSITIONS

The thickness and stiffness of the five measuring sites over the soles in sitting and standing are listed in Table 4.3. Paired t-test showed that the plantar soft tissue was significantly thinner, with a range from 0.92 mm to 1.97 mm decrease in thickness, at different measurement sites when changing from sitting to standing position (all $p<0.001$). Also, the stiffness of plantar soft tissue was significantly increased in a standing position at different measurement sites (with an increase ranged from 84.19 kPa to 243.49 kPa) as compared with the measurements recorded in a sitting position (between-group difference: all $p<0.05$).

Table 4.3

The thickness (mm) and stiffness (kPa) recorded in sitting and standing recorded by the use of Ultrasound Foot Scanner System#.

Site	Sitting	Standing	*p*-value
Thickness (mm)			
Big toe	9.03 ± 1.34	8.11 ± 1.20	<0.001**
First metatarsal head	11.19 ± 1.05	9.79 ± 1.24	<0.001**
Second metatarsal head	10.64 ± 1.53	9.18 ± 1.33	<0.001**
Fifth metatarsal head	8.43 ± 1.44	7.47 ± 1.27	<0.001**
Heel	15.27 ± 3.99	13.30 ± 3.65	<0.001**
Stiffness (kPa)			
Big toe	66.50 ± 33.35	150.69 ± 75.03	<0.001**
First metatarsal head	73.59 ± 60.44	238.25 ± 278.34	0.013*
Second metatarsal head	57.15 ± 28.81	149.48 ± 108.75	0.001**
Fifth metatarsal head	108.38 ± 99.9	351.87 ± 440.69	0.018*
Heel	143.59 ± 46.29	379.63 ± 87.72	<0.001**

*$p<0.05$

**$p\leq 0.001$

Values are Mean ± standard deviation. All the shown data were the mean obtained from the left and right legs.

4.3.3 POWER ANALYSIS

The *post hoc* power analysis was performed by using G*Power with the data obtained in 1st metatarsal head with sample size of 15 subjects in 2 groups and alpha set at 0.05, it yielded an effect size ranging from 0.734 to 2.040 and power from 0.753 to 1.000.

4.4 DISCUSSION

Foot ulceration is one of the common complications reported by people with diabetes. One of the risk factors is an increase in stiffness of plantar soft tissue (Reihsner et al., 2000). The morbidity, mortality and additional medical cost are substantially increased for patients with diabetes who developed foot ulcer (Ramsey et al., 1999). Therefore, an accurate and convenient assessment tool is essential to monitor the mechanical changes over the sole of foot for early detection among people with diabetes who are at risk of developing foot ulceration. Several devices or imaging systems have been adopted to assess the stiffness and thickness of plantar soft tissue (Gefen et al., 2001; Rome et al., 2001). But they are either expensive imaging system such as magnetic resonance imaging (Gefen et al., 2001) or system that only provides indirect measurement of the plantar soft tissue during the indentation (Rome et al., 2001). These factors limit their feasibility to be applied in clinical settings.

Ultrasound is a relatively inexpensive and safe imaging technology. The foot scanner system adopted in the present study is an advanced model based on a previously-designed Tissue Ultrasound Palpation System (TUPS). The foot scanner can reflect the plantar pressure that the foot received during weight-bearing. Since plantar pressure changes when transfer from non-weight bearing positions to weight bearing positions (Kwan et al., 2010; Zheng et al., 2000), therefore assessing the plantar soft tissue in weight-bearing positions is clinically relevant especially for people with diabetes because they are prone to develop foot deformities in weight bearing activities The redistribution of plantar pressure occurs when the subjects change from a non-weight bearing position to a weight bearing position (Cowley, Boyko, Shofer, Ahroni, & Ledoux, 2008). Moreover, TUPS requires the assessor to perform a manual indentation of the ultrasound probe by hand that needs a great deal of practice. Measuring errors may occur if the alignment of the probe is not perpendicular to the skin. One earlier study reported that the Ultrasound Foot Scanner System used in the present study was able to measure stiffness and thickness of plantar soft tissue at different bodyweight loading (Zheng et al., 2012). The present study further demonstrated that this system is a potential clinical device to monitor people’s plantar soft tissue conditions over time.

Our findings demonstrated a high test-retest reliability of using the Ultrasound Foot Scanner System in assessing the thickness and stiffness of plantar tissue. The ultrasound probe was fixated in the system to ensure its perpendicular alignment to the surface of the skin during each measurement. Also, an electronic scale was built in the foot platform that ensures the subject distributing equal body weight on both feet during the measurement; software was implemented to standardize the speed and depth of penetration, which contributed to the consistency of the measurements of stiffness at different time points.

The present study was the first one to compare the change in thickness and stiffness of the plantar soft tissue over the pulp of big toe, first metatarsal head, second metatarsal head, fifth metatarsal head, and heel when subjects transferred from sitting to standing. There was a significant thinning and stiffening of plantar tissue at these points when subjects get up from sitting to standing position. Specifically, there was a 10% to 14%

decrease in thickness of the plantar soft tissue at the five measuring sites; and there was a range of 123% to 164% increase in stiffness of the plantar soft tissue among those measurement sites. When a subject gets up from a sitting to standing position, the body weight exerts a higher force over the skin of the foot, the vertical compression force results in horizontal squeezing of the tissue in standing, which is commonly observed in biological soft tissue for protection from tissue breakdown (Zheng et al., 2012). Our results also showed that the stiffness of the plantar soft tissue was highest at the heel, followed by the fifth metatarsal head, first metatarsal head, pulp of big toe and then the second metatarsal head. This trend was consistent in both sitting and standing. This is the first study that reports this trend; future study can verify if this trend is altered in an aging population or a disease group such as diabetes.

Our findings demonstrated that the weight bearing status alters the stiffness of plantar tissue. More importantly, the change in stiffness of plantar tissue would increase the plantar soft tissue pressure. Cheung et al. reported that the stiffness of plantar soft tissue increase by five-fold that can lead to an increase in the pressure on the plantar soft tissue for more than 30 percent (Cheung et al., 2005); Flynn et al. further showed that the plantar pressure was reduced during weight supported walking as compared with normal walking (Flynn, Canavan, Cavcanagh, & Chiang, 1997). Vela et al. also found that an increase in body weight would significantly increase the plantar pressure (Vela, Lavery, Armstrong, & Anaim, 1998). These findings further support the use of the present foot scanner system in assessing the plantar soft tissue in weight bearing positions; which is an important functional position to estimate the risk of developing foot ulcers. Further investigation is required to explore how exactly the change of plantar soft tissue stiffness would affect the plantar pressure using the present foot scanner system. The present device can potentially be used in assessing plantar pressure in clinical settings,

The present study performed the foot assessment in static postures and we found that the percentage decrease in tissue thickness over the heel from sit to stand was around 13%. This figure was lower than the results reported by Gefen et al. who found that there was a deformation heel tissue thickness by about 40% during heel strike using an X ray-based system (Gefen, Megido-Ravid, & Itzchak, 2011). This discrepancy was probably caused by the ground reaction force exerted on the heel during walking. The device used by Gefen et al. (2001) only allowed a one-dimensional lateral view of the foot, which is not feasible to provide accurate measurement of the deformation of one particular point on the heel. Besides, the exposure to radiation and also the expenses would be a concern if regular assessments need to be conducted over time in clinical setting.

Plantar soft tissues over the metatarsal heads are common sites of developing foot ulceration. A previous study showed that toe extension produced a significant increase in stiffness on the plantar soft tissue over metatarsal heads, which would cause an increase in plantar soft tissue pressure during push off phase in walking (Garcia, Hoffman, Hastings, Klaesner, & Mueller, 2008). Modification of the current system such as putting a tilting system to fixate the toes in extension position would be technically feasible to measure how would toes extension change the soft tissue stiffness and thickness over the metatarsal heads, but further investigation is required to prove this hypothesis. According to Table 4.3, the 1st and 5th metatarsal heads showed a relatively higher standard deviation. This might be due to the reason that some of the subjects were relatively active in sport activities and callus might have formed over these two spots.

The Ultrasound Foot Scanner System was designed to minimize the possible human error made during measurement. Assessors were only required to ensure that the subjects were able to keep an erect proper during the measurement; and the same posture can be maintained during the repeated measurements made at each site in either sitting or standing. Therefore, the present system can potentially be used in clinical settings to allow accurate and efficient assessment with good test-retest reliability. It is important to assess the change in the biomechanical properties of plantar tissues in various weight bearing positions because it allows early detection of people who are prone to develop foot complication such as diabetic ulcers.

4.5 LIMITATION

The present study was conducted in healthy subjects. Therefore future study should be conducted to use the present device to measure thickness and stiffness of plantar soft tissue in a specific client group such as elderly or people with diabetes.

4.6 CONCLUSION

The Ultrasound Foot Scanner System is a reliable tool for measuring the thickness and stiffness of the plantar soft tissue in either a sitting or standing position. The plantar soft tissues become significantly thinner and stiffer in standing when compared to sitting, which implies that weight-bearing status can change the plantar pressure. The system can potentially be used as a clinical device to identify the risk of developing foot ulcers in various disease groups such as people with diabetes.

Foot ulceration is not the only complication found in people with diabetes. In the next chapter, I will introduce another common complication, a decrease in mobility performance found in people with DM. I will also explain the findings on the relationship between the ankle characteristics found in elderly with type 2 DM and their mobility performance.

CHAPTER 5

RELATIONSHIP BETWEEN THE PHYSICAL CHARACTERISTICS OF THE ANKLE AND THE POSTURAL CONTROL IN ELDERLY WITH TYPE 2 DIABETES

5.1 INTRODUCTION

Decrease in mobility performance is one of the major concerns in people with diabetes (Gregg et al., 2000; Orr, Tsang, Lam, Comino, & Singh, 2006). The decline in quality of life and balance performance were associated with the decline in mobility performance (Bootsma-van der Wiel et al., 2002; Ijzerman et al., 2012). Diabetes affects the distal circulation and may lead to various complications on the ankle joint, including a decrease in ankle muscle strength, increase in stiffness of the ankle joint in dorsiflexion, and decrease in ankle proprioception sense (Andersen et al., 2004; Giacomozzi et al., 2008; van Deursen & Simoneau, 1999). These physical characteristics are potential factors affecting the mobility performance in this client group. However, no previous study has examined these relationships.

A decrease in lower limb muscle strength due to sarcopenia is commonly found among elderly people, but the rate of decline in the distal muscle strength was found to be faster among elderly with diabetes than age-matched control (Andersen et al., 2004; Andreassen et al., 2006). This accelerated decline in muscle strength is caused by hyperglycemia which speed up the muscles break down, thus reducing the mass and quality of the muscles as reflected by muscle force per unit of mass (Cesari et al., 2004; Park et al., 2006; Visser et al., 2002). A reduced range of motion in dorsiflexion is another complication caused by hyperglycemia that trigger a chain of reaction and ended up with an increase in the density of disorganized collagen fiber and formed abnormal fiber morphology with adhesive fiber in the Achilles tendon (Giacomozzi et al., 2008; Grant et al., 1997). These changes were found to alter the stretch distribution of the Achilles tendon during walking (Cronin et al., 2010), which may in turn influence the walking efficiency in diabetic patients. Besides, a decrease in proprioception of the ankles may occur even before any sign of diabetic neuropathy is reported; this sensory deficits may affect their stability of walking and increase their risk of fall during walking (Liu et al., 2010; van Deursen & Simoneau, 1999).

The abovementioned ankle characteristics are believed to contribute to the decline in mobility performance among elderly with diabetes. However, no study has investigated how much each of these physical characteristics contributes to the decline in mobility performance among this client population. With a better understanding of the contribution of each ankle characteristics to mobility performance of people with diabetes, a specific training program can be designed to enhance the mobility status for this client group. Therefore, the objective of present study was to examine the relationship between physical characteristics of the ankle (muscle strength, ankle stiffness, and proprioception) and the mobility performance of people with type 2 diabetes. Since demographic characteristics are factors affecting the mobility performance, multiple regression analysis was used to assess the degrees of association between demographic characteristics, ankle joint characteristics, and mobility performance. The mobility performance was measured by the Timed Up and Go test (TUG). TUG is a clinical test which has been widely used to assess mobility performance in elderly population including people with diabetes (Beauchet et al., 2011; Brandon, Gaasch, Boyette, & Lloyd, 2003).

5.2 METHOD

5.2.1 SUBJECTS

Subjects with type 2 diabetes and age 65 or above were recruited in local community elderly centers. Inclusion criteria were a diagnosis of type 2 diabetes with the ability to walk without walking aids and able to understand instructions. Subjects were excluded if they had peripheral neuropathy screened by 10g monofilament (Nather et al., 2008), retinopathy, or other visual impairments assessed by visual acuity test using the Snellen chart (Falkenstein et al., 2008), recent foot lesions or surgery, a history of neurological disorders, and unstable hypertension as reported by the patients. Ethical approval for conducting the study was obtained from a local university; written informed consent was obtained from all the participants.

5.2.2 MATERIALS AND EXPERIMENTAL SETUP

5.2.2.1 TIMED UP AND GO TEST

The Timed Up and Go test (TUG) was conducted by first asking the subjects to sit on a chair with backrest and their arms relaxed on the armrests. Subjects were then instructed to stand up, walk for 3 meters, turn around at a mark on the ground, then walk back to the chair and sit down with their back touching the backrest (Shumway-Cook et al., 2000). The details of timing can be referred to chapter 3 (section 3.6). Three trials were conducted on each subject and the average time measured to the nearest 0.01 second was calculated for analysis. This test is commonly used in assessing the general mobility status of elderly people, and high test-retest reliability has been demonstrated (Steffen et al., 2002).

5.2.2.2 MUSCLE STRENGTH OF ANKLE PLANTAR FLEXORS AND DORSIFLEXORS

The isokinetic muscle strength of ankle plantar flexors and dorsiflexors was tested using the Cybex Norm dynamometer (Computer Sports Medicine Inc, Stoughton, MA, USA) with the angular velocity set at 60º/seconds. Details of the test can be referred to chapter 3 (section 3.2). A total of three trials with three repetitions in each trial were performed for each leg, and the average peak torque normalized by each subject's weight in Newton meters per kilogram (Nm/kg) was calculated for analysis (Li et al., 2009).

5.2.2.3 ACITVE ANKLE JOINT REPOSITIONING TEST

The proprioception of the ankle joint was measured by an active ankle joint repositioning test using the built-in goniometer of the Cybex Norm dynamometer (Computer Sports Medicine Inc, Stoughton, MA, USA). The inter-tester reliability of the test was previously reported to be excellent (Deshpande et al., 2003). The details of the assessment can be referred to chapter 3 (section 3.3). A total of three trials were performed and the mean value of the three trials was calculated for subsequent analysis (Sefton et al., 2009).

5.2.2.4 WEIGHT –BEARING LUNGE TEST

The ankle joint mobility in terms of dorsiflexion was assessed by the weight-bearing lunge test (WBLT), based on the knee-to-wall principle (Hoch et al., 2011). The detail of assessment can be found in chapter 3 (section 3.4). Excellent inter-tester and intra-tester reliability for the WBLT had been reported in a previous study (Bennell et al., 1998).

5.2.3. STATISTICAL ANALYSIS

All analyses were performed with the IBM® SPSS® Statistics 19.0 (IBM Corporation, Chicago, IL, USA). Pearson correlation coefficient was used to analyze the pairwise relationship between gender (coded 0/1), age, duration of diabetes, body mass index (BMI), glycated hemoglobin (HbA1c), normalized peak torque of ankle dorsiflexors, normalized peak torque of ankle plantar flexors, WBLT, and active ankle joint repositioning error. Pearson correlation coefficient was also used to assess the association between TUG and each independent variable as abovementioned. Multiple regression analysis (Enter method) was used to examine the degree of association between those independent variables and TUG when examined simultaneously. Three separate regression models adopted in the present analysis were: (i) only demographic variables were entered into the model; (ii) only ankle characteristics were entered; (iii) all variables, including demographic and ankle characteristics were entered. Comparing these three nested models would enable us to examine the partial correlation between TUG and ankle characteristics after partialling out the effect of demographic characteristics, and vice versa. Since there was no significant difference between the left and right leg in the results obtained on the normalized peak torque of ankle muscles, WBLT, and active joint repositioning error, the average of the data obtained for the two legs was used for subsequent data analyses. The level of significance was set at $p < 0.05$.

5.3 RESULTS

5.3.1 DESCRIPTIVE STATISTIC

85 elderly subjects with type 2 diabetes were recruited from four community elderly centers. The demographic characteristics are shown in Table 5.1. In general, the mean duration of diabetes among our subjects was more than 10 years. The glycemic control in our subjects was not satisfactory (7.7±1.4%) as American Diabetic Association recommended people with diabetes should keep the HbA1c level below 7% in order to reduce the risk of developing microvascular complications ("Executive summary: standards of medical care in diabetes-2009," 2009).

Table 5.1

Demographic characteristics of the subjects (mean ± SD)

Characteristic	n=85
Age (year)	72.5 ± 7.2
Female (%)	70.6
History of diabetes (year)	10.6 ± 8.3
Glycated haemoglobin - HbA1c (%)	7.7 ± 1.4
Height (cm)	153 ± 7.3
Weight (kg)	63.4 ± 14.4
Body Mass Index (kg/m^2)	26.9 ± 6.6

The performance of TUG, normalized peak torque of ankle plantar flexors and dorsiflexors, weight-bearing lunge test distance and active ankle joint repositioning errors are shown in Table 5.2. A linear relationship between TUG and each independent variable was observed. Table 5.3 shows the pairwise relationship of the independent variables (demographics and ankle characteristics). The correlations between several pairs of the independent variables were statistically significant; however the level of correlations were only low to moderate. Therefore, each variable provides independent information in the regression model.

Table 5.2

Descriptive statistic of the performance (mean $\pm$ SD)

Variables	Descriptive statistic
TUG (second)	10.1 $\pm$ 3.1
Normalized peak torque of dorsiflexors (Nm/kg)	0.2 $\pm$ 0.1
Normalized peak torque of plantarflexors (Nm/kg)	0.3 $\pm$ 0.1
Lunge test distance (cm)	8.6 $\pm$ 4.1
Active ankle joint repositioning error (degree)	5.4 $\pm$ 3.1

Data on the active ankle joint repositioning error, lunge distance and normalized peak torques represent the mean obtained in the left and right legs

Table 5.3

Pearson correlation coefficient of the independent variables

Independent variables	TUG	Age	History of diabetes	Gender	BMI	HbA1c	Normalized peak torque of dorsiflexors	Normalized peak torque of plantarflexors	Lunge test distance	Active ankle joint repositioning error
Age (year)										
r	0.44		0.00	-0.01	0.19	-0.08	-0.31	-0.20	-0.28	0.30
p	(<0.001)‡	-----	(0.985)	(0.920)	(0.082)	(0.494)	(0.005†)	(0.071)	(0.009†)	(0.006†)
History of diabetes (year)										
r	0.04		-----	0.16	-0.04	-0.22	0.02	0.07	-0.06	-0.12
p	(0.747)			(0.142)	(0.732)	(0.052)	(0.890)	(0.518)	(0.611)	(0.291)
Gender										
r	0.16				0.07	0.20	-0.39	-0.13	-0.21	0.19
p	(0.134)			----	(0.539)	(0.071)	(<0.001‡)	(0.240)	(0.059)	(0.094)
Body mass index (kg/m^2)										
r	0.42					0.03	-0.36	-0.36	-0.32	0.02
p	(<0.001)‡				-----	(0.783)	(0.001†)	(0.001†)	(0.003†)	(0.838)
Glycated haemoglobin - HbA1c (%)										
r	-0.15						0.05	0.17	0.06	0.06
p	(0.194)					-----	(0.647)	(0.133)	(0.591)	(0.579)
Normalized peak torque of dorsiflexors (Nm/kg)										
r	-0.63						-----	0.74	0.53	-0.18
p	(<0.001)‡							(<0.001‡)	(<0.001†)	(0.111)

Normalized peak torque of plantarflexors (Nm/kg)		-----		
r	-0.61		0.48	-0.10
p	(<0.001)‡		(<0.001‡)	(0.374)
Lunge test distance (cm)				
r	-0.56			-0.37
p	(<0.001)‡		-----	(0.001†)
Active ankle joint repositioning error (degree)				
r	0.43			-----
p	(<0.001)‡			

†*p*<.01; ‡*p*<.001

5.3.2 CORRELATION BETWEEN THE INDEPENDENT VARIABLES AND THE TIMED UP AND GO TEST

Pearson correlation coefficient showed that age (r=0.44), body mass index (r=0.42) and active ankle joint repositioning error (r=0.43) were positively correlated with TUG while normalized peak torque of ankle dorsiflexors (r=-0.63), plantar flexors (r=-0.61) and weight-bearing lunge test distance (r=-0.56) were negatively correlated to the Timed Up and Go test (with all $p<0.05$) (Table 5.3).

5.3.3 MULTIPLE REGRESSION ANALYSES

When only demographic variables were included in the model, the R^2 was 0.375. When both demographic and ankle characteristics were included, the R^2 increased to 0.599. Hence, by adding ankle characteristics, there was a 22.4% increase in variation explained. However, when only ankle characteristics were included in the model, the R^2 was 0.546; implying that the additional variance explained by demographic variables was only 5.3%. The independent contribution made by ankle characteristics was therefore a lot bigger than demographic characteristics. Table 5.4 presents results of the full regression model; the multiple R (0.774) was statistically significant ($p<0.001$). The strength of the ankle dorsiflexors and ankle plantar flexors, stiffness in dorsiflexion and proprioception, together with the demographic data, accounted for 59.9% of the variance of TUG. Significant contributors included BMI (β= 0.235, p=0.009; partial correlation= 0.314), active ankle joint repositioning error (β= 0.252, p=0.005; partial correlation= 0.338), and normalized peak torque of plantar flexors (β= -0.296, p=0.027; partial correlation= -0.268).

5.3.4 POWER ANALYSIS

The *post hoc* power analysis was performed by G*Power with the result obtained from the multiple regression analysis. It yielded an effect suze of 0.270 and power 0.62.

Table 5.4

Multiple Regression Analysis of the Timed Up and Go test with Demographic Data and Ankle Characteristics

Independent variables	Standardized coefficient (β)	R^2	F	p-value
Age (year)	0.133	0.599	10.953†	0.134
Gender	-0.010			0.912
Duration of diabetes (year)	0.078			0.366
Body Mass Index (kg/m^2)	0.235			0.009*
Glycated haemoglobin-HbA1c (%)	-0.087			0.312
Normalized peak torque of dorsiflexors (Nm/kg)	-0.176			0.233
Normalized peak torque of plantarflexors (Nm/kg)	-0.296			0.027*
Weight-bearing lunge test distance (cm)	-0.084			0.396
Active ankle joint repositioning error (degree)	0.252			0.005*

The dependent variable is the Timed Up and Go test.

*p<0.05; †p<0.001

5.4 DISCUSSION

This is the first study that examined the association between ankle characteristic and mobility performance in elderly with type 2 diabetes. We measured ankle muscle strength, proprioception and the dorsiflexion stiffness in each patient, and found that all these ankle characteristics were significantly associated with TUG. Multiple regression analysis revealed that BMI, normalized peak torque of the ankle plantar flexors, and ankle joint proprioception are significant contributors to the mobility performance of elderly with diabetes, as reflected by TUG.

5.4.1 DEMOGRAPHIC DATA AND TIMED UP AND GO TEST

BMI was one of the significant factors contributing to TUG (β= 0.235, p=0.009). This finding was consistent to what an earlier study reported that BMI is one of the factors that contribute to the loss of walking ability in people with diabetes (van Sloten et al., 2011). Studies have reported the problems brought by obesity in people with diabetes including risk of developing coronary heart disease (Cho et al., 2002). Our results further suggested that obesity in this client group would reduce their mobility status. People who are relatively obese need stronger lower limb muscle to ambulate and transfer. Launer et al. (1994) suggested that people with high BMI would result in reduction in neurological and musculoskeletal reserve or capacity, which would form a vicious cycle that cause further decline in mobility performance (Launer, Harris, Rumpel, & Madans, 1994). Therefore, weight control and reduction is essential for the diabetic population.

Age was found to be significantly correlated with TUG (r=0.44, p<0.001). This association was expected because there is a general decline in different systems during the process of aging, such as reduced general muscle strength or visual deterioration, which would affect physical mobility (Finlayson & Perterson, 2010). Surprisingly, our findings illustrated that glycated haemoglobin level (HbA1c) and the duration of diabetes did not correlate with TUG. This was inconsistent to our original hypothesis since previous studies reported that HbA1c level and duration of diabetes were associated with the physical function in elderly with type 2 diabetes (Park et al., 2006; Sayer et al., 2005). The reason behind this contradicting result can be explained by the convenience sampling method that we adopted. This is well known that most elderly people with type 2 diabetes adopt a more sedentary life style. We recruited subjects from community centres, who subjects were relatively active and had a better general health. The convenient sampling adopted in present study may lead to a selection bias in which the recruited subjects did not represent the typical people with diabetes, therefore, the influence of diabetic duration or blood glucose level seemed to bring little impact to the physical performance in our subjects.

5.4.2 ANKLE MUSCLE PEAK TORQUE AND THE TIMED UP AND GO TEST

The major components of TUG included sit-to-stand transfer, walking and turning. Our results showed that the normalized peak torque of the plantar flexors was a significant factor contributing to TUG (β= -0.296, p=0.027). This finding was consistent to the result reported by Ijzerman et al who found both ankle dorsiflexors and plantar flexors were associated to TUG for people with diabetes (Ijzerman et al., 2012). The present study presented the ankle peak torque by normalizing the body weight. This is because lower limb muscle strength is supposed to be related to a person's own body weight (Bazett-Jones, Cobb, Joshi, Cashin, & Earl, 2011). The strength of plantar flexors is a crucial factor affecting walking speed and that is the key factor discriminating the physical performance of individuals (Graf, Judge, Ounpuu, & Thelen, 2005; Kerrigan, Todd, Croce, Lipsitz, & Collins, 1998). The push-off power of the ankles is essential in propelling the weight of the body forward and it was found that the decrease in push-off power by ankle plantar flexors contributed more than the reduction of cadence to the reduction in walking speed when people are getting old (Winter, Patla, Frank, & Walt, 1990). Besides, it was found that the preferred walking speed can be increased by 7% if the push-off energy is increased by 15% (Norris, Granata, Mitros, Byrne, & Marsh, 2007). This finding was particularly important for elderly people with diabetes because they are experiencing an accelerated decline in muscle strength as compared with healthy subjects (Andersen et al., 2004). In addition to forward walking, ankle plantar flexors strength is particularly important for making a smooth turn because an efficient ankle push-off of the outer limb is needed in order to push the center of gravity in the direction of turning (Orendurff et al., 2006). In addition, extra push–off power enables a person to make a spin turn (takes a shorter time to complete the turning) rather than a step turn (Hase & Stein, 1999).

We found that the strength of ankle dorsiflexors was associated with TUG. This finding was consistent to a previous study that reported a positive correlation between strength of ankle dorsiflexors and walking velocity in people with type 2 diabetes (MacGilchrist et al., 2010). The muscle strength of ankle dorsiflexors is important in creating effective toe clearance during walking and turning (Orendurff et al., 2006). Kemoun and colleagues demonstrated that elderly fallers have a greater delay in the recruitment of ankle dorsiflexor rather than a decrease in dorsiflexors strength during swing phase of walking as compared to elderly non-fallers (Kemoun, Thoumie, Boisson, & Guieu, 2002). This implies that the neuromuscular component of ankle dorsiflexors might be a more important factor than muscle strength in determining the walking efficiency. This could be more obvious in people with diabetes who commonly present with a decrease in nerve conduction in distal muscle as the disease progresses. Further study is needed to verify this hypothesis.

For the sit-to-stand phase of the TUG, some studies reported that the strength of ankle dorsiflexors was correlated to the sit-to-stand performance in which the subjects who had weaker dorsiflexor strength took longer time to perform sit-to-stand transfer. However, those studies focused on the performance on either healthy elderly or elderly in other disease group but not in people with diabetes (Lord, Murray, Chapman, Munro, & Tiedemann, 2002; Scott-Okafor, Silver, Parker, Almy-Albert, & Gardner, 2001). Previously, it was believed that hip and knee extensors were the main contributors to sit-to-stand transfer, Scott-Okafor and colleagues suggested there might be a subtle role of ankle dorsiflexor on maintaining the balance of the center of gravity of during the transition phase from sitting to standing (Scott-Okafor et al., 2001). Until now, there is no clear explanation on the relationship between ankle dorsiflexor strength and the sit-to-stand performance.

Although we found that the normalized peak torque of ankle dorsiflexors has a significant and moderate correlation with the performance of TUG (r=-0.63, p<0.001), we still found that it was not significantly associated with the performance of TUG in the multiple regression model. This can be explained statistically. As shown in Table 5.3, there are significant correlations between several pairs of independent variables. Among those pairs, the correlation between the normalized peak torque of ankle dorsiflexors and the normalized peak torque of plantar flexors (r=0.74, p<0.001) is relatively high as compared with the rest. When multiple regression analysis was applied to predict the performance of TUG, the explanatory power of the peak torque of dorsiflexors might be overshadowed by that of plantar flexors, hence making the impact of the peak torque of dorsiflexors on the performance of TUG less substantial.

5.4.3 ANKLE JOINT REPOSITIONING TEST AND TIMED UP AND GO TEST

Ankle joint proprioception is another significant factor contributing to TUG (β= 0.252, p=0.005). Ankle proprioception is essential in coordinating various muscle groups of the lower limbs for ambulation (Abelew, Miller, Cope, & Nichols, 2000) Accurate ankle proprioception enables human to detect the correct placement of the foot during the initial heel contact, and it also contributes to a stable single-leg stance in mid-stance during walking(Konradsen, Ravn, & Sorensen, 1993), it is also important for providing correct information on the location and acceleration of the center of the mass with respect to the supporting surface during the swing phase when walking (Sorensen & Hollands, 2002). A systematic review demonstrated that the afferent input from the ankle contributes 30% to 60% of the output of ankle extensor muscles during the stance phase (Donelan &

Pearson, 2004). Therefore, ankle proprioception affects the stance and swing phases during walking and turning, and its statistical significance in the regression model in the present study further reflects its importance found in previous studies. Although no previous study has investigated the relationship between ankle proprioception and sit to stand performance, the alignment of ankle would be affected in preparation of sit-to-stand transfer if there was a deficit in estimation of ankle placement, thus affecting the performance during the transfer.

5.4.4 WEIGHT-BEARING LUNGE TEST AND THE TIMED UP AND GO TEST

The present study demonstrated a significant correlation between the stiffness of ankle dorsiflexion and TUG performance. The range of motion of ankle dorsiflexion is important for toe clearance and for generating the peak torque of plantar flexors during walking (Mueller, Minor, Schaaf, Strube, & Sahrmann, 1995). It was found that the passive ankle range of motion in dorsiflexion was associated with the time for rearfoot re-inversion and heel-off during walking, a greater deficit in the range would result in further decline in walking performance (Cornwall & McPoil, 1999). For sit-to-stand performance, decreased range of motion in ankle dorsiflexion would result in poor alignment of ankle, which may increase the total center of mass distance traveled before rising up from sitting and more time would be required for transfer (Perry, Marchetti, Wagner, & Wilton, 2006). However, the present study found that ankle joint stiffness in dorsiflexion was not a significant contributing factor to TUG, this can be explained by the satisfactory performance of our subjects as the mean WBLT distance of our subjects (8.56 cm) was comparable to the mean values measured in young healthy subjects (7.80

cm to 8.90 cm) as reported by Jones and colleagues (Jones, Carter, Moore, & Wills, 2005). In addition, the toe clearance could be compensated for by increasing the range of hip flexion during the test. Therefore, the influence of ankle dorsiflexion stiffness on TUG in terms of WBLT was reduced in the regression model.

5.5 LIMITATION

Convenient sampling method is one of the limitation of present study. Since the subjects of present study were recruited from community centers. It is logical to deduced that this group of population were physically more active. This can be one of the reason why we found that the strength of ankle dorsiflexors and the stiffness of ankle joint in dorsiflexion were not significant contributor to TUG.

5.6 CONCLUSION

To conclude, age, BMI, peak torque of ankle plantar flexors and dorsiflexors, stiffness of the ankle joint in dorsiflexion, and ankle joint proprioception are correlated with TUG. Multiple regression analysis showed that the physical characteristics of the ankle joint together with demographic factors contributed to 59.9% of the variance in the performance of TUG. BMI, ankle joint proprioception, and the strength of the ankle plantar flexors are significant contributors to functional mobility in elderly people with type 2 diabetes.

The research gap between the ankle characteristics and the mobility performance in elderly with type 2 diabetes has been filled through the present study. The next step is to investigate it exercise with content targeting at these characteristics could enhance the mobility performance. However, previous studies were performed to investigate it exercise could improve the balance and mobility performance in this group of population. In the next chapter, the result of a systematic review on this aspect will be presented.

CHAPTER 6

EFFECTS OF EXERCISE ON MOBILITY PERFORMANCE AND BALANCE STATUS IN PEOPLE WITH TYPE 2 DIABETES: A SYSTEMATIC REVIEW

6.1 INTRODUCTION

According to the fact sheet from World Health Organization, there are around 350 million people diagnosed with diabetes worldwide and this number is still rising (*Diabetes Mellitus. Fact Sheet number 312*, 2011). Diabetes is well known in some of its complications including impaired balance and mobility (Tilling, Darawil, & Mary, 2006). The consequences of fall vary from physical injury to psychological impact and both cause a decline in quality of life to the sufferers and their care givers (Jung, 2008).

One possible reason behind the increased fall risk is diabetic peripheral neuropathy. It affects the transmission of the somatosensory signal from the sole of feet. Poor afferent inputs subsequently cause a deterioration in postural control and gait stability (Menz et al., 2004). However, it was found that people with diabetes without peripheral neuropathy demonstrated a deterioration in ankle joint proprioception, thus causing them an altered gait performance when walking across obstacle as compared with healthy control (Liu et al., 2010). Besides, the decrease in the range of ankle dorsiflexion caused by increased collagen cross-link in Achilles tendon in diabetic subjects was found to contribute to the abnormal gait pattern which may cause mobility impairment (Abate et al., 2011; Grant et al., 1997). Therefore, it is likely that the diabetic-associated decline in the musculoskeletal system contributes to the increase in risk of fall (Andreassen et al., 2006; Hilton et al., 2008).

Various studies have evaluated the effects of exercise in people with balance disorders. A systematic review suggested that exercise is effective in enhancing balance in healthy elderly (Howe, Rochester, Neil, Skelton, & Ballinger, 2011). However, there is lack of similar review for diabetic population. Previous reviews only showed that exercise is effective in glycemic control, reduction of visceral adipose tissue and reduce the incidence of type 2 diabetes (Orozco et al., 2008; D. Thomas, Elliott, & Naughton, 2009). Therefore, the present chapter will present the result of a systematical review on the effectiveness of exercise on the enhancement of balance and mobility status in people with type 2 diabetes.

6.2 METHODOLOGY

6.2.1 LITERATURE SEARCH STRATEGY

A literature search was conducted to identify all possible studies published until March 2012 in order to answer the research question. Medline (1950 to present), CINAHL (1982 to present), Cochrane Central Register of Controlled Trials and EMBASE were examined. Search terms included controlled terms such as from MeSH in CENTRAL and free text terms. Hand search on the bibliography of the relevant articles and existing reviews on the effect of exercise in people with diabetes were performed in order to avoid missing any relevant articles that were not identified in the abovementioned electronic databases. Published or unpublished article, such as conference paper or dissertations in all languages were included. The literature search was done with the combination of keywords with an example of Medline in Appendix I. Search terms stand for diabetes (such as diabet*, NIDDM, glucose intolerance etc); exercise (such as strengthening, training, Tai Chi etc) and balance and mobility (such as balance, timed up and go test etc) were used. The literature search was performed by two authors independently (TN and

EC), the identified articles were screened and included after reviewing the abstract. Full texts of articles which matched the inclusion criteria or for those with unclear abstracts were identified for further review. Any disagreement was resolved by discussion and a third author (GC) was referred for adjudication if necessary.

6.2.2 INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria were defined under the PICO model (population, intervention, control group/comparison group and outcome measures).

- Population: people diagnosed with type 2 diabetes at any age and in any setting
- Intervention: any kind of exercise therapy aimed at improving balance and mobility status. Specific exercise (such as Tai Chi or Pilates) or non-specific exercise (such as resistance training or balance training); land exercise or hydrotherapy; home exercise or center-based exercise; individual training or group exercise were included.
- Control group/ comparison group: Randomized controlled trial or Quasi-randomized controlled trial were included.
- Outcome measures: All kinds of objective assessments to evaluate the balance and mobility status of the subjects were included. Assessments could be clinical test (such as Timed Up and Go test, single leg stance test) or laboratory test (such as gait analysis, Sensory Organization Test, Chattecx Dynamic Balance System). Subjective assessments such as questionnaire or subject self-reported performance were excluded.

6.2.3 QUALITY ASSESSMENT

The quality assessment was performed by the same authors as mentioned above (TN and EC) independently, any disagreement was resolved by discussion and if necessary, the third author (GC) was referred for decision. The quality assessment on the included articles was done using the Cochrane Collaboration's Risk of bias tool (Higgins & Altman, 2008). This tool includes 7 domains: (1) sequence generation, (2) allocation concealment, (3) blinding of participants, (4) blinding of outcome assessor, (5) incomplete outcome data, (6) selective outcome reporting, and (7) free of other bias. In each domain, answer 'low' indicates low risk of bias; 'high' indicates high risk of bias and 'unclear' indicates the authors could not make the judgment due to lack of sufficient detail.

6.2.4 DATA EXTRACTION

Details of the articles were extracted and summarized in Appendix II. The data that were extracted included:

- Authors, year and country of publication
- Study design
- Demographic data (age, number of subjects in each group)
- Intervention and control group management (form and intensity)
- Intervention duration and/or follow up period
- Balance or mobility outcome measures
- Drop out
- Summary of results

- Intervention adverse effects

6.2.5 STATISTICAL ANALYSIS

Since there was no limitation in the type of therapeutic exercise in the present study, in order not to misrepresent the extracted data, a meta-analysis was not conducted. The clinical significance was set at $p<0.05$ in all outcome measures in the included articles, unless if specific statistical analysis such as Bonferroni correction.

6.3 RESULTS

A total of 3394 abstracts were identified by the electronic databases. After selection based on the title and keywords, a total of 27 studies were found. Fig 6.1 showed the flow chart of the search result. After initial screening, 27 articles were extracted with full text for further investigation.

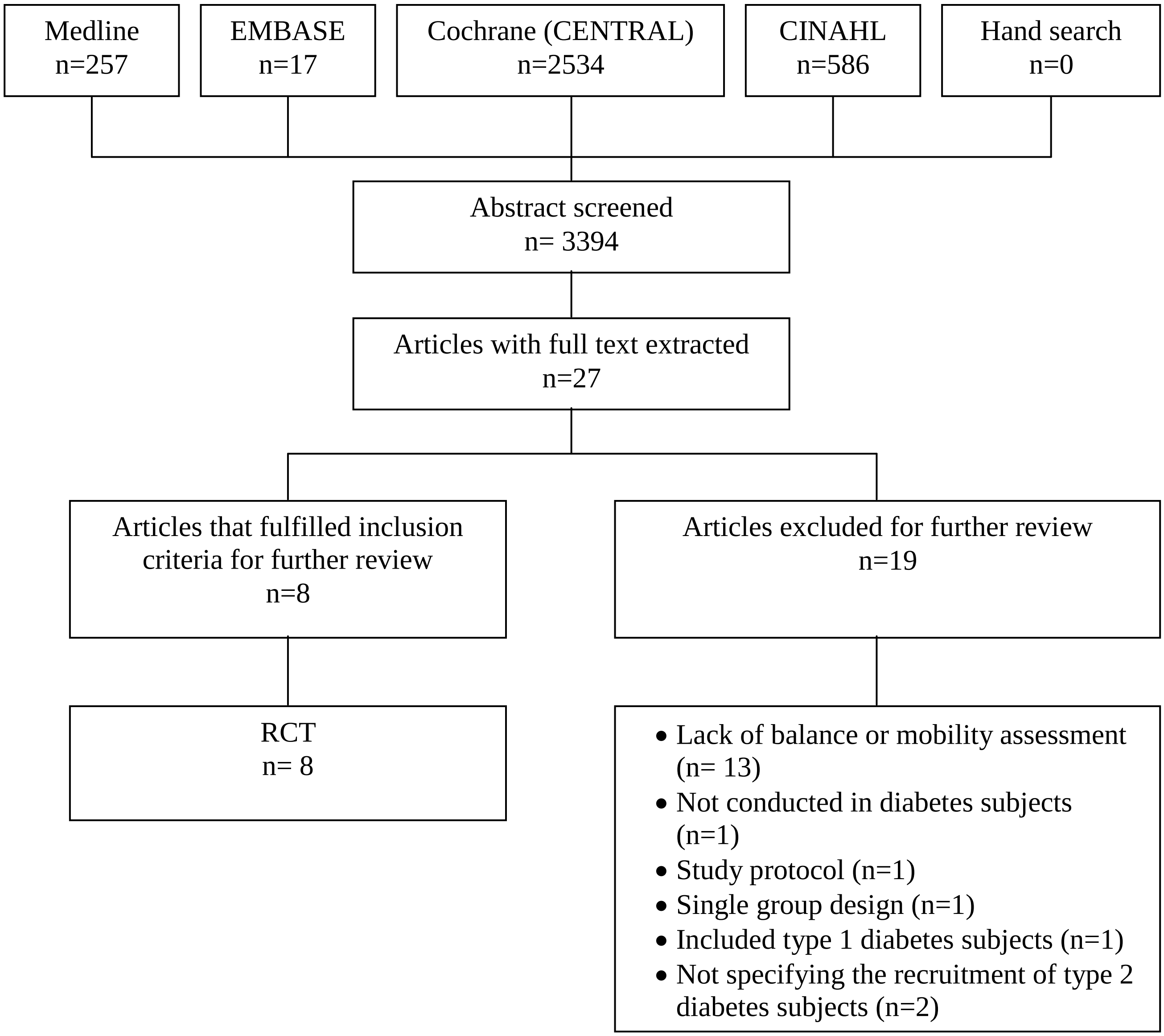


Figure 6.1 Flow chat of the search result

After extracting the full text of the articles, 19 articles were excluded due to the absence of objective balance or mobility assessment (n=13) (Agurs-Collins, Kumanyika, Ten Have, & Adams-Campbell, 1997; Araiza, Hewes, Gashetewa, Vella, & Burge, 2006; Collins et al., 2011; Davies et al., 2008; Dutton, Provost, Tan, & Smith, 2008; Dutton et al., 2009; Kim, Hwang, & Yoo, 2004; Kim & Kang, 2006; King et al., 2006; Larose et al., 2010; Praet et al., 2008; Schneider et al., 2011; Weinstock et al., 2011); did not specify the recruitment of type 2 diabetes patients (n=2) (Brandon et al., 2003; Richardson, Sandman, & Vela, 2001); recruitment of type 1 diabetes patient (Kruse, Lemaster, & Madsen, 2010); recruitment of non-diabetic patients (n=1) (Levinger, Goodman, Hare, Jerums, & Selig, 2007); absence of control group (n=1) (Morrison, Colberg, Mariano, Parson, & Vinik, 2010); and 1 of them was only a study protocol (Vadstrup, Frolic, Perrild, Borg, & Roder, 2009). A total of 8 articles were included for further review. The summary of the data extraction is shown in Appendix II.

6.3.1 QAULITY ASSESSMENT

Cochrane risk of bias tool was used to assess the risk of bias in each article, the summary of the assessment is shown in Table 6.1. The randomizations of the subjects were done properly except the one done by Orr et al. (2006), in which the randomization process was not clearly mentioned. The concealments of allocation were done properly in 4 studies (Allet et al., 2010a; Allet et al., 2010b; Lam, Dennis, Diamond, & Zwar, 2008; Tsang, Orr, Lam, Comino, & Singh, 2007), the remaining studies were not able to be judged due to lack of sufficient information (Lambers, van Laethem, van Acker, & Calders, 2008; Negri et al., 2010; Orr et al., 2006; Ozdirenc, Kocak, & Guntekin, 2004).

Blinding of the participants, including the assessors and the subjects were not satisfactory, the authors either admitted that they could not completely blind the subjects and assessors due to the nature of the study or the limited manpower (Allet et al., 2010a,b; Tsang et al., 2007), some did not state the details of the blinding (Negri et al., 2010; Orr et al., 2006; Ozdirenc et al., 2004). Drop out subjects was reported in all the 8 articles and several methods in handling the missing data were used. Allet et al. (2010a,b) handled the incomplete data by putting the "last observation carried forward" (Allet et al., 2010a,b), which is a less bias method in handling incomplete data, but it was performed based on the assumption that the exercise was beneficial to the subjects, therefore the risk of bias was not able to be identified. The rest of the studies either did not state clearly the drop out or the statistical method in handling incomplete data (Lam et al., 2008; Negri et al., 2010; Orr et al., 2006; Ozdirenc et al., 2004), or the as-treated analysis was probably used by analyzing the tables in the full texts, in which the authors analyzed the subjects who had completed the whole study and the result might not be able to reflect the true effect of the treatment (Lambers et al., 2008). There were 7 out of the 8 articles reported the outcomes clearly without selective reporting except one did a second analysis which was not mentioned in the methodology. In the analysis, those subjects who had high attendance to the exercise class were included for data analysis and the authors chose to report the result of this analysis (Negri et al., 2010). The details of risk of bias in each domain are shown in Appendix III.

Table 6.1

The summary of the risk of bias in the included studies

	Adequate sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessors	Incomplete data addressed	Selective reporting	Other bias
Allet et al. (2010a)	Low risk	Low risk	High risk	High risk	Unclear risk	Low risk	
Allet et al. (2010b)	Low risk	Low risk	High risk	High risk	Unclear risk	Low risk	
Lam et al. (2008)	Low risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk
Lambers et al. [36]	Low risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Unclear risk
Negri et al. (2010)	Low risk	Unclear risk	Unclear risk	Unclear risk	High risk	High risk	Unclear risk
Orr et al. (2006)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk	Low risk	Unclear risk
Ozdirenc et al. (2004)	Low risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk
Tsang et al. (2007)	Low risk	Low risk	Low risk	High risk	Unclear risk	Low risk	

6.3.2 STUDY POPULATION

In the 8 included studies, there were a total of 426 subjects recruited with 233 subjects in the intervention group and 193 subjects in the control group. The subject number varied from 35 to 71. We included studies with type 2 diabetes in all age group and the subjects in each included study were between 52 to 66 years old. There was no limitation in the duration of diabetes in the current review. However, one study recruited subjects with a duration of diabetes for more than 6 months (Lam et al., 2008) , while the other study recruited subjects with a history of diabetes more than 2 years (Negri et al., 2010). Two of the included studies specifically recruited type 2 diabetes subjects with peripheral neuropathy and this was assessed by vibration perception threshold using a tuning fork (Allet et al., 2010a,b). Most studies recruited subjects from outpatient clinic of hospitals (Allet et al., 2010a,b; Lambers et al., 2008; Negri et al., 2010); but two studies recruited subjects from the community (Lam et al., 2008; Tsang et al., 2007); one study recruited subjects in in-patient setting and investigated the acute effect of exercise on functional capacity for people with diabetes (Ozdirenc et al., 2004). One of the included studies did not mention how and where the subjects were recruited (Orr et al., 2006).

6.3.3 EXERCISE PROGRAM

Various studies have adopted different types of exercise. Some studies performed balance and gait training program with a focus on improving mobility and balance of the subjects (Allet et al., 2010a,b); a study delivered an endurance or combined endurance and strengthening exercise program (Lambers et al., 2008); other studies were conducted on evaluating effectivessnes of walking exercise under supervision (Negri et al., 2010); cardiovascular and theraband exercise (Ozdirenc et al., 2004); or Tai Chi exercise (Lam et al., 2008; Orr et al., 2006; Tsang et al., 2007). The authors tried to compare the effectiveness of exercise with no treatment (Allet et al., 2010a,b; Lam et al., 2008; Negri et al., 2010; Ozdirenc et al., 2004); sham exercise (Orr et al., 2006; Tsang et al., 2007). One of the studies compared the effectiveness of combined endurance and strengthening exercise with strengthening exercise alone and control group (Lambers et al., 2008). Despite that most exercise programs were delivered in out-patient setting or community setting, one study was done in in-patient setting to investigate the acute effect of the exercise for people with diabetes (Ozdirenc et al., 2004). The exercise duration for various studies ranged between 45 minutes to 60 minutes, the exercise frequencies were mainly twice to three times a week, lasted from 3 weeks to 12 weeks except for the study done by Ozdirenc et al. (2004). Ozdirenc et al. (2004) delivered daily exercise for five times a week in in-patient. Among all included studies, only Allet et al. (2010a, b) reassessed the subjects at the 6-month follow-up after the completion of a 12-week program.

6.3.4 DROPOUT AND COMPLIANCE OF THE STUDIES

Dropout from the study was defined as the number of randomized participants who did not attend the post intervention assessment. There were 7 of the 8 included studies reported the dropout rate and the range was between 5.26% (Tsang et al., 2007) to 18.9% (Lam et al., 2008). None of the included studies reported 100% attendance and two studies did not report the dropout rate (Orr et al., 2006; Ozdirenc et al., 2004).

6.3.5 EFFECTIVENESS OF EXERCISE IN BALANCE AND MOBILITY PERFORMANCE

6.3.5.1 BALANCE

The balance assessments included walking on a 5-meter beam as quickly as possible, Biodex balance system (Allet et al., 2010b) in which, the subject was required to stand barefoot on a platform that was locked in a fixed position. During the test, the platform was unlocked and the subject was required to find a position at which he or she could maintain platform stability. The index was calculated using the time and deviation (in degrees) of the platform against the original position. Besides, Chattecx balance platform was used to generate a balance index in which, the subject was required to stand on a platform and underwent six tests with eyes closed or opened, the index was generated as a summary score by summating all anterior-posterior, medio-lateral sway measures (Orr et al., 2006; Tsang et al., 2007); single leg stance test with eyes opened and eyes closed

(Orr et al., 2006; Tsang et al., 2007), tandem walk score, which was the time to complete 3-meter tandem walk plus the number of error made (Orr et al., 2006; Tsang et al., 2007).

Table 6.2 shows the summary of the outcomes in balance assessment. To summarize, after exercise training, Allet et al. (2010b) found that the intervention group showed a 31% improvement in walking performance as reviewed by the biodex balance system, in contrast to the decline of performance observed in the control group (Allet et al., 2010b). Besides, Tsang et al. (2007) and Orr et al. (2006) did not find significant group difference in the balance index as assessed by the Chattecx balance platform between the “Tai Chi for Diabetes” group and the control group (Orr et al., 2006; Tsang et al., 2007). For single leg stance test, trends of improvement were noted in exercise groups in eye closed or eyes opened conditions but the difference between the exercise group and control group did not reach significance (Orr et al., 2006; Tsang et al., 2007). The time used to walk on 5-meter beam as fast as possible was significantly reduced in the intervention group as reported by Allet et al. (2010b) while Orr et al. (2006) found no significant change in the 3-meter tandem walk score and both Tai Chi and control group showed trend of improvement (Allet et al., 2010b; Orr et al., 2006). Table 6.2 shows the summary of the outcomes in balance assessment.

Table 6.2
Summary of balance performance for people with diabetes participated in previous studies

	Allet et al. (2010b)	Orr et al. (2006)	Tsang et al. (2007)
Dynamic balance test: walk as fast as possible on a 5-meter beam(second)	Intervention: improved from 9.78 ± 5.58 to 7.10 ± 3.55, then to 7.08 ± 3.61 at the follow-up C: deteriorated from 8.35 ± 3.89 to 9.32 ± 5.19, then to 9.32 ± 4.05 at the follow- up (significant group effect in post-intervention and at the follow-up)		
Biodex Balance system level 6 and 8 (sway index)	Level 6 Intervention : improved from 5.97 ± 2.59 to 3.74 ± 1.12 then to 4.74 ± 1.51 in the follow-up Control: changed from 6.00 ± 2.79 to 5.99 ± 2.76 then to 6.42 ± 2.83 in follow-up Level 8 Intervention: improved from 4.29 ± 2.18 to 2.94 ± 1.06 then to 3.31 ± 1.02 in follow-up Control: changed from 4.58 ± 2.02 to 4.72 ± 1.94 then to 4.77 ± 1.93 in follow-up (significant group effect in post-intervention but not in follow-up)		
Balance index-Chattecx balance platform		Intervention: improved from 111.1 ± 23.1 to 107.3 ± 23.1 Control: improved from 111.5 ± 22.2 to 104.1 ± 22.2 (significant changes were made over time but not for group effect)	Intervention: improved from 111.1 ± 23.1 to 107.3 ± 23.1 Control: improved from 111.5 ± 22.2 to 104.1 ± 22.2 (significant changes were made over time, but not for group effect)
Unilateral stance, eyes open (second)		Intervention: median improved from 8.96 to 17.9 Control: median deteriorated from 30 to 24.2	Intervention: improved from 13.6 ± 13.1 to 16.9 ± 13.2 Control changed from 19.4 ± 12.7 to 19.4 ± 12.1

		(no significant time and group effect)	(no significant time and group effect)
Unilateral stance, eyes closed (second)		Intervention: changed from 3.9 to 2.8 Control: changed from 2.2 to 2.0 (no significant time and group effect)	Intervention: median decreased from 3.9 to 2.8 Control: median decreased from 2.2 to 2.0 (no significant time and group effect)
Tandem walk score (time to complete 3-meter tandem walk plus number of error made)		Intervention: improved from 19.1 $\pm$ 7.0 to 18.1 $\pm$ 8.3 Control: improved from 18.5 $\pm$ 6.3 to 17.2 $\pm$ 6.2 (no significant time and group effect)	Intervention: improved from 19.1 $\pm$ 7.0 to 18.1 $\pm$ 8.3 Control: improved from 18.5 $\pm$ 6.3 to 17.2 $\pm$ 6.2 (no significant time and group effect)

6.3.5.2 MOBILITY PERFORMANCE

Mobility performance was assessed by using the 6-minute walk test (Lambers et al., 2008; Negri et al., 2010; Orr et al., 2006; Ozdirenc et al., 2004; Tsang et al., 2007), gait speed (Allet et al., 2010a,b; Orr et al., 2006; Tsang et al., 2007), functional sit to stand test (Lambers et al., 2008) or 6-meter walk test (Lam et al., 2008). Negri et al. (2010) reported significant improvement in the 6-minute walk test, in which the intervention group showed improvement in supervised walking from 521 $\pm$ 37.2 meters to 612 $\pm$ 78.8meters ($p<0.001$). Although the control group also showed significant within-group changes in the performance over time, the change observed in the intervention group was significantly higher than did the control group (Negri et al., 2010). Lambers et al. (2008) found that combined endurance and muscle strengthening exercise produced better improvement in the 6-minute walk distance than endurance training alone, and similar finding was also found in the 30-second functional sit to stand test in the same study (Lambers et al., 2008). Ozdirenc et al. (2004) found that cardiovascular training together with theraband exercise in in-patient setting resulted in significantly greater improvement in the 6-minute walk test as compared with control (83.4 meters versus 46.5 meters, $p<0.05$) (Ozdirenc et al., 2004). However, Orr et al. (2006) and Tsang et al. (2007) both found that Tai Chi did not produce significant improvement in the 6-minute walk test and gait speed as compared with the sham exercise group whom performed exercise which was not related to the improvement on mobility performance such as seated callisthenics and stretching exercise (Orr et al., 2006; Tsang et al., 2007). The study performed by Allet et al. (2010b) found that balance and gait training produced significant improvement in habitual gait speed in tarred pathway as compared with the control while another study conducted by the same team showed that the habitual gait speed in tarred pathway and cobblestones pathway improved after intervention (Allet et al., 2010a).

In the study performed by Lam et al. (2008), the "6 meters walk test" was used to assess the mobility performance in elderly with type 2 diabetes after practising Tai Chi for 3 months. The author found no significant change in the Tai Chi group over time. However, the control group used longer time to complete the 6-meter walk test after the 3month study period as compared with the Tai Chi group, in which the walking performance was maintained after the Tai Chi training (Lam et al., 2008). Table 6.3 and 6.4 show the summary of the outcome measures in mobility performance adopted by previous studies.

Table 6.3

Summary of mobility performance reported by previous studies

	Allet et al. (2010b)	Allet et al. (2010a)	Lam et al. (2008)	Lambers et al. (2008)
Habitual gait speed on tarred terrain (meter per second)	Intervention: improved from 1.21 ± 0.17 to 1.36 ± 0.19, then to 1.31 ± 0.18 at the follow-up Control: changed from 1.26 ± 0.18 to 1.24 ± 0.19 then to 1.24 ± 0.15 at the follow- up (significant group effect in post-intervention and at the follow-up)	Intervention: improved from 1.22 ± 0.17 to 1.36 ± 0.19 and to 1.31 ± 0.18 at follow-up Control: from 1.26 ± 0.18 to 1.24 ± 0.19 on and to 1.24 ± 0.15 at follow-up (significant group effect in post-intervention and at follow-up)		
Habitual gait speed on cobblestone pathway (meter per second)		Intervention: improved from1.05 ± 0.21 to 1.22 ± 0.23 then to 1.19 ± 0.23 at follow-up Control: from 1.10 ± 0.21 to 1.08 ± 0.21 and to 1.09 ± 0.21 at follow-up (significant group effect in post-intervention and at the follow-up)		
6 meters walk test (second)			Intervention: changed from 5.1± 0.7 to 5.7 ± 1.6 (p=0.34) Control: changed from 5.2 ± 1.1 to 10.7 ± 25.5 (p-value: unknown)	

6-minute walk test (meter)	Combined exercise: improved from 539.8 $\pm$ 61.26 to 594.2 $\pm$ 60.25 Endurance exercise: improved from 538.1 $\pm$ 76.32 to 583.4 $\pm$ 61.48 Control: deteriorated from 528.9 $\pm$ 88.36 to 521.3 $\pm$ 86.27 Significant group-time interaction were found between combined exercise group and control, and between endurance exercise group and control
Functional sit-to-stand test (number per 30 seconds)	Combined exercise: improved from 14.2 $\pm$ 2.59 to 16.8 $\pm$ 2.30 Endurance exercise: improved from 13.4 $\pm$ 2.73 to 15.3 $\pm$ 4.41 Control: decreased from 13.1 $\pm$ 2.17 to 12.8 $\pm$ 1.72 Significant group-time interaction was found between combined exercise group and control group

Table 6.4

Summary of mobility performance reported by previous studies (continue)

	Negri et al. (2010)	Orr et al. (2006)	Ozdirenc et al. (2004)	Tsang et al. (2007)
6-minute walk test (meter)	Intervention: improved from 521 ± 37.2 to 612 ± 78.8 Control: improved from 554 ± 49.2 to 574 ± 60.8 The change in intervention was significantly higher than that in control group	Intervention: changed from 474.0 ± 76.1 to 481.8 ± 83.0 Control: changed from 456.6 ± 117.8 to 470.1 ± 118.2 Significant time effect was found	Intervention: improved from 455.2 ± 76.6 to 537.6 ± 61.6 Control: improved from 454 ± 45.1 to 511.5 ± 42.8 significant between-group difference was noted after the intervention)	Intervention: improved from 474.0 ± 76.1 to 481.8 ± 83.0; Control: improved from 456.6 ± 117.8 to 470.1 ± 118.2 Significant time effect was found
Habitual gait speed in non-specific environment (meter per second)		Intervention: improved from 1.0 ± 0.2 to 1.1 ± 0.2 Control: improved from 1.1 ± 0.2 to 1.2 ± 0.3 Significant time effect was found		Intervention: median improved from 1.0 to 1.2 Control: median improved from 1.1 to 1.2 Significant time effect was found
Maximal gait speed in non-specific environment (meter per second)		Intervention: improved from 1.6 ± 0.3 to 1.7 ± 0.3 Control: improved from 1.6 ± 0.3 to 1.7 ± 0.3 Significant time effect was found		Intervention: improved from 1.6 ± 0.3 to 1.7 ± 0.3 Control: improved from 1.6 ± 0.3 to 1.7 ± 0.3 Significant time effect was found

6.3.5.3 ADVERSE EFFECT

Several adverse effects of exercise training were reported in these studies including hypoglycemia (n=9) (Lambers et al., 2008; Negri et al., 2010); pain over the ankles and foot (n=4) (Allet et al., 2010a,b); Tsang et al. (2007) reported one subject in intervention group complained of pain and fatigue after the exercise but no further detail was provided.

6.4 DISCUSSION

The current review included 8 randomized controlled trials that evaluated the effectiveness of exercise on mobility and balance performance in people with type 2 diabetes. All of the included studies showed certain degree of improvement in mobility and balance performance, although some of them did not reach statistical significance. Although one of the inclusion criteria in the present review was the adoption of objective assessment on either balance or mobility performance, this was not be the main objective of 5 out of 8 included studies. These 5 studies mainly evaluated the effect of exercise on the functional capacity or physical performance of people with type 2 diabetes (Allet et al., 2010a; Lam et al., 2008; Lambers et al., 2008; Negri et al., 2010; Ozdirenc et al., 2004). Therefore, the exercise programs adopted in these studies might not be effective in enhancing balance or mobility performance. Also, these studies adopted various types of exercises. Therefore, combining the findings in these studies using a pooled analysis seems inappropriate.

The diagnosis of type 2 diabetes in these studies was confirmed by blood test, either adopting the criteria of HbA1c $\geq$ 6.5% or fasting blood glucose test > 7mmol^{-1}. There was no restriction of age of subjects in the present review but majority of the included studies only recruited subjects who were equal to or younger than 50 years old because aging is a known factor contributing to the deterioration of mobility.

Most of the exercise programs were delivered in either an out-patient or community setting, only one study investigated the acute effect of exercise in in-patient setting, in which the subjects underwent an intensive exercise five times a week and the result was promising as compared with control (Lambers et al., 2008). Although the mean length of hospital stay was around 12 days, the frequency of exercise was more intense as compared with that in other exercise programs included in the present review. This suggested that the frequency of exercise is an essential factor that determiness the rehabilitation outcome, therefore the practice of exercise at home should be emphasized. However, only two studies recommended subjects to continue the practice of home exercise that they learned in the program, and they reported that the home exercise compliance was not recorded. Therefore, the effect of home exercise was unclear (Allet et al., 2010a,b). As exercising at home allows a more flexible schedule, and subjects can perform exercise in a more familiar environment, future study can investigate the effect of home exercise or combine home exercise and center-based exercise in this group of population. It would be important to include the compliance of home exercise in the study as it may bring significant impact on the performance of subjects in the post-intervention assessment. If the exercise compliance is poor, it may reflect the acceptance of the exercise program for the subjects. Also, the long term effect of exercise after the study period was not provided by these studies. Only 2 out of 8 included articles provided a follow-up period, and they showed a significant long term effect that outlasted the exercise program (Allet et al., 2010a,b).

The included studies reported that exercise training was safe for people with diabetes without any serious complications brought by the exercise in class. Common complications reported are hypoglycemia (more than 60%) (Lambers et al., 2008; Negri et al., 2010), or pain over the ankle including Achilles tendon; and muscle fatigue. The studies that reported subjects having hypoglycemia were aerobic in nature, which was not uncommon to see this occur during aerobic exercise. Therefore, researchers should pay more attention in this issue in future study. Subjects should be advised to eat something before the start of the exercise; the starting time of the exercise program would be crucial as the blood glucose varies in between meals. Ideally, taking the blood glucose level before the start of each exercise session provides most updated information about the glucose level and the risk of hypoglycemia would then be minimized. For other complications reported, the cause was not mentioned and it is unclear whether it was due the past medical history of the patients or new injury that was induced during the exercise program. The drop out rates in the included studies was high that varied from 5.26% to 18.9%. The reasons for attrition varied and no obvious trend was observed. The drop out number can be used in calculating sample size for future study.

The major information on the methodology quality was not provided in many studies even though most of them were claimed to be RCTs. Among the 8 included studies, half of them did not mention the blinding the participants (Lam et al., 2008; Negri et al., 2010; Orr et al., 2006; Ozdirenc et al., 2004); and 3 of them did not mention the blinding of assessors (Negri et al., 2010; Orr et al., 2006; Ozdirenc et al., 2004). Unlike research on drug effects, participants in the study of exercise are not easily blinded. Because participants in the exercise group are aware of what intervention they received. The expectation of the participants may become a bias of the outcomes. Therefore, we suggest that sham exercise group should be implemented to eliminate the bias such as stretching exercise of the upper limbs or exercise that does not involve lower limbs. Blinding of the assessors was another factor that may cause high risk of bias in these studies. Two of the studies used assessors who were working in the center where the subjects received the exercise and this would cause high risk of bias during the post-intervention assessment (Allet et al., 2010a,b). While in another study, the investigator was the one who led the exercise in the intervention group and the sham group (Tsang et al., 2007). These would cause high risk of bias during the post-intervention assessment. The results may tend to flavor the intervention group.

Mobility and balance deterioration are common problems found in elderly due to a decline in the sensory and musculoskeletal systems, but it was shown that elderly with type 2 diabetes showed higher risk of fall than healthy age-matched control (Tilling et al., 2006). Therefore, there must be some specific problems found in people with diabetes which contribute the increase in risk of fall and deteriorated mobility and the exercise should be specific also. However, the exercises adopted in the 8 included studies were not designed to suit this group of population. They adopted exercise programs that showed success in normal elderly population (Allet et al., 2010a,b), or exercise programs that appear to be non-specific to people with diabetes (Lambers et al., 2008; Negri et al., 2010; Ozdirenc et al., 2004). Three studies implemented ‘Tai Chi for diabetes’ without clarifying the specific component on the exercise (Lam et al., 2008; Orr et al., 2006; Tsang et al., 2007). Previous studies found that diabetes people have a decrease in ankle muscle strength, ankle proprioception sense and an increase in the stiffness of the ankle joint in dorsiflexion as compared with healthy control. These factors are supposed to be related to the decline in mobility in this client group. Therefore, in order to produce significant benefits on mobility performance, exercise training must be tailored made to the disease group.

6.5 LIMITATION

Like other systematic review, this review is limited by the quality of the studies that included as reflected by high risk of bias in different aspects as shown in Table 6.1. Another potential limitation of the present review was the selection bias by the journal articles, as studies that showed positive results tend to be easier be get accepted by editors while those showing negative effects were less likely to be accepted. Therefore, the actually positive effect of the exercise would be over-estimated. Besides, the reporting of exercise compliance was not fully provided by all included studies and the method in handling to missing data (ie intention-to-treat analysis) was not being mentioned in several studies. Readers should pay attention as it affect the actual effect of the program.

6.6 CONCLUSIONS

To conclude, few studies on exercise have been adopted that aimed at improving the balance and mobility status in elderly with type 2 diabetes. After reviewing the included articles, exercise generally showed positive effect on the mobility performance in this patient group. Only mild adverse responses to the exercise were reported. Due to the wide spectrum of exercise included in present study, a meta-analysis was not performed to give a conclusion on the effect of exercise in enhancing the mobility and balance performance in people with type 2 diabetes. Further study with better quality is necessary to provide a more concrete conclusion.

Based on the findings in chapter 5 and the lack of a specific exercise program to enhance the balance and mobility performance in people with type 2 diabetes as shown in present chapter, an exercise program with specific content was designed in order to improve the balance and mobility performance in elderly with type 2 diabetes. The details will be shown in the next chapter.

CHAPTER 7

EFFECTIVENESS OF EXERCISE PROGRAM WITH SPECIFIC REGIMEN ON IMPROVING POSTURAL CONTROL AND MOBILITY PERFORMANCE IN ELDERLY WITH TYPE 2 DIABETES

7.1 INTRODUCTION

People with diabetes often present with a decrease in postural control and mobility performance (Morrison, Colberg, Parson, & Vinik, 2012), which may contribute to subsequent complications (Schwartz et al., 2002; Tilling et al., 2006). People with diabetes were found to have reduced ankle muscle strength, ankle proprioception sense and greater stiffness of the ankle joint in dorsiflexion (Andersen et al., 2004; Giacomozzi et al., 2008; van Deursen & Simoneau, 1999). In chapter 5, we showed that these physical characteristics of the ankle are significantly correlated with mobility performance in elderly people with diabetes as measured by the Timed Up and Go test (TUG) (Ng & Cheing, 2011). It is therefore logical to deduce that specific exercise regimen focusing on ankle strength and flexibility training; and substituting the deteriorated ankle proprioception might improve postural control and mobility performance in this client group.

Previous studies have shown that exercise training improves glycemic control and general fitness in people with diabetes (Maiorana, O'Driscoll, Goodman, Taylor, & Green, 2002; Tessier et al., 2000). However, limited studies have investigated the effects of exercise on balance control and mobility performance in elderly with type 2 diabetes; and in chapter 6, we know that those studies demonstrated that exercise only produced modest improvement or their findings were non-conclusive due to poor study design. In addition, the exercise protocols implemented in previous studies were not specific to our target population. Therefore, it is necessary to design a new study with specific exercise content.

Beside center-based training, home exercise has been demonstrated to be effective in improving the mobility performance of community-dwelling and frail elderly people (Matsuda, Shumway-Cook, & Ciol, 2010; Miller, Magel, & Hayes, 2010). However no such study has been conducted in people with diabetes. Therefore, the objective of the present study was to evaluate the effect of a specially designed exercise program, which focused on the ankle characteristics that would affect the mobility performanace as found in Chapter 5 (ie the deteriorated ankle muscle strength, range of motion in dorsiflexion and deficit in joint proprioceotion), would improve postural control and mobility performance for people with type 2 diabetes.

7.2 METHOD

7.2.1 SUBJECTS

This was a prospective non-randomized controlled trial. Subjects were recruited from four local community centers. Inclusion criteria were people aged 65 or above, with a diagnosis of type 2 diabetes confirmed by blood test with HbA1c $\geq$ 6.5%. They were self ambulatory without walking aids, and cognitively competent in understanding instructions. Exclusion criteria included the presence of visual impairments such as retinopathy assessed by Snellen chart, a recent foot lesion or surgery, a history of neurological disorders, or unstable hypertension by self-reporting. The flow diagram of study enrollment and participation is shown in Fig. 7.1

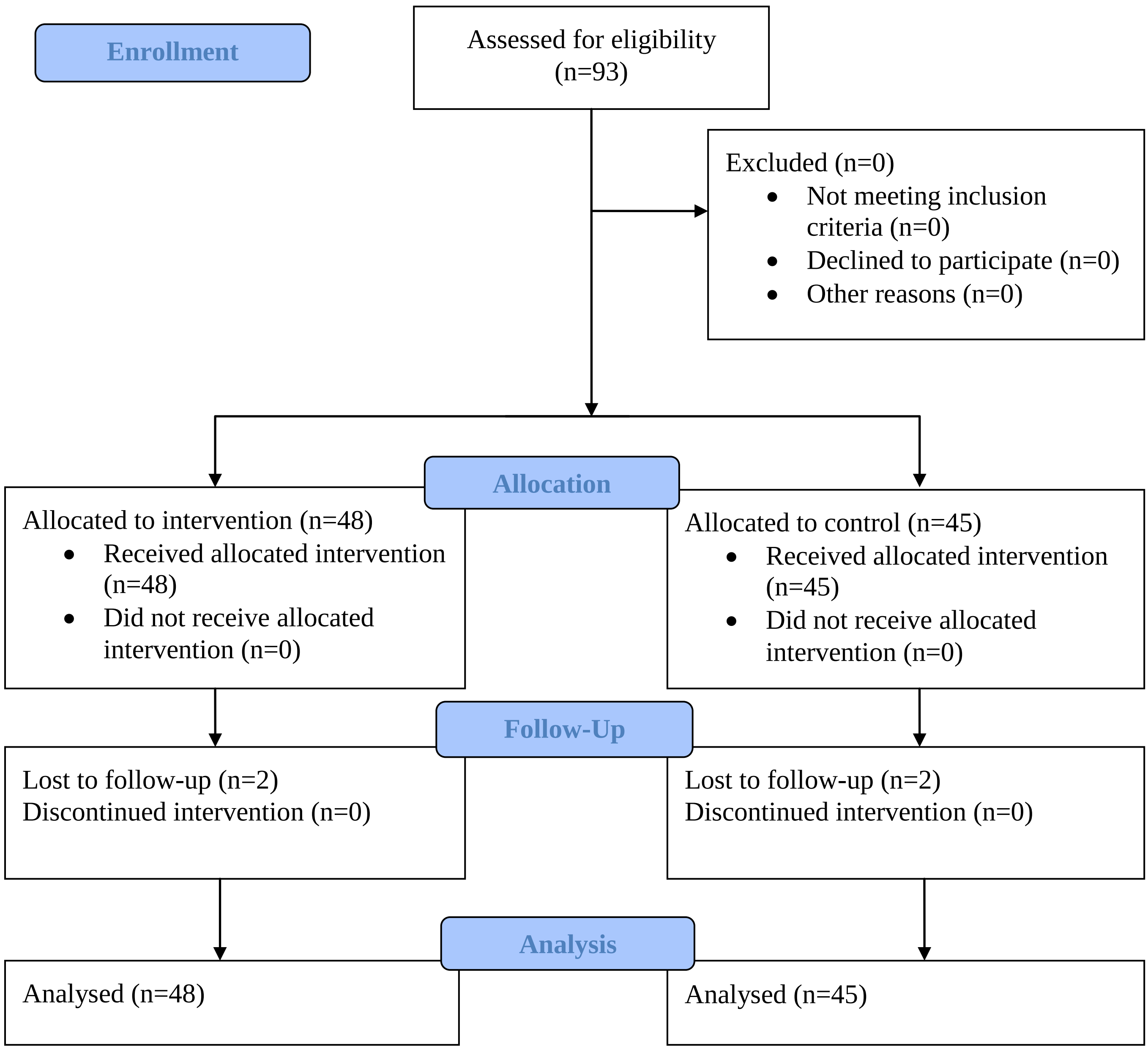


Figure 7.1

Flow diagram of study enrollment and participation.

7.2.2 MATERIALS AND EXPERIMENTAL SETUP

7.2.2.1 EXERCISE PROGRAM

The intervention group participated in a 10-week exercise program delivered twice a week in community centers, together with daily home exercise with compliance recorded. The frequency of the center-based exercise program was based of the frequencies adopted in the studies found in last chapter. The subjects in the control group were required to maintain their usual daily activities and not to attend any exercise classes during the 10-week study period. For ethical reason, identical exercise classes together with home exercise program were delivered to the control group after the 10-week study period.

Each exercise session held in the community centre lasted for 60 minutes with therapist/subject ratio around 1:15. The exercise program was designed by registered physiotherapists, which targeted at improving physical characteristics of the ankle joint. First, strengthening exercise of the ankle dorsiflexors and plantarflexors muscles using an elastic theraband band was performed (Theraband, Hygenic Corporation, Akron, OH, USA) (Ribeiro, Teixeira, Brochado, & Oliveira, 2009). During the theraband exercise, the subjects were encouraged to adjust the tension of the band based on their own physical condition and abilities; and exercises were modified according to the progress of each subject. Second, intensive stretching exercise was performed to improve the range of ankle dorsiflexion (Christiansen, 2008). Third, subjects learned to adopt compensation strategies for the deficit in ankle proprioception by enhancing the use of visual and vestibular inputs for postural control. This was achieved by using an ankle disc (Theraband, Hygenic Corporation, Akron, OH, USA). It is a 13-inch latex-free polyvinyl chloride disc that is inflated by air. The subjects were required to stand on the ankle disc using either both legs or one leg. While performing ankle movements alone or in combination with the movement of their upper limbs to challenge their balance, the subjects held on to stable furniture to prevent themselves from falling. Fourthly, a 15-minute rhythmic exercise was performed in each exercise class in which the subjects were instructed to follow music and performed rhythmic movements such as walking backwards, sideways, turning and lunging in different directions.

Daily home exercise program was emphasized in the intervention group. Elastic therabands with resistance levels based on their physical ability and an exercise pamphlet were distributed to each subject. The exercise pamphlet illustrated the exercise protocol clearly by means of photographs and written instructions. Home exercises were also practiced during exercise class and individual feedback was given to the subjects before they practiced at home. A home exercise diary was enclosed in the exercise pamphlet for subjects to record their attempts of home exercise.

7.2.2.2 OUTCOME MEASURES

Demographic data was collected at the baseline including age, duration of diabetes, Glycated haemoglobin (HbA1c) and Body Mass Index (BMI). The primary outcome measure was SOT while TUG and SLST were secondary outcome measures.

7.2.2.2.1 SENSORY ORGANIZATION TEST

In order to assess the ability to use visual, vestibular, and somatosensory information to maintain postural stability, Sensory Organization Test (SOT) using a computerized posturography machine (Smart EquiTest$^{@}$, NeuroCom International Inc, Clackamas, OR, USA) was performed. This device is comprised of a platform and a visual surround, both of which can be sway-referenced. SOT has been shown to have good test-retest reliability among community-dwelling elderly people (Ford-Smith et al., 1995). The details of the test and the interpretation of the result can be found in chapter 3 (section 3.5).

7.2.2.2.2 TIMED UP AND GO TEST

Timed Up and Go test (TUG) was performed by requesting the subject to sit on a chair with his/her back against the back rest and arms placed on the arm rest, then stood up, walked for 3 meters, turned around a marker made on the floor, walking back and sitting on the chair again with the back leaned against the back rest. The details can be referred to chapter 3 (section 3.6). TUG was shown to be a sensitive measurement for detecting changes in mobility in the elderly with high inter-rater and intra-rater reliability (Steffen et al., 2002; van Iersel, Munneke, Esselink, Benraad, & Olde Rikkert, 2008).

7.2.2.2.3 SINGLE LEG STANCE TEST

Single leg stance test (SLST) was performed by asking the subjects to stand in an upright position with their arms put along their sides. The timer was started once the non-tested leg was lifted up and stopped once the foot of the lifted leg touched the floor; the stance foot was displaced; or the subject used the lifted foot to support the stance leg (Hurvitz et al., 2000). Further details can be referred to chapter 3 (section 3.7). The present study did not find a significant difference in SLST between the left and the right legs; therefore, the average time (in seconds) obtained in the two legs was calculated for subsequent analysis.

7.2.3 STATISTICAL ANALYSIS

SPSS® V17.0 (Chicago, IL, USA) was used for the statistical analysis. Independent t-test and chi-sq test were used to analyze the difference in demographic characteristics between the intervention and control groups. Two-way repeated measures analysis of covariance (ANCOVA) was used to analyze the group x time interaction after the 10-week study period. Pair t-test and independent t-test used after the ANCOVA analysis in order to investigate the within-group difference in each group at two time points and between-group difference at the same time point respectively. ANCOVA was used since there was significant between-group difference in HbA1c, it was entered as a covariate in. The level of significance was set at 0.05. Intention-to-treat analysis with the last observation carried forward (LOCF) was used for subjects who did not attend the post-assessment session (Portney & Watkins, 2000).

7.3 RESULTS

7.3.1 DEMOGRAPHIC DATA

Ninety-three subjects were recruited (control *n*= 45, mean age 72.8 years old; intervention *n*= 48, mean age 71.4 years old) from four community elderly centers. The mean duration of diabetes history was 10 years and subjects in both groups were obese according to their Body Mass Index (Table 7.1). No significant differences in demographic characteristics were found between the two groups, with the exception of HbA1c. No adverse effects were reported during the center-based exercise and home exercise. None of the subjects in the intervention group withdrew from the program. However, two subjects in the intervention group and two subjects in the control group did not attend the reassessment session after the 10-week exercise program (Figure 7.1). The mean rate of attendance in the center-based exercise was 75.5% while the average home exercise compliance was 53.49%. Some subjects were absent from several center-based exercise classes due to time conflicts with some traditional Chinese festivals or family commitment. For home exercise compliance, some subjects stated that they had forgotten to mark down their exercise compliance in their exercise diaries. Therefore, the actual level of compliance with home exercise should be higher than the reported figure. Therefore, the effect of our exercise training could be increased if the compliance of both center-based and home-based exercise was improved.

Table 7.1

Demographic data for people participating in the present study

Demographic data	Exercise (n=48)	Control (n=45)	*p*-value
Age (year)	71.4 (7.9)	72.8 (6.5)	0.36
Sex (female), n (%)	35 (72.9)	33 (73.3)	0.95
History of diabetes (years)	10.2 (8.7)	10.2 (7.3)	0.99
Glycated haemoglobin (HbA1c) (%)	8.0 (1.2)	6.9 (0.8)	<0.001*
Body mass index (kg/m^2)	27.6 (7.9)	25.4 (4.0)	0.10

All values are presented as mean (SD).

7.3.2 DESCRIPTIVE STATISTIC AND ANCOVA

The results of two-way repeated measures ANCOVA are reported in Table 2. In the analysis, HbA1c was entered as covariate since there was significant difference between 2 groups at the baseline. Significant time x group interactions between intervention group and control group were found in SOT (condition 4, condition 5, composite score, vestibular ratio and visual ratio). Subsequent analyses showed significant within-group improvement in the intervention group in SOT condition 4, 5, 6; composite scores, vestibular and visual ratios while the control group showed no significant difference (Table 2.). For the TUG, the intervention group showed a greater trend of improvement as compared with control group (-0.25 second versus -0.07 second). For the SLST, the intervention group showed a trend of being able to stand for a longer period of time after the exercise training (1.77 second versus -1.38 second)

Table 7.2

Two-way repeated measures ANCOVA, between-group and within-group comparisons

	Exercise group	Control group	Between-group *p*-value
SOT condition 1			
Pretest	91.33(4.93)	92.43(2.60)	0.189
Posttest	92.02(2.29)	91.81(3.01)	0.706
Within-group *p*-value	0.340	0.080	
Overall within-group effect p= 0.470, overall between-group effect p=0.373 *Time x group interaction p= 0.081*			
SOT condition 2			
Pretest	90.13(3.12)	90.05(3.25)	0.911

Posttest	89.75(2.92)	89.83(3.27)	0.907
Within-group *p*-value	0.265	0.641	
Overall within-group effect p=0.913, overall between-group effect p=0.976 *Time x group interaction p= 0.846*			
SOT condition 3			
Pretest	88.65(5.75)	88.97(5.61)	0.786
Posttest	89.24(6.02)	89.46(3.70)	0.836
Within-group *p*-value	0.136	0.523	
Overall within-group effect p=0.548, overall between-group effect p=0.501 *Time x group interaction p= 0.936*			
SOT condition 4			
Pretest	68.76(11.17)	70.73(9.50)	0.372
Posttest	74.47(7.89)	70.86(10.44)	0.065
Within-group *p*-value	<0.001*	0.916	
Overall within-group effect p=0.152, overall between-group effect p=0.811 *Time x group interaction p= 0.002**			
SOT condition 5			
Pretest	47.99(13.12)	59.24(10.17)	<0.001*
Posttest	59.36(11.82)	59.06(9.97)	0.896
Within-group *p*-value	<0.001*	0.899	
*Overall within-group effect p=0.521, overall between-group effect p= 0.009**			

*Time x group interaction p= <0.001**			
SOT condition 6			
Pretest	49.62(14.53)	56.35(11.84)	0.019*
Posttest	55.07(13.40)	57.10(11.42)	0.443
Within-group *p*-value	0.021*	0.652	
Overall within-group effect p= 0.255, overall between-group effect p= 0.071 *Time x group interaction p= 0.455*			
SOT composite score			
Pretest	66.26(12.19)	70.34(12.19)	0.114
Posttest	71.0(12.4)	72.10(5.7)	0.443
Within-group *p*-value	<0.001*	0.875	
*Overall within-group effect p= 0.897, overall between-group effect p=0.040** *Time x group interaction p= 0.005**			
SOT somatosensory ratio			
Pretest	0.99(0.076)	0.97(0.03)	0.207
Posttest	0.98(0.03)	0.98(0.03)	0.614
Within-group *p*-value	0.203	0.442	
Overall within-group effect p=0.542, overall between-group effect p=0.366 *Time x group interaction p= 0.130*			
SOT vestibular ratio			
Pretest	0.53(0.15)	0.64(0.11)	<0.001*
Posttest	0.64(0.13)	0.64(0.11)	0.968
Within-group *p*-value	<0.001*	0.889	

*Overall within-group effect p= 0.608, overall between-group effect p= 0.012** *Time x group interaction p= <0.001**			
SOT visual ratio			
Pretest	0.75(0.12)	0.77(0.10)	0.620
Posttest	0.81(0.08)	0.77(0.11)	0.074
Within-group *p*-value	<0.001*	0.623	
Overall within-group effect p= 0.216, overall between-group effect p= 0.662 *Time x group interaction p= 0.010**			
TUG (seconds)			
Pretest	9.83(3.02)	11.46(3.27)	0.014*
Posttest	9.58(2.95)	11.39(3.31)	0.006*
Within-group *p*-value	0.121	0.663	
*Overall within-group effect p= 0.272, overall between-group effect p= 0.015** *Time x group interaction p= 0.258*			
SLST (seconds)			
Pretest	15.57(14.27)	15.81(13.72)	0.937
Posttest	17.34(16.11)	14.43(13.59)	0.353
Within-group *p*-value	0.240	0.296	
Overall within-group effect p= 0.914, overall between-group effect p= 0.620 *Time x group interaction p= 0.153*			

All values are presented as mean (SD)

*$p \leq 0.05$

SOT: Sensory Organization Test; TUG: Timed Up and Go test; SLST: Single leg stance test

The results of the single leg stance test were obtained by the average value obtained in the left legs and right leg

7.3.3 POWER ANALYSIS

The *post hoc* power analysis was performed by using G*Power. By using the result of SOT composite score, it yielded an effect size ranging from 0.185 to 0.386 and power from 0.143 to 0.664.

7.4 DISCUSSION

The present study examined the effectiveness of a specific exercise program emphasizing on training postural control and mobility performance in older adults with type 2 diabetes. Our exercise program was developed with reference to the findings of a previous study (Ng, Lo, & Cheing, 2012), and we focused on the training of the physical characteristics at the ankle in older adults with type 2. Specifically, our program aimed at training the ankle muscle strength, the ankle flexibility in dorsiflexion; and to enhance the use of vestibular and visual systems in order to compensate the deteriorated ankle proprioception. Our exercise program produced significantly greater improvement in the postural stability than did a control group. The intervention group also demonstrated a trend of improvement in mobility performance in Timed Up and Go test and balance test in single leg standing although the between-group differences was not statistically significant.

It was suggested that balance training should comprised of tasks with varying difficulties in order to challenge the subjects' balance control (Tiedemann, Sherrington, Close, & Lord, 2011). In the present study, we did not adopt an exercise protocol with fixed tasks and intensities. Instead, the level of difficulty of the exercise protocol was increased after several sessions according to the progress made by the subjects. The duration and frequency of the exercise classes were designed based on previous successful balance programs (Cheung, Au, Lam, & Jones, 2008; Kaesler, Mellifont, Swete Kelly, & Taaffe, 2007).

7.4.1 SENSORY ORGANIZATION TEST

Significant (time x group) interactions were noted in conditions 4 and 5 of SOT (i.e. visual ratio and vestibular ratio, details of the calculation of sensory scores can be referred to Chapter 3, section 3.5) and also in the composite score in two-way repeated measures ANCOVA. Pair t-test showed significant within-group improvements were shown in the intervention group in the abovementioned outcomes. The significant improvement in vestibular ratio and visual ratios indicated that our participants had more utilization ratio on the vestibular and visual information to maintain postural stability. This served as a good compensatory strategy that accounts for the improvement in their overall static postural control after the training as shown in the composite score.

The integration of inputs from the visual, vestibular, and somatosensory system is important for maintaining balance. The inability to use correct information that being received from the changing environment may result in fall. This is particularly true for elderly people whose sensory systems have deteriorated due to ageing. It was reported that a decrease in ankle proprioception occur in elderly with diabetes even before they present with any symptom of neuropathy (Liu et al., 2010). Indeed, the risk of fall for diabetic elderly should not be underestimated even if these people do not present any symptom of peripheral neuropathy. What made the situation worse was our subjects showed relatively low sensory ratios in the visual and vestibular systems (Table 7.2) at the baseline measurement, this reflected that the participants relied more on the somatosensory system which might not be providing accurate information before the training. The exercise training for this client group should aim at adopting a compensatory strategy for the decline in ankle proprioception inputs, which can be achieved by enhancing the use of visual and vestibular systems for postural control.

Visual inputs provide useful information on the spatial orientation between our body and the environment, which allow us to detect movements between ourselves and our surroundings. This is particularly true for movements with low frequency such as standing in a room while the surrounding environment is static (Redfern, Yardley, & Bronstein, 2001). In order to facilitate the use of visual inputs, our subjects were trained to use visual fixation while they were standing on the ankle disc and performing movements. Subjects were required to look at a fixed target during the movement, and the ankle disc served as a media that disturb the proprioception over the ankles, therefore, subjects had to rely on the visual information and vestibular information to maintain balance. By requesting the subjects to visually fixate a target, it provides information to distinguish the change in the body orientation and the surroundings. Therefore, it increases their visual attention that prevents falling.

In order to enhance the use of vestibular systems, music was played during our center-based exercise. Subjects were requested to follow the beat of music and perform rhythmic movements by rotating their head or turning their whole body. The subjects were also required to change their base of support during the dynamic movements and to combine the movement of their upper limbs. At the same time, they fixed their vision on their hands to enhance the adaptability of the vestibular system, which is one of the strategies for vestibular rehabilitation (Herdman, 1993). The vestibular system allows one to detect head movements in relation to the gravity and it is the most important sensory system for maintaining balance. The vestibular system provides true afferent information when a person encounters conflicting visual and somatosensory information. As aforementioned, people with diabetes are at risk of reduced ankle proprioception, their vestibular system would be the major afferent inputs that they rely on when they encounter an environment with conflicting visual information or in a dark environment. This explains why elderly people are prone to fall in dark environment (Connell & Wolf, 1997).

The vestibular or visual ratios were computed by comparing the data obtained in two testing conditions (both were compared with condition 1), the contribution from motor systems was eliminated. Therefore, the improvements achieved by our subjects were likely due to the relative change in the emphasis of various sensory systems. For the composite score, the intervention group showed a 7.1% improvement, in contrast, there was almost no change in control group over time. This improvement might be explained by the ankle muscle strengthening and the improvement in the ankle range of motion on top of the enhanced use of visual and vestibular systems. Spink et al. did demonstrate that ankle muscle strength and range of motion were associated with the amplitude of sway during postural control in quiet standing (Spink et al., 2011). Therefore, further study is warranted to examine if the improvement in composite score of the SOT was contributed by the increase in muscle strength and range of motion at the ankle.

7.4.2 TIMED UP AND GO TEST (TUG)

The intervention group showed a greater trend of improvement in TUG than the control group (Table 7.2.). The test itself comprises of three components: sit-to-stand transfer, walking and turning. It was shown that the muscle strength of ankle dorsiflexors and plantarflexors were correlated with the walking speed in elderly (Tiedemann, Sherrington, & Lord, 2005); sufficient push off power by plantarflexors was found to be essential for a quick turning during daily activities (Orendurff et al., 2006); the increase in stiffness of ankle dorsiflexion range of motion not only affect the toe clearance during walking, it would result in poor alignment of the ankle joint during sitting, causing an increase in the travelling distance of center of mass for rising up during the initial phase of TUG (Mueller et al., 1995; Perry et al., 2006).

We found that the intervention group tended to have modest effect in TUG. This could be explained by the fact that the intervention group did well in the baseline assessment and took an average of 9.8 seconds to complete the TUG. Note that the cut-off score of TUG to indicate risk of fall is 12-second (Bischoff et al., 2003). Therefore, the baseline performance of the intervention group was considered to be satisfactory, which might have caused a ceiling effect. The other reason might be due to the compliance of the subjects as aforementioned. Our findings may not be generalized to people with diabetes who have relatively poorer mobility performance. Future study may be needed to examine the effects of exercise training for people with diabetes who have poorer mobility performance.

7.4.3 SINGLE LEG STANCE TEST (SLST)

SLST is another functional test for detecting risk of fall in elderly (Hurvitz et al., 2000). The exercise group showed a trend of improvement (11.5%) in contrast to the deterioration observed in the control group (decreased for 8.9%). This might be explained by the improvement in using visual information achieved by our subjects after the training. Hazime and colleagues found that visual information produced a major effect on single leg standing (Hazime et al., 2012). Moreover, the strength of ankle dosiflexors and plantar flexors were related to the anterior-posterior and medial-lateral sway during single leg standing (Reimer & Wilkstrom, 2010). Previous study reported a wide range of SLST performance (6.9-32.9 seconds) observed among the group of people aged between 70 to 79 years old, but there is no common consensus on the cut-off score (Michikawa, Nishiwaki, Takebayashi, & Toyama, 2009). In the present study, four subjects were unable to attend the post assessment. We carried forward the last observation (i.e. baseline assessment) for these cases over to the post assessment, this was based on the assumption that their performance did not change in the 10-week period. Therefore, the actual effect of exercise might have been underestimated.

7.5. LIMITATION

Convenient sampling method was the limitation of present study. Same was Chapter 5, the subjects recruited in present study were from community centers, who were considered to be relatively active physically. Therefore, we hypothesized that the effect of the present exercise program might be more prominent for those who adopted a more sedentary life-style. But further study is essential to prove this hypothesis. Besides, ehe exercise compliance of the present study might hinder the effect of the program. Therefore, future study should include a measure to ensure a higher compliance.

7.6 CONCLUSION

A 10-week exercise program, incorporated with a home exercise program, focused on ankle training was effective in improving the postural control in elderly with type 2 diabetes. It also produced a trend of improvement in mobility performance and single leg balance. Clinicians should consider this strategy to reduce the risk of falls among elderly people with diabetes.

CHAPTER 8

CONCLUSIONS

The prevalence of diabetes is increasing and it is a global health concern. Since this is a chronic disease associated with many complications, it is essential to take measures to prevent complications. Starting from chapter 4, different studies were done to achieve the purposes. In chapter 4, we examined the reliability of an innovative Ultrasound Foot Scanner System based on a previously validated TUPS to investigate the thickness and stiffness of plantar soft tissue (Zheng & Mak, 1996). The merit of developing the current foot scanner system was to overcome the shortcoming of TUPS as this system can not be used to measure the thickness and stiffness of plantar soft tissue in weight-bearing positions, which implies that TUPS can not be used to predict the risk of developing foot ulceration in people with diabetes. In that chapter, we found that the innovative Ultrasound Foot Scanner System is a reliable tool for measuring the thickness and stiffness in sitting and standing positions. This system is a potential tool for assessing the risk of developing foot ulceration in people with diabetes.

Besides diabetic foot ulceration, a decrease in mobility performance is another common complication found in people with diabetes (Gregg et al., 2000; Orr et al., 2006), especially among elderly. However, there is a lack of research trying to investigate the factors contributing to the decrease in the mobility in this client group. In chapter 5, we found that the mobility performance of the elderly with type 2 diabetes is correlated with age, BMI, peak torque of ankle plantar flexors and dorsoflexors, stiffness of the ankle joint in dorsiflexion and ankle joint proprioception. Besides, multiple regression analysis showed that the demographic characteristics, together with the ankle plantarflexors and dorsiflexors strength, ankle joint proprioception and stiffness in ankle dorsiflexion account for 59.9% of the variance in the performance of TUG. We also found that the ankle joint proprioception sense and the strength of ankle plantarflexors are significant contributors to TUG. The findings of chapter 5 provide a rationale for developing a rehabilitation program which consists of specific regimen to improve the mobility performance in elderly with diabetes.

In chapter 6, a systematic review was done to review the existing literatures about the effect of exercise on balance and mobility performance in people with type 2 diabetes. Although meta-analysis was unable to be carried out, exercise generally showed positive result on mobility and balance performance in this group of population. However, all of the studies included in this review were not specific to this client group.

Since there are very limited research work been done to investigate the effect of exercise on mobility and balance for people with diabetes. There is lack of consent on optimal rehabilitation program to improve the mobility and balance performance in this client group. Therefore, chapter 7 reported a quasi-randomized control trial to investigate the effectiveness of a 10-week exercise program which has specific regimen in enhancing the postural control and mobility performance in elderly with type 2 diabetes. The exercise regimen was based on the results obtained in chapter 5. Our results reflected that this program, incorporated with home exercise was effective in improving the postural control in elderly with type 2 diabetes, a trend of improvement was shown in mobility performance and single leg balance. There were limitations in which chapter in which we suggest that future study should address.

APPENDICS

Appendix I (Search keywords of the systematic review)

Filter for diabetes

1. Diabet*
2. NIDDM
3. Non-insulin* depend*
4. Glucose intolerance
5. Insulin* resistanc*
6. Metabo* syndrom*

7. 1 or 2 or 3 or 4 or 5 or 6

Filter for exercise

8. Exercis*
9. Training
10. physical
11. Strengthening
12. Weight lifting
13. Wright-lifting
14. Weight bearing
15. Weight-bearing
16. Resist*
17. Stretch*
18. Flexib*
19. Range of motion*
20. Balanc*
21. Mobilit* training*
22. Sport*
23. Exert*
24. Home program*
25. Tai Ji
26. Tai Chi
27. Chi, Tai
28. Taiji
29. Ji Quan, Tai
30. Pilates*
31. Hydrotherap*
32. aquatic
33. Ai chi

34. 8 or 9 or 10 or 11 or 12 or 13 or14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

Filter for balance and mobility

35. Balance*
36. Postur*
37. BBS
38. Single leg*
39. one leg*
40. Functional reach
41. Timed up and go test
42. TUG*
43. Timed-up-and-go
44. Stability
45. equilibrium
46. fall*
47. mobilit*
48. ambulat*
49. walk*
50. gait*
51.Performanc*
52. Locomot*
53. Disorder*
54. Activit*
55. SOT
56. Sensory Organization Test

57. 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57

Final: 7 and 34 and 57

Appendix II (summary of the included articles)

Authors, year and country of publication	Study design	Demographic data	Intervention and control group management	Intervention duration and follow up period	Balance or mobility outcome measures	Drop Out	Summary of results	Intervention adverse effects
Negri et al., 2010, Italy	RCT, blinding was not mentioned	n=60 I=39 C= 21 (mean age 65.7 $\pm$ 5.2) Subjects in intervention groups were analyzed if they have higher than 50% attendance. Adjust I=21 (mean age 65.7 $\pm$ 4.9)	I=Supervised walking exercise with intensity increased from low to moderate gradually C= standard instruction aimed at encouraging physical activity At 2 months, both groups received interim visit	45 minutes, 3 times weekly for 4 months No follow up	Six minute walk test (meter)	I=9 (lack of time = 5, persistent articular pain =3, difficulty in completing the walking exercise and excluded =1) C=1, due to lost to follow-up	Based on the statistical analysis after excluding those with poor attendance I: improved from 521 $\pm$ 37.2 to 612 $\pm$ 78.8 ($p<0.001$) C: improved from 554 $\pm$ 49.2 to 574 $\pm$ 60.8 ($p<0.05$) The change in I is significantly higher than C	Hypoglyce mia n= 7
Allet et al., 2010a Switzerland	RCT, double-blinded	n=71 I=35 (mean age 63 $\pm$ 7.99) C=36 (mean age 64 $\pm$ 8.89)	I= balance and gait training C= no treatment or advice	60 minutes, twice a week for 12 weeks. After the program the subjects were encouraged to perform home exercise in the following 6 months Follow up at 6 months after the 12-week program	1. Gait speed (meter per second) 2. Coefficient of variation of gait cycle time (%) 3. Dynamic balance test: walk as fast as possible on a 5 - meter beam (second)	I= 5 (foot problem =1, fatigue = 1, holidays= 1, discus hernia =1, illness of spouse=1) C= 8 (fatigue= 3, no motivation =1, no time=1, illness=2, not	1. I: increased habitual gait speed from (1.21 $\pm$ 0.17 to 1.36 $\pm$ 0.19, then to 1.31 $\pm$ 0.18) C: changed habitual gait speed from (1.26 $\pm$ 0.18 to 1.24 $\pm$ 0.19 then to 1.24 $\pm$ 0.15 in follow up)	Achilles tendon pain n=2

					4. Static balance test by Biodex Balance System (level 6 and 8)(Sway index)	specified=1	2. I: increased (from 2.60 + 0.72 to 2.68 + 0.99 then to 2.52 + 0.95 in follow up) C: changed (from 2.75 <u>+</u> 0.96 to 2.70 <u>+</u> 1.12 then to 1.09 <u>+</u> 0.21 in follow up) 3. I: improved (from 9.78 <u>+</u> 5.58 to 7.10 <u>+</u> 3.55, then to 7.08 <u>+</u> 3.61 in follow up) C: deteriorated from (8.35 <u>+</u> 3.89 to 9.32 <u>+</u> 5.19, then to 9.32 <u>+</u> 4.05 in follow up) 4. Level 6 I : improved (from 5.97 <u>+</u> 2.59 to 3.74 <u>+</u> 1.12 then to 4.74 <u>+</u> 1.51 in follow up) C: changed (from 6.00 <u>+</u> 2.79 to 5.99 <u>+</u> 2.76 then to 6.42 <u>+</u> 2.83 in follow up) Level 8 I: improved from 4.29 <u>+</u> 2.18 to 2.94 <u>+</u> 1.06 then to 3.31 <u>+</u> 1.02) C: changed (from	

							4.58 + 2.02 to 4.72 + 1.94 then to 4.77 + 1.93 in follow up) All variables showed significant improvement post-intervention and in follow up in I except for 2. while all variables showed deterioration in C.	
Allet et al., 2010b Switzerland	RCT, double-blinded	n=71 I=35 (mean age 63 + 8.0) C=36 (mean age 64 + 8.9)	I= balance and gait training C= no treatment or advice	60 minutes, twice a week for 12 weeks, encouraged to perform home exercise in the following 6 months Follow up at 6 months after the 12-week program	Outdoor gait assessment in tarred 50 meters tarred pathway and 20 meters cobblestone pathways 1. gait speed(meter per second) 2. Cadence (Stride per minute 3. Gait cycle time (second) 4. Stance time (%) 5. Coefficient of variation of gait cycle time (%) 6. Stride length	I= 5 (foot problem =1, fatigue = 1, holidays= 1, discus hernia =1, illness of spouse=1) C= 8 (fatigue= 3, no motivation =1, no time=1, illness=2, not specified=1	1. I: improved (from 1.22 + 0.17 to 1.36 + 0.19on tarred pathway after the intervention and to 1.31 + 0.18 at follow up; from 1.05 + 0.21 to 1.22 + 0.23 on cobblestones pathway after intervention and to 1.19 + 0.23 at follow up) (*p*<0.001). C: changed (from 1.26 + 0.18 to 1.24 + 0.19 on tarred pathway after the intervention and to 1.24 + 0.15 at follow up; from 1.10 + 0.21 to 1.08 + 0.21 on cobblestones	Achilles tendon pain n=2

							pathway after the intervention and to 1.09 ± 0.21 at follow up) (no significant change) 2. I: Improved (from 55.03 ± 5.41 to 60.31 ± 6.24 on tarred pathway after the intervention and to 56.10 ± 4.37 at follow up; from 50.92 ± 5.8 to 56.82 ± 6.75 on cobblestone pathway after the intervention and to 55.80 ± 5.68 at follow up) (*p*<0.001) C: changed (from 56.34 ± 5.27 to 55.57 ± 4..74 on tarred pathway after the intervention and to 56.10 ± 4.37 at follow up; from 52.59 ± 5.78 to 51.79 ± 5.52 on cobblestone pathway after the intervention and to 52.72 ± 5.45 at	

							follow up) (no significant change) 3. I: decreased (from 1.10 ± 0.12 to 1.01 ± 0.11 on tarred pathway after the intervention and to 1.03 ± 0.1 at follow up; from 1.20 ± 0.15 to 1.07 ± 0.14 on cobblestone pathway after the intervention and to 1.09 ± 0.12 at follow up) ($p<0.001$) C: changed (from 1.08 ± 0.1 to 1.09 ± 0.1 on tarred pathway after the intervention and to 1.08 ± 0.08 at follow up; from 1.16 ± 0.14 to 1.18 ± 0.15 on cobblestone pathway after the intervention and to 1.16 ± 0.13 at follow up) (no significant change) 4. I: decreased (from 60.67 ± 1.87 to	

							56.69 ± 2.47 on tarred pathway and to 60.14 ± 2.28at follow up; from 61.38 ± 2.65 to 59.89 ± 2.39 on cobblestone pathway after the intervention and to 60.36 ± 2.52 at follow up) (p<0.001 after intervention but not significant at follow up) C: changed (from 60.35 ± 1.78 to 60.55 ± 1.96 on tarred pathway after the intervention and to 60.49 ± 2.03 at follow up; from 60.68 ± 1.97 to 60.91 ± 2.27 on cobblestone pathway after the intervention and to 60.69 ± 2.07 at follow up) (no significant change) 5. I: changed (from 2.60 ± 0.73 to 2.69 ± 0.99 on tarred pathway after the intervention and to	

							2.52 + 0.95 at follow up; from 4.93 + 2.61 to 4.29 + 1.97 on cobblestone pathway after the intervention and to 4.69 + 2.32 at follow up) (no significant change) C: changed (from 2.75 + 0.96 to 2.70 + 1.12 on tarred pathway after intervention and to 2.72 + 0.88 at follow up; from 5.11 + 2.27 to 5.12 + 2.23 after intervention and to 5.12 + 2.82 at follow up) (no significant change) 6. I: increased (from 1.32 + 0.13 to 1.35 + 0.14 (p=0.039) on tarred pathway after the intervention and to 1.27 + 0.17 (p=0.012)at follow up; from 1.24 + 0.17 to 1.29 + 0.15 (p=0.009) on cobblestone pathway and to 1.27	

							+ 0.17 (p=0.012) at follow up) C: changed (from 1.35 + 0.15 to 1.33 + 0.17 on tarred pathway after intervention and to 1.33 + 0.16 at follow up; from 1.25 + 0.17 to 1.24 + 0.19 on cobblestone pathway after intervention and to 1.24 + 0.2 at follow up) (no significant change).	
Lambers et al., 2008, Holland and Belgium	RCT, double-blinded	n=54 Icom (combined training) =19 (mean age 55.8 + 9.66) Iend(endurance training)= 19 (mean age 52.2 + 8.26) C= 16 (mean age 57.5 + 8.69)	Icom= endurance and muscle strengthening Iend= endurance taining C= remained normal activities without additional guided physical activity	Icom and Iend: 40 sessions (3 times a week), 1 hour training No follow up	1. Six-minute walk test (meter) 2. Functional sit-to-stand test (number per 30 seconds)	Icom=2 (illness) Iend=1 (illness) C=5 (lost to follow up)	1. Icom improved from 539.8 + 61.26 to 594.2 + 60.25; Iend improved from 538.1 + 76.32 to 583.4 + 61.48; C deteriorated from 528.9 + 88.36 to 521.3 + 86.27 Both Icom and Iend performed significantly better than control group (p<0.01) 2. Icom improved from 14.2 + 2.59 to	Hypoglycemia I=2

							16.8 ± 2.30; Iend improved from 13.4 ± 2.73 to 15.3 ± 4.41; C decreased from 13.1 ± 2.17 to 12.8 ± 1.72 Significant difference was found between Icom and C (p<0.05)	
Lam et al., 2008, Australia	RCT, single-blind	(n=53) I=28 (mean age 63.2 ± 8.6) C=25 (mean age 60.7 ± 12.2)	I= Tai Chi program based on ‘yang and sun style 20-form C= maintain usual activities	1 hour, twice a week for 3 months, then once a week for 3 months No follow up	6 meters walk test (second)	I= 7 C= 3 Illness= 5 Time commitments= 2 Non-specified= 3	I changed from 5.1± 0.7 to 5.7 ± 1.6 (p=0.34); C changed from 5.2 ± 1.1 to 10.7 ± 25.5 (statistical significance not mentioned	Not mentioned
Ozdirenc et al., 2004, Turkey	RCT, blinding was not mentioned	(n=44) I=23 (61.9 ± 7.4) C=21 (60.4 ± 5.6)	I= cardiovascular training and theraband exercise for training lower limbs, exercise intensity was in submaximal level C=did not receive any recommendations regarding exercise	20-45 minutes, five times a week in in-patient setting (mean stay=12 ± 2.4 days) No follow up	6-minute walk test (meters)	Withdrawal was not reported	I: improved (from 455.2 ± 76.6 to 537.6 ± 61.6); C improved (from 454 ± 45.1 to 511.5 ± 42.8) (both group showed significant within-group difference p<0.05, significant between-group difference was noted after the intervention)	No adverse effect

Orr et al., 2006, Australia	RCT, single-blinded	(n=35) I=17 (mean age 65.9 + 7.4) C=18 (mean age 64.9 + 8.1)	I=Tai Chi for Diabetes (a 12-movement hybrid from Sun and Yang style C= sham exercise (seated calisthenics, stretching etc.)	I and C: twice a week for 16 weeks (10 minutes warm up and cool down, 45 minutes exercise) No follow up	1. Balance index (Chattecx balance platform) 2. Unilateral stance, eyes open (second) 3. Unilateral stance, eyes closed (second) 4. Tandem walk score (time to complete 3-meter tandem walk plus number of error made) 5. 6-minute walk test (meter) 6. Habitual gait speed (meter per second) 7. Maximal gait speed (meter per second)	Not mentioned	1. I improved from 111.1 + 23.1 to 107.3 + 23.1; C improved from 111.5 + 22.2 to 104.1 + 22.2 (*p*=0.03) 2. I improved from 8.96 to 17.9; C deteriorated from 30 to 24.2 (*p*=0.60)# 3. I changed from 3.9 to 2.8; C changed from 2.2 to 2.0 (*p*=0.20)# 4. I improved from 19.1 + 7.0 to 18.1 + 8.3; C improved from 18.5 + 6.3 to 17.2 + 6.2 (*p*=0.20) 5. I changed from 474.0 + 76.1 to 481.8 + 83.0; C changed from 456.6 + 117.8 to 470.1 + 118.2 (*p*=0.06) 6. I improved from 1.0 + 0.2 to 1.1 + 0.2; C improved from	Not mentioned

							1.1 ± 0.2 to 1.2 ± 0.3 (*p*=0.053) 7. I improved from 1.6 ± 0.3 to 1.7 ± 0.3; C improved from 1.6 ± 0.3 to 1.7 ± 0.3 (*p*=0.005) # median value *p*-value is the significance of change over time	
Richardson et al., 2001, USA	Quasi-RCT, single-blinded	n=20 I=10 (mean age 64 ± 6.3) C=10 (age 63.3 ± 7.6)	I=focused exercise program to improve distal strength and balance C=sham exercise on upper limbs	I=daily exercise for 3 weeks C= 5 or more times per week for 3 weeks No follow up	1. Tandem stance (second) 2. Functional reach (inch) 3. Unipedal stance (second)	I=1 (ankle and foot pain) C=3 (illness=1, non-specified=2)	1. I improved from 17.5 ± 13.4 to 23.5 ± 10.9 (p=0.004); C improved from 19.0 ± 11.8 to 22.0 ± 12.0 (p=0.13) 2. I improved from 10.5 ± 2.1 to 11.5 ± 2.2 (p=0.012); C improved from 11.3 ± 3.6 to 11.9 ± 2.8 (p=0.23) 3. I improved from 5.4 ± 4.7 to 11.6 ± 10.2 (p=0.0014); C decreased from 9.3 ± 8.6 to 7.9 ± 5.9 (p=0.33)	Ankle and foot pain I=1

Tsang et al., 2007, Australia	RCT, single-blinded	(n=38) I=18 (age 66 ± 8) C=20 (age 65 ± 8)	I= Tai Chi for Diabetes (a form of 12 movements form Sun and Yang Tai Chi styles) C= sham exercise (seated calisthenics and stretching)	I and C: twice a week for 16 weeks (10 minutes warm up and cool down, 45 minutes exercise) No follow up	1. Balance index (Chattecx balance plateform) 2. Unilateral stance, eyes open (second) 3. Unilateral stance, eyes closed (second) 4. Tandem walk score (time to complete 3-meter tandem walk plus number of error made) 5. 6-minute walk test (meter) 6. Habitual gait speed (meter per second) 7. Maximal gait speed (meter per second)		1. I improved from 111.1 ± 23.1 to 107.3 ± 23.1); C improved from 111.5 ± 22.2 to 104.1 ± 22.2 (*p*=0.03) 2. I improved from 13.6 ± 13.1 to 16.9 ± 13.2; C changed from 19.4 ± 12.7 to 19.4 ± 12.1(*p*=0.40) 3. I decreased from 3.9 to 2.9; C decreased from 22.2 to 2.0 (*p*=1.00)# 4. I improved from 19.1 ± 7.0 to 18.1 ± 8.3; C improved from 18.5 ± 6.3 to 17.2 ± 6.2 (*p*=0.20) 5. I improved from 474.0 ± 76.1 to 481.8 ± 83.0; C improved from 456.6 ± 117.8 to 470.1 ± 118.2 (*p*=0.06) 6. I improved from 1.0	Pain and fatigue I=1

							to 1.2; C improved from 1.1 to 1.2 (*p*=0.054)# 7. I improved from 1.6 + 0.3 to 1.7 + 0.3; C improved from 1.6 + 0.3 to 1.7 + 0.3 (*p*=0.005) #median value p-value is the significance of change over time	

I=intervention C=control

Appendix III (Cochrane Risk of Bias Tables)

(Allet et al., 2010a) Diabetologia

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Electronic randomization was performed	“ For each of these starting points a new randomization list was electronically generated…”
Allocation concealment	Low risk	Allocation was probably not foreseeable by electronic randomization	“new randomisation list was electronically generated…..by a person not involved in the recruitment, evaluation or treatment processes…the allocation was accomplished by a secretary in a central office”
Blinding of participants	High risk	The nature of the study made it less likely to blind the subjects	“Patients were kept unaware of the study hypothesis. However, the nature of the study made it impossible to blind patients and therapists.” “Patients allocated to the IG received a timetable containing all planned sessions over 12 weeks.”
Blinding of outcome assessors	High risk	The assessor worked in the same center and could see who is receiving training during the class	“The assessor was kept as much as possible unaware of the group assignment. However, as she worked in this hospital during the experiment, she saw some patients arriving for training sessions.”
Incomplete outcome data addressed	Unclear risk	Incomplete data was handles by method of intention-to-treat analysis with last observation carry forward	“An intention to treat analysis was performed and in the event of missing value for any variables, these values were imputed by means of the last observation carried forward method”
Selective reporting	Low risk	In the article, all pre-specified outcome measures were reported	
Other bias			

(Allet et al., 2010b) Gait and Posture

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Electronic randomization was performed	"a new randomization list was electronically generated…"
Allocation concealment	Low risk	Allocation was probably not foreseeable by electronic randomization	"a new randomization list was electronically generated and was used by a person uninvolved in the recruitment, evaluation or treatment process"
Blinding of participants	High risk	The nature of the study made it less likely to blind the subjects	"Patients were kept unaware of the study hypothesis. However, the nature of the study made it impossible to blind patients and therapists"
Blinding of outcome assessors	High risk	The assessor worked in the same center and could see who is receiving training during the class	"All outcome measures were taken at baseline, after 12 weeks and after six months and performed by the same experienced physiotherapist" "However, the nature of the study made it impossible to blind patients and therapists"
Incomplete outcome data addressed	Unclear risk	Incomplete data was handles by method of intention-to-treat analysis with details described	" An intention to treat analysis was performed and in case of missing values of variables, values were imputed by means of the last observation carried forward methods"
Selective reporting	Low risk	All pre-specified outcome measures were reported with details described in tables	
Other bias			

(Lam et al., 2008)

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Computer generated randomization was used	"randomized to tai chi or wait list control using a centralized computer generated allocation method…"
Allocation concealment	Low risk	Subjects were less likely to foresee the assignment before the start of the program	"randomized to…using a centralized computer generated allocation method…"
Blinding of participants	Unclear risk	Blinding of subjects was not mentioned	
Blinding of outcome assessors	Low risk	Assessors were blinded to the treatment allocation	"subjects were assessed at baseline…by either an exercise physiologist or trained nurse, both blinded to the treatment allocation"
Incomplete outcome data addressed	Unclear risk	Attrition was mentioned in the article but the handling of incomplete data was not mentioned	" A total of 53 patients were randomised to the study. There were 10 patients who withdrew from the study because of illness (5) or time commitments (2). Three patients withdrew toward the end of the study but returned for final blood tests and were included in the analysis."
Selective reporting	Low risk	All pre-specified outcome measures were reported with details presented in tables	
Other bias	Unclear risk	?uneven baseline data between two groups	

(Lambers et al., 2008)

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Randomization using envelope	“ the randomization was performed using envelopes”
Allocation concealment	Unclear risk	Writers did not mention the detail on the concealment of envelop	
Blinding of participants	Low risk	Blinding of subjects was probably done	“ the message inside stated that they were in group 1 (combined exercise training), 2 (endurance training) or 3 (control group)”
Blinding of outcome assessors	Low risk	Blinding of assessors were mentioned	“The measurements were done by masked assessors. They examined the participants without being aware of the programme followed by each individual.”
Incomplete outcome data addressed	High risk	Incomplete and missing data management was not mentioned, according to flow diagram, the writers probably adopted as-treated analysis	“During the experimental period 8 patients dropped out (2 in the combination group, 1 in the endurance group and 5 in the control group) due to non-compliance, illness and lost to follow-up.”
Selective reporting	Low risk	All pre-specified outcome measures were reported with details presented in tables	
Other bias	Unclear risk	1. 29 males and 17 males 2. There was significant difference in baseline on weight and waist circumference	1.” So, 29 males and 17 females with stable type 2 diabetes, all free of exercise-limiting co-morbidities…were enrolled in a 40-session rehabilitation programme.” 2. In general all groups were matched except for weight (P<0.05) and waist circumference (P<0.05).”

(Negri et al., 2010)

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Randomization table was used	" subjects were assigned with a 1:2 ratio by a randomization table…"
Allocation concealment	Unclear risk	Details of concealment was not mentioned	
Blinding of participants	Unclear risk	Blinding not mentioned	
Blinding of outcome assessors	Unclear risk	Blinding not mentioned	
Incomplete outcome data addressed	High risk	1. Number of attrition and exclusion addressed, but the number of drop out between two groups were not balanced 2. Incomplete outcome data was handled by intention-to-treat without further details	1. "Eight subjects in the intervention group abandoned the protocol because of lack of time (n=5) or persistent articular pain (n=3). One subject was excluded because of difficulties in completing the walking sessions. One subject in the control group was lost to follow up." 2. "By intention-to-treat analysis, at the end of study…."
Selective reporting	High risk	All pre-specified outcomes were reported but the author performed a second analysis to draw the conclusion	"Because there was a wide individual range (14-90%) in participation in scheduled activities, a secondary analysis was carried our including only subjects whose attendance was at least 50% (n=21)."
Other bias	Unclear risk	Practice effect of the intervention	

(Orr et al., 2006)

	Judgment	Description	Quote
Adequate sequence generation	Unclear risk	The method of randomization was not clear	“ participants were randomly allocated to the Tai Chi or control groups, named Eastern or Western exercise….”
Allocation concealment	Unclear risk	The method of concealment was not mentioned	
Blinding of participants	Unclear risk	Blinding of participants was not mentioned	
Blinding of outcome assessors	Unclear risk	Blinding of assessor was not mentioned	
Incomplete outcome data addressed	High risk	The number of attrition and drop out was not mentioned. Intention-to-treat analysis was mentioned in methodology part without much details, it appeared that the as-treated analysis was used according to the table	“ We conducted a 16-week single –blind, randomized, sham-exercise controlled trial with an intention-to-treat design.”
Selective reporting	Low risk	All pre-specified outcome measures were reported and presented in table.	
Other bias	Unclear risk	79% of the subjects were female	

(Ozdirenc et al., 2004)

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Random number table was used	“randomly allocated by means of a random numbers table to one of two groups”
Allocation concealment	Unclear risk	Method of concealment was not mentioned	
Blinding of participants	Unclear risk	Blinding subjects was not mentioned	
Blinding of outcome assessors	Unclear risk	Blinding of assess was not mentioned	
Incomplete outcome data addressed	Unclear risk	Number of missing data or drop out not mentioned	
Selective reporting	Low risk	All pre-specified outcome measures were reported and described in tables	
Other bias	Unclear risk	All subjects were recruited from the same hospital The treatment period was not standardized	

(Tsang et al., 2007)

	Judgment	Description	Quote
Adequate sequence generation	Low risk	Computerized randomization program was used	“randomly allocated to intervention or control groups. Permuted block randomization in blocks of four, stratified by gender…computerized randomization program”
Allocation concealment	Low risk	The randomization was done by a third party and a sealed envelope was used	“…stratified by gender was generated by an investigator no otherwise involved with study subjects…” “Subjects were randomized following baseline assessment by handing them their group allocation in a sealed opaque envelope.”
Blinding of participants	Low risk	Subjects were blinded	“ both forms of exercise were presented to the subjects as being potentially beneficial to them, and naming the program, ”Move It for Diabetes” assisted in the blinding of the subjects to the hypothesized beneficial exercise mode.”
Blinding of outcome assessors	High risk	Assessor was not blinded	“ All classes were run by the same investigator extensively trained in both forms of exercise. The same investigator performed the outcome measures also, due to limited staff availability”
Incomplete outcome data addressed	Unclear risk	Attrition and exclusion of subjects described but the method handling the incomplete data was not mentioned	“ There was one dropout in the Tai Chi group (at week 4) who refused follow-up testing due to illness and difficulty with transport.” “One subject (with pre-existing spinal stenosis) in the Tai Chi group found the exercise intolerable secondary to pain and fatigue, and did not attend after session 1.”
Selective reporting	Low risk	All pre-specified outcome measures were reported and described in table	
Other bias			

Appendix VI (Consent form-English version)

The Hong Kong Polytechnic University
Department of Rehabilitation Sciences

Research Project Information letter

Project Title:	The use of foot scanner in evaluating the biomechanical properties of plantar tissue in people with diabetes
Name of Researcher:	Mr. Thomas Ng, MPhil candidate, Department of Rehabilitation Science, The Hong Kong Polytechnic University
Name of Supervisors:	Dr. Gladys Cheing, PhD, Department of Rehabilitation Sciences, The Hong Kong Polytechnic University
	Dr. Yong-ping Zheng, PhD, Department of Health Technology & Informatics, The Hong Kong Polytechnic University

<u>Project information:</u>

The purposes of this study are (i) to examine the validity of a newly developed ultrasound platform in measuring the mechanical property of the plantar tissues of diabetic foot in standing position, and (ii) to examine the biomechanical properties of plantar tissues among people with diabetic polyneuropathy as compared to healthy control subjects.

For the first part of this study, a novel ultrasound platform will be modified and implemented to measure the mechanical properties of plantar tissues in standing. The validity of this ultrasound platform system will be tested in people with diabetic peripheral neuropathy using the tissue ultrasound palpation system (TUPS).

For the second part of the study, subjects with Type 2 diabetic with or without peripheral neuropathy and age-matched healthy control subjects will be recruited. Comparison will be made on (i) plantar tissue thickness and stiffness and (ii) postural control in standing. Equipments include (i) a newly developed ultrasound plantar foot scanner and (ii) a computerized posturography machine (Smart EquiTest@, NeuroCom International, Inc) will be used for the testing.

All measurements include change in mechanical property of plantar tissues, and the postural control are absolutely safe with no known side-effects. Subjects will not be exposed to any painful stimulation during assessment. Subjects are under no obligation to take part in this study and free to withdraw from the study at any time during the sessions. Subject's personal information and data acquired from this study is confidential and will not be disclosed to people who are not related to this study.

If you have any complaint about the conduct of this research study, please do not hesitate to contact Mrs. Michelle Leung, Secretary of Departmental Research Committee of The Hong Kong Polytechnic University at tel. no. 2766 5397.

If you would like more information about this study, please contact Dr. Gladys Cheing at tel. no. 2766 6738.

Thank you for your interest in participating in this study.

Appendix V (Consent form-Chinese version)

香港理工大學康復治療科學系科研同意書

科研題目： 超聲波足部平臺系統測試糖尿病周邊神經病變患者的足底部生物力學之研究

科研人員： 吳家偉先生 (香港理工大學康復治療科學系碩士學生)
鄭荔英博士 (香港理工大學康復治療科學系助理教授)
鄭永平博士 (香港理工大學醫療科技及資訊學系副教授)

科研內容：

本研究之目的包括: (一) 檢測新研發的超聲波足部平臺系統測試方法來測試足底部生物力學之可靠度及準確度，(二) 研究糖尿病周邊神經病變患者相對非糖尿病健康人士之平衡表現與及摔跌的風險因素。

此研究的第一部份是檢測新研發的超聲波足部平臺系統測試方法的使用在 2 型糖尿病周邊神經病變患者的可靠度及準確度。

此科研的第二部份研究對象包括: (一) 2 型糖尿病患者、(二) 2 型糖尿病周邊神經病變患者、(三)非糖尿病健康人士。研究對象將會接受兩種不同類形的測試與檢查，包括: (一)足底軟組織的厚度與彈性、(二)直立時的姿勢控制能力。測試儀器包括: (一)超聲波足部平臺、(二)電腦化姿勢描記術儀器。

對項目參與人士和社會的益處：

此研究為糖尿病周邊神經病變患者跌倒的風險因素提供更有效的檢測及理解，研究結果將對今後糖尿病足的治療提供寶貴資料。

潛在危險性：

此研究的所有測試包括足底軟組織生物力學特性之改變、與及平衡測試都十分安全，沒有潛在危險性，測試過程中不會引起疼痛。參與者有權在任何時候、無任何原因放棄參與此次研究，不會導致任何懲罰或不公平對待。參與者的資料將不會洩露給與此研究無關的人員。

研究對象如有關於此項研究的疑問，可在辦工時間內致電鄭荔英博士(2766 6738)查詢。若研究對象對此研究有任何投訴，可聯繫梁女士（部門科研委員會秘書），電話：27665397。

多謝閣下的積極參與。

<u>同意書</u>：

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、無任何原因放棄參與此次研究，而此舉不會導致我受到任何懲罰或不公平對待。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，我的名字或相片不會出現在任何出版物上。

若本人對此研究有何疑問，可致電研究負責人鄭荔英博士 (電話：2766 6738)查詢。若本人對此研究人員有任何投訴，可以聯繫梁女士（部門科研委員會秘書），電話：2766 5397。本人亦明白，參與此研究課題需要本人簽署一份同意書。

參與者簽名：＿＿＿＿＿＿＿＿＿＿ 日期：＿＿＿＿＿＿＿＿＿＿

見證人簽名：＿＿＿＿＿＿＿＿＿＿ 日期：＿＿＿＿＿＿＿＿＿＿

科研人員簽名：＿＿＿＿＿＿＿＿＿＿ 日期：＿＿＿＿＿＿＿＿＿＿

Appendix VI (Abstract I of 13th Hong Kong Diabetes and Cardiovascular Risk Factors- East Meets West Symposium)

THE CHANGE OF PLANTAR SOFT TISSUES BIOMECHANICAL PROPERTIES IN DIFFERENT WEIGHT BEARING POSITIONS

Thomas Ka Wai Ng; Yong-Ping Zheng; Rachel Lai Chu Kwan; Gladys Lai Ying Cheing

Purpose of the study
This study was to investigate the thickness and stiffness of the plantar soft tissue in sitting and standing positions by the use of an Ultrasound Foot Scanner System.

Methods
Fifteen healthy young subjects (mean age: 22.5±2.2 yrs; 7 males and 8 females) were recruited. The Ultrasound Foot Scanner System was used to assess the thickness and stiffness of the plantar soft tissue at the pulp of the big toe, the first metatarsal head, second metatarsal head, fifth metatarsal head, and heel in both a sitting and standing position. Paired t-test was used to compare the result obtained in the sitting and standing positions made by the Ultrasound Foot Scanner System.

Summary of the results
Paired t-test showed that the thickness and stiffness of plantar soft tissue at all measuring sites were significantly thinner (all $p<0.001$) and stiffer (all $p<0.05$) in a standing position as compared with the measurements recorded in a sitting position.

Conclusions
The plantar soft tissues become significantly thinner and stiffer when subjects change from a sitting to a standing position, which implies that weight-bearing status is related to the plantar pressure. Assessment of the biomechanical properties of the plantar tissue by the Ultrasound Foot Scanner System enables us to monitor the change of the plantar pressure during different weight bearing activities, also to estimate the risk of developing foot ulcer or foot complications in various disease groups such as people with diabetes.

Appendix VII (Abstract II of 13th Hong Kong Diabetes and Cardiovascular Risk Factors- East Meets West Symposium)

PHYSICAL CHARACTERISTICS OVER THE ANKLE JOINT PREDICT THE MOBILITY PERFORMANCE FOR ELDERLY WITH TYPE II DIABETES

Thomas Ka Wai Ng; Gladys Lai Ying Cheing

Purpose of the study

The purpose of the present study was to investigate if the physical characteristics of the ankle joint are significant predictors of the mobility status in elderly with diabetes.

Methods

Eighty-five subjects with type II diabetes (mean age: 72.52±7.17 years) were recruited from the community elderly centres. The mobility performance status was measured by Timed Up and Go test. The active ankle joint repositioning test for ankle proprioception sense and the ankle peak torque were investigated by Cybex Norm dynamometer (Cybex International Inc, Ronkonkomam NY). The stiffness of ankle dorsiflexion was examined by weight bearing lunge test. Multiple regression analysis was used to predict Timed Up and Go test from the ankle proprioception sense, ankle peak torque of plantarflexors and dorsiflexors, ankle dorsiflexion stiffness and the demographic data.

Summary of the results

Multiple regression analysis shows that the multiple R (0.774) was statistically significant ($F(9,66)=10.953$, $p<0.001$). Our findings demonstrated that body mass index, normalized peak torque of plantarflexors and active ankle joint repositioning test errors are significant predictors of Timed Up and Go test (all $p<0.05$). These factors, together with the demographic data of the subjects count for 59.9% of the variance of Timed Up and Go test.

Conclusions

The body mass index, ankle plantarflexors strength and the ankle proprioception are important factors affecting the physical mobility of elderly with diabetes. The physical characteristics of ankle together with demographic factors contribute to more than 50% of variance of Timed Up and Go test. Future rehabilitation programs should target on improving these physical characteristics for elderly with diabetes in order to reduce the risk of fall in this population.

Appendix VIII (Abstract of Diabetic Foot Global Conference 2012)

Effectiveness of exercise on balance and mobility performance in people with type 2 diabetes

Thomas KW Ng[1,2]; Gladys LY Cheing, PhD[1]

[1] Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China
[2] Physiotherapy Department, Kowloon Hospital, Hong Kong SAR, China

Purpose

To investigate the effectiveness of a 10-week balance exercise program on the balance and mobility performance in elderly people with type 2 diabetes.

Methods

One hundred and eight subjects with type 2 diabetes without neuropathy were recruited from four community elderly centers. They were divided into either the intervention group (n=62, mean age=72.0 years) or control group (n=46, mean age=72.7 years).The intervention group attended exercise class twice a week for 10 weeks, with daily home exercise prescribed. Sensory Organization Test and single leg standing test for balance performance, and Timed Up and Go test for mobility performance were examined before and after the exercise program, and the change in performance over time was calculated, Independent t-test was used to examine the difference between the groups.

Results

The intervention group had significantly greater improvement than did the control in performing the Sensory Organization Test in condition 4 (9.56% versus 1.57%); condition 5 (32.23% versus 1.80%) and condition 6 (28.58% versus 3.79%). In addition, the composite score (7.83% versus 0.66%), visual ratio (8.93% versus 2.11%) and vestibular ratio (31.58 % versus 2.44%) of the intervention group were higher than the control group (all $p<0.05$). The performance of single leg standing and Timed Up and Go test also favor the intervention group but the group difference did not reach statistical significance.

Conclusion

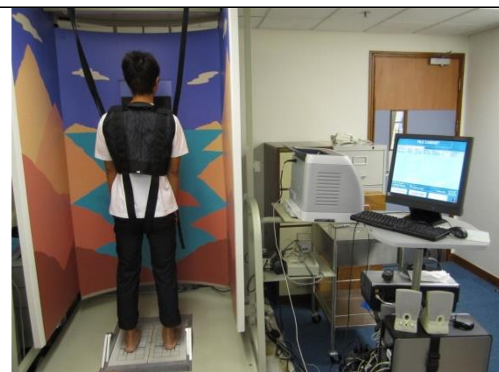
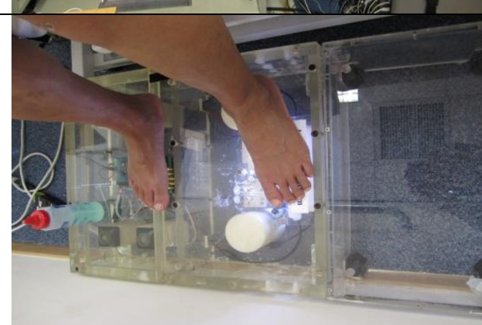
A 10-week exercise program together with home exercise significantly improved the balance performance in elderly with type 2 diabetes, and it may also bring benefits to their mobility performance.

Appendix IX (Leaflet of exercise program)

日 期	2010 年 11 月 8 日至 2011 年 1 月 27 日(逢一、四)
時 間	早上十時半 (每節 45 分鐘) 為期十週
名額	二十人， 報名從速
地 址	鄰舍輔導會雅研社鄰里康齡中心

活動特色：

- 此活動與理工大學合辦，由**<u>註冊物理治療師</u>**針對糖尿病人設計的運動班
- 活動包括糖尿病患者防跌家居講座
- **<u>免費血糖驗血</u>**及視力檢查
- 派發家居運動小錦囊
- 由物理治療師為您作出專業的跌倒風險評估、驗查下肢肌肉力量、平衡表現及柔軟度，並提供**<u>詳盡報告</u>**

<table>
<tr><td colspan="2">臨床測試包括：</td></tr>
<tr><td colspan="2">1. 測試平衡及運動功能
2. 評估足踝關節柔軟度</td></tr>
<tr><td>3. 用六種不同模擬現實狀況評估平衡反應
4. 重心移動測試及反應度</td><td></td></tr>
<tr><td>5. 以香港理工大學研製超聲波皮層感應儀量度足部軟組織厚度及韌度</td><td></td></tr>
<tr><td>6. 以均速力量測試儀測試足踝肌肉力量及關節感覺測試</td><td></td></tr>
</table>

Appendix X (Home exercise pamphlet)

糖尿患者家居平衡運動手冊

糖尿病人防跌運動包括以下三部份：伸展、平衡及強化肌力運動。導師將根據每位患者的運動表現作出相應的調整及篩選，以設計適合個別學員的家居運動。

目的：

1. 增加小腿及踝關節柔軟度
2. 增加足底軟組織柔軟度
3. 改善足部關節平衡感應能力
4. 增強下肢肌肉力量

注意事項：

1. 學員需由導師指導後進行運動，並依照手冊列明之次數進行家居運動
2. 學員必須每日填妥練習進度表
3. 如在運動期間或後感到不適，需暫時停止運動並馬上通知導師有關情況。

香港理工大學康復治療學系及九龍醫院物理治療部編制
二零一零年

小腿伸展運動 (1)

1. 準備附有背靠的椅子或桌子，面向椅子以雙手輕力支撐
2. 分開雙腿站立，前腿屈曲、後腿伸直，腳跟貼地
3. 重心向前移直至小腿後面有拉緊感覺
4. 停留 10 秒，放鬆，每邊重覆動作 10 次，每日 2 次，雙腳交替，每天進行

小腿伸展運動 (2)

1. 開始位置和擺設與運動(1)一樣
2. 後腿膝蓋輕微屈曲
3. 重心向前移直至小腿後面有拉緊感覺
4. 停留 10 秒，放鬆，重覆動作 10 次，每日 2 次，雙腳交替，每天進行

足底軟組織伸展運動

1. 坐著，以腳跟著地，腳尖靠牆
2. 然後腳跟上提，腳指貼牆
3. 直至後足底軟組織有拉緊感覺，
4. 停留 10 秒，放鬆，重覆動 10 次，每日 2 次，雙腳交替，每天進行

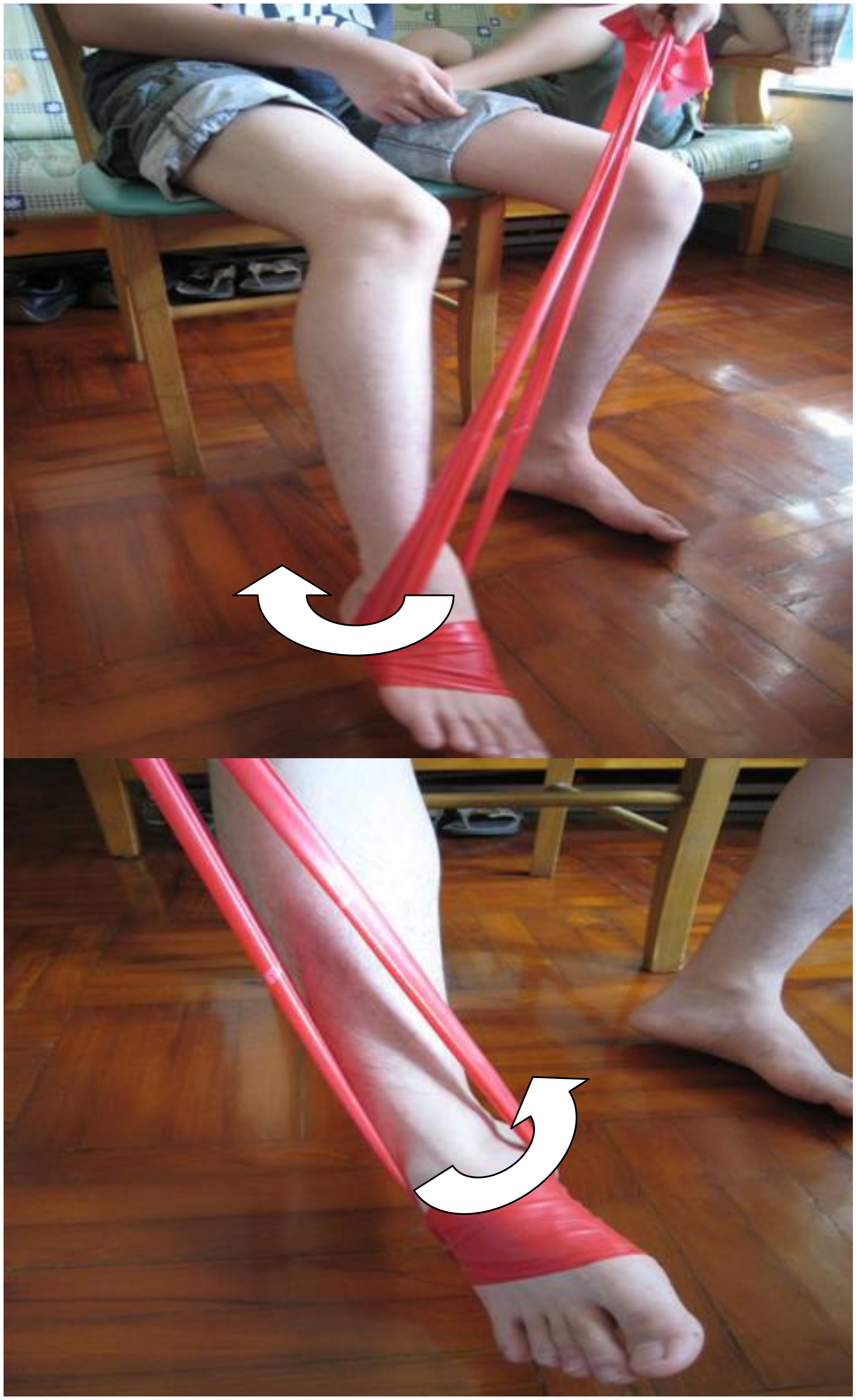
站立踮腳

1. 準備附有背靠的椅子或桌子，面向椅子以雙手輕力支撐
2. 雙腿以腳尖站立停留約 3 秒
3. 雙腳再以腳跟站立停留約 3 秒
4. 每日 2 次，每次 3 組，每組重覆 10 次，每天進行

小腿肌肉力量訓練(1)

1. 坐在一張穩固的座椅上
2. 把運動橡筋於腳掌及雙手各圍兩圈
3. 膝關節伸直，腳掌做向下按的動作
4. 運動橡筋的阻力應令你感到有些困難
5. 每日 2 次，每次 3 組，每組重覆 10 次，每天進行

小腿肌肉力量訓練(2)



1. 坐在一張穩固的座椅上
2. 把運動橡筋於腳掌圍兩圈
3. 用單手拿起運動橡筋的兩端及圍圈
4. 把運動橡筋拉向肩膀
5. 腳掌做外翻及內翻的動作
6. 運動橡筋的阻力應令你感到有些困難
7. 每日 2 次，每次 3 組，每組重覆 10 次，每天進行

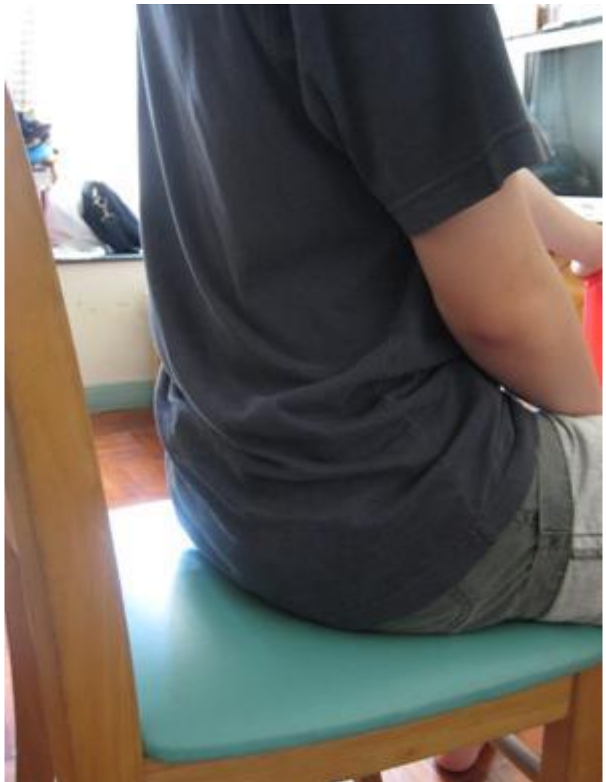
大腿肌肉力量訓練(1)

1. 坐在一張穩固的座椅上
2. 把運動橡筋於足踝上方圍兩圈
3. 另外一隻腳踏在運動橡筋上
4. 用另外一方的手拿起運動橡筋兩端
5. 小腿作向前踢的動作
6. 運動橡筋的阻力應令你感到有些困難
7. 每日 2 次，每次 3 組，每組重覆 10 次 ，每天進行

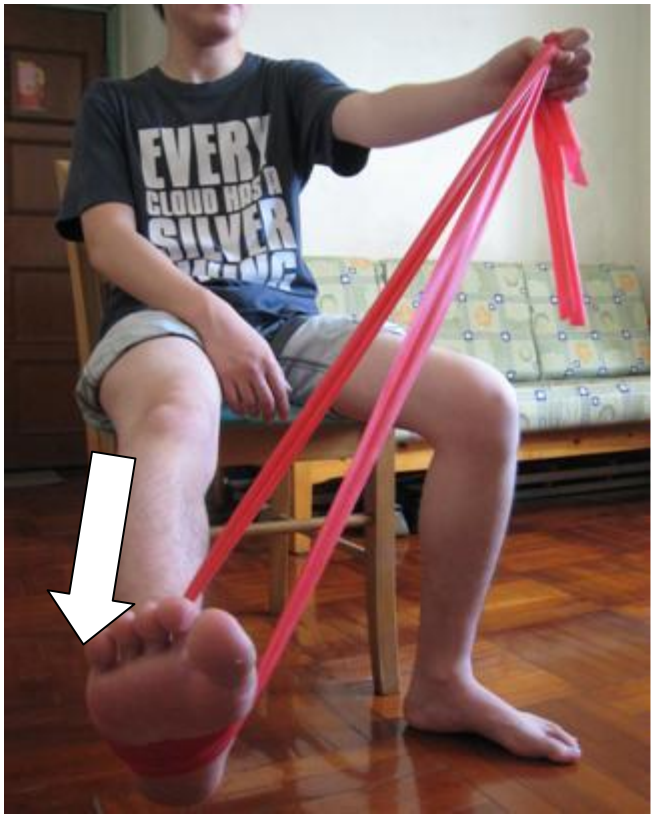
髖關節肌肉力量訓練

1. 站在一張穩固的座椅旁
2. 把運動橡筋於足踝上方圍兩圈
3. 另外一隻腳踏在運動橡筋上
4. 用另外一方的手拿起運動橡筋兩端
5. 膝關節保持伸直及作向前，後及外側踢的動作
6. 運動橡筋的阻力應令你感到有些困難
7. 每日 2 次，每次 3 組，每組重覆 10 次，每天進行

軀幹穩定訓練




EVERY
CLOUD HAS



1. 坐在一張穩固的座椅上，背部不可靠椅背
2. 把運動橡筋於腳掌上方圍兩圈
3. 髖關節及膝關節輕微屈曲
4. 用另外一方的手拿起運動橡筋兩端
5. 手肘輕微屈曲
6. 下肢作向外踢的動作
7. 運動橡筋的阻力應令你感到有些困難
8. 每日 2 次，每次 1 組，每組 10 次
每天進行

練習進度表

(填寫方法:完成 ✓；部分完成 O；無法完成 ×)

八月

	星期一	星期二	星期三	星期四	星期五	星期六	星期日
週一 上午	9	10	11	12	13	14	15
下午							
週二 上午	16	17	18	19	20	21	22
下午							
週三 上午	23	24	25	26	27	28	29
下午							
週四 上午	30	31					
下午							

九月

	星期一	星期二	星期三	星期四	星期五	星期六	星期日
週四 上午			1	2	3	4	5
下午							
週五 上午	6	7	8	9	10	11	12
下午							
週六 上午	13	14	15	16	17	18	19
下午							
週七 上午	20	21	22	23	24	25	26
下午							
週八 上午	27	28	29	30			
下午							

十月

	星期一	星期二	星期三	星期四	星期五	星期六	星期日
週八 上午					1	2	3
下午							
週九 上午	4	5	6	7	8	9	10
下午							
週十 上午	11	12	13	14	15	16	17
下午							

REFENERCES

2011 National Diabetes Fact Sheet. (2011). Centers for Disease Control and Prevention.

Abate, M., Schiavone, C., Pelotti, P., & Salini, V. (2011). Limited joint mobility (LJM) in elderly subjects with type II diabetes mellitus. . *Archives of Gerontology and Geriatrics, 53*(2), 135-140.

Abelew, T. A., Miller, M. D., Cope, T. C., & Nichols, T. R. (2000). Local loss of proprioception results in disruption of interjoint coordination during locomotion in the cat. . *Journal of Neurophysiology, 84*(5), 2709-2714.

Abouaesha, F., van Schie, C. H., Griffths, G. D., Young, R. J., & Boulton, A. J. (2001). Plantar tissue thickness is related to peak plantar pressure in the high-risk diabetic foot. *Diabetes Care, 24*(7), 1270-1274.

Agurs-Collins, T. D., Kumanyika, S. K., Ten Have, T. R., & Adams-Campbell, L. L. (1997). A randomized controlled trial of weight reduction and exercise for diabetes management in older African-American subjects. *Diabetes Care, 20*(10), 1503-1511.

Allet, L., Armand, S., Aminian, K., Pataky, Z., Golay, A., de Bie, R. A., et al. (2010a). An exercise intervention to improve diabetic patients' gait in a real-life environment. *Gait & Posture, 32*(2), 185-190.

Allet, L., Armand, S., de Bie, R. A., Golay, A., Monnin, D., Aminian, K., et al. (2010b). The gait and balance of patients with diabetes can be improved: a randomized controlled trial. *Diabetologia, 53*(3), 458-466.

Andersen, H., Nielsen, S., Mogensen, C. E., & Jakobsen, J. (2004). Muscle strength in type 2 diabetes. *Diabetes, 53*(6), 1543-1548.

Andreassen, C. S., Jakobsen, J., & Andersen, H. (2006). Muscle weakness: a progressive late complication in diabetic distal symmetric polyneuropathy. *Diabetes, 55*(3), 806-812.

Aoki, T., Ohashi, T., Matsumoto, T., & Sato, M. (1997). The pipette aspiration applied to the local stiffness measurement of soft tissue. *Annals of Biomedical Engineering, 25*(3), 581-587.

Araiza, P., Hewes, H., Gashetewa, C., Vella, C. A., & Burge, M. R. (2006). Efficacy of a pedometer-based physical activity program on parameters of diabetes control in type 2 daibetes mellitus. *Metabolism Clinical and Experimental, 55*(10), 1382-1387.

Bazett-Jones, D. M., Cobb, S. C., Joshi, M. N., Cashin, S. E., & Earl, J. E. (2011). Normalizing hip muscle strength: establishing body-size-independent measurements. *Archives of Physical Medicine and Rehabilitation, 92*(1), 76-82.

Beauchet, O., Fantino, B., Allali, G., Muir, S. W., Montero-Odasso, M., & Annweiler, C. (2011). Timed up and go test and risks of falls in older adults: a systematic review. *Journal of Nutrition, Health & Aging, 15*(10), 933-938.

Bennell, K., Talbot, R., Wajswelner, H., & Kelly, D. (1998). Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Australian Journal of Physiotherapy, 44*(3), 175-180.

Bischoff, H. A., Stahelin, H. B., Monsch, A. U., Iversen, M. D., Weyh, A., von Dechend, M., et al. (2003). Identifying a cut-off point for normal mobility: a comparison of the timed 'up and go' test in community-dwelling and institutionalized elderly women. *Age and Ageing, 32*(3), 315-320.

Bootsma-van der Wiel, A., Gussekloo, J., De Craen, A. J. M., Van Exel, E., Bloem, B. R., & Westendorp, R. G. J. (2002). Common chronic diseases and general impairments as determinants of walking disability in the oldest-old population. *Journal of the American Geriatrics Society, 50*(8), 1405-1410.

Boulton, A. J. (2000). The diabetic foot: a global view. *Diabetes/metabolism research and reviews, 16*(suppl 1), S2-S5.

Brandon, L. J., Gaasch, D. A., Boyette, L. W., & Lloyd, A. M. (2003). Effects of long-term resistive training on mobility and strength in older adults with diabetes. *Journal of Gerontology: Medicine Sciences, 58*(8), 740-745.

Briggs, R. C., Gossman, M. R., Birch, R., Drews, J. E., & Shaddeau, S. A. (1989). Balance performance among noninstitutionalized elderly women. *Physical Therapy, 69*(9), 748-756.

Bus, S. A., Yang, Q. X., Wang, J. H., Smith, M. B., Wunderlich, R., & Cacanagh, P. R. (2002). Intrinsic muscle atrophy and toe deformity in the diabetic neuropathic foot: a magnetic resonance imaging study. *Diabetes Care, 25*(8), 1444-1450.

Cavanagh, P. R. (1999). Plantar soft tissue thickness during ground contact in walking. *Journal of Biomechanics, 32*(623-628).

Cesari, M., Penninx, B. W., Pahor, M., Lauretani, F., Corsi, A. M., Rhys Williams, G., et al. (2004). Inflammatory markers and physical performance in older persons: the InCHIANTI study. *Journal of Gerontology. Series A. Biological Sciences and Medical Sciences*, *59*(3), M242-M248.

Chao, C. Y., Zheng, Y., & Cheing, G. L. (2011). Epidermal thickness and biomechanical properties of plantar tissues in diabetic foot. *Ultrasound in Medicine and Biology, 37*(7), 1029-1038.

Cheung, J. T., Zhang, M., Leung, A. K., & Fan, Y. b. (2005). Three dimensional finite element analysis of the foot during standing- a material sensitivity study. *Journal of Biomechanics, 38*(5), 1045-1054.

Cheung, K. K., Au, K. Y., Lam, W. W., & Jones, A. Y. (2008). Effects of a structured exercise programme on functional balance in visual impaired elderly living in a residential setting. *Hong Kong Physiotherapy Journal, 26*, 45-50.

Cho, E., Manson, J. E., Stampfer, M. J., Solomon, C. G., Colditz, G. A., Speizer, F. E., et al. (2002). A prospective study of obesity and risk of coronary heart disease among diabetic women. *Diabetes Care, 25*(7), 1142-1148.

Christiansen, C. L. (2008). The effects of hip and ankle stretching on gait function of older people. *Archives of Physical Medicine and Rehabilitation, 89*(8), 1421-1428.

Collins, N., Teys, P., & Vicenzino, B. (2004). The initial effects of a Mulligan's mobilization with movement technique on dorsiflexion and pain in subacute ankle sprains. *Manual Therapy, 9*(2), 77-82.

Collins, T. C., Lunos, S., Carlson, T., Henderson, K., Lightbourne, M., Nelson, B., et al. (2011). Effects of a home-based walking intervention on mobility and quality of life in people with diabetes and peripheral arterial disease: a radnomized controlled trial. . *Diabetes Care*, *34*(10), 2174-2179.

Connell, B. R., & Wolf, S. L. (1997). Environmental and behavioral circumstances associated with falls at home among healthy elderly individuals. Atlanta FIC SIT Group. *Archives of Physical Medicine and Rehabilitation, 78*(2), 179-186.

Cornwall, M. W., & McPoil, T. G. (1999). Effect of ankle dorsiflexion range of motion on rearfoot motion during walking. *Journal of the American Podiatric Medical Association*, *89*(6), 272-277.

Cowley, M. S., Boyko, E. J., Shofer, J. B., Ahroni, J. H., & Ledoux, W. R. (2008). Foot ulcer risk and location in relation to prospective clinical assessment of foot shape and mobility among persons with diabetes. *Diabetes Research and Clinical Practice*, *82*(2), 226-232.

Crawford, F., Inkster, M., Kleijnen, J., & Fahey, T. (2007). Predicting foot ulcers in patient with diabetes: a systematic review and meta-analysis. . *The Quarterly Journal of Medicine, 100*(2), 65-86.

Cronin, N. J., Peltonen, J., Ishikawa, M., Komi, P. V., Avela, J., Sinkjaer, T., et al. (2010). Achilles tendon length changes during walking in long-term diabetes patients. *Clinical Biomechanics, 25*(5), 476-782.

Davies, M. J., Heller, S., Skinner, T. C., Campbell, M. J., Carey, M. E., Cradock, S., et al. (2008). Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. *BMJ*(336), 491-495.

Definition, diagnosis and classification of diabetes mellitus. (1999). Geneva: World Health Organization.

Deshpande, N., Connelly, D. N., Culham, E. G., & Costigan, P. A. (2003). Reliability and validity of ankle proprioceptive measures. *Archives of Physical Medicine and Rehabilitation, 84*(6), 883-889.

Deshpande, N., Metter, E. J., & Ferrucci, L. (2010). Validity of clinically derived cumulative somatosensory impairment index. *Archives of Physical Medicine and Rehabilitation*, *91*(2), 226-232.

Diabetes Mellitus. Fact Sheet number 312. (2011). Geneva: World Health Organization.

Diabetes mellitus. Report of a WHO Expert Committee. (1965). Geneva: World Health Organization.

Diabetes Mellitus: Report of a WHO Study Group. Technical Report Series 727. (1985). Geneva: World Health Organization.

Donelan, J. M., & Pearson, K. G. (2004). Contribution of sensory feedback to ongoing ankle extensor activity during the stance phase of walking. *Canadian Journal of Physiology and Pharmacology, 82*(8-9), 589-598.

Dutton, G. R., Provost, B. C., Tan, F., & Smith, D. (2008). A tailored print-based physical activity intervention for patients with type 2 diabetes. *Preventive Medicine, 47*(4), 409-411.

Dutton, G. R., Tan, F., Provost, B. C., Sorenson, J. L., Allen, B., & Smith, D. (2009). Relationship between self-efficacy and physical activity among patients with type 2 diabetes. *Journal of Behavioural Medicine*, *32*(3), 270-277.

Edelstein, J. E. (1992). Physical therapy for elderly patients with foot disorders. *Topics in Geriatric Rehabilitation, 7*(3), 24-35.

Edwards, J. L., Vincent, A. M., Cheng, H. T., & Feldman, E. L. (2008). Diabetic neuropathy: Mechanisms to management. *Pharmacology & Therapeutics, 120*(1), 1-34.

Executive summary: standards of medical care in diabetes-2009. (2009). *Diabetes Care, 32*(4), 754.

Falkenstein, I. A., Cochran, D. E., Azen, S. P., Dustin, L., Tammewar, A. M., Kozak, I., et al. (2008). Comparison of visual acuity in macular degeneration patients measured with Snellen and early treatment diabetic retinopathy study chart. *Ophthalomology, 115*(2), 319-323.

Finlayson, M. L., & Perterson, E. W. (2010). Falls, Aging and Disability. . *Physical Medicine and Rehabilitation Clinics of North America, 21*(2), 357-373.

Flynn, T. W., Canavan, P. K., Cavcanagh, P. R., & Chiang, J. H. (1997). Plantar pressure reduction in an incremental weight-bearing system. *Physical Therapy, 77*(4), 410-416.

Fong, S. S., Tsang, W. W., & Ng, G. Y. (2012). Altered postural control strategies and sensory organization in children with developmental coordination disorder. *Human Movement Science, 31*(5), 1317-1327.

Ford-Smith, C. D., Wyman, J. F., Jr, E. R. K., Fernandex, T., & Newton, R. A. (1995). Test-retest reliability of the Sensory Organization Test in noninstitutionalized older adults. *Archives of Physical Medicine and Rehabilitation, 76*(1), 77-81.

Frykberg, R. G. (1998). Diabetic foot ulcers: current concepts. *The Journal of foot and ankle surgery: official publication of the American College of Foot and Ankle Surgeons, 37*(5), 440-446.

Fu, A. S., & Hui-Chan, C. W. (2007). Ankle joint proprioception and postural control in basketball players with bilateral ankle sprains. *The American journal of Sports Medicine, 33*(8), 1174-1182.

Garcia, C. A., Hoffman, S. L., Hastings, M. K., Klaesner, J. W., & Mueller, M. J. (2008). Effect of metatarsal phalangeal joint extension on plantar soft tissue stiffness and thickness. *The Foot, 18*(2), 61-67.

Garra, B. S., Cespedes, E. I., Ophir, J., Spratt, S. T., Zurbier, R. A., Magnant, C. M., et al. (1997). Elastography of breast lesions: initial clinical results. *Radiology, 202*(1), 79-86.

Gefen, A., Megido-Ravid, M., Azariah, M., Itzchak, Y., & Arcan, M. (2001). Integration of plantar soft tissue stiffness measurements in reoutine MRI of the diabetic foot. *Clinical Biomechanics, 16*(10), 921-925.

Gefen, A., Megido-Ravid, M., & Itzchak, Y. (2011). In vivo biomechanical behavior of the human heel pad during the stance phase of gait. *Journal of Biomechanics, 34*(12), 1661-1665.

Giacomozzi, C., D' Ambrogi, E., Cesinaro, S., Macellari, V., & Uccioli, L. (2008). Muscle performance and ankle joint mobility in long-term patients with diabetes. *BMC: Musculoskeletal Disorder, 4*(9), 99.

Ginat, D. T., Destounis, S. V., Barr, R. G., Castaneda, B., Strang, J. G., & Rubens, D. J. (2009). US elastography of breast and prostate lesions. *Radiographics, 29*(7), 2007-2016.

Gokulakrishnan, K., Monhanavalli, K. T., Monickaraj, F., Mohan, V., & Balasubramanyam, M. (2009). Subclinical inflammation/ oxidation as revealed by altered gene expression profiles in subjects with impaired glucose tolerance and type 2 diabetes patients. . *Molecular & Cellular Biochemistry, 324*(1-2), 173-181.

Gooding, G. A., Stess, R. M., Graf, P. M., Moss, K. M., Louie, K. S., & Grunfeld, C. (1986). Sonography of the sole of the foot: evidence for loss of foot pad thickness

in diabetes and its relationship to ulceration of the foot. *Investigative Radiology, 21*(1), 45-48.
Gordois, A., Scuffham, P., Shearer, A., Oglesby, A., & Tobian, J. A. (2003). The health care costs of diabetic peripheral neuropahty in the US. *Diabetes Care, 26*(6), 1790-1795.
Goulle, J.-P., Larcorix, C., & Bouige, D. (2002). Glycated hemoglobin: a useful post-mortem reference marker in determining diabetes. *Forensic Science International, 14*(128(1-2)), 44-49.
Graf, A., Judge, J. O., Ounpuu, S., & Thelen, D. G. (2005). The effect of walking speed on lower-extremity joint power among elderly adults who exhibit low physical performance. *Archives of Physical Medicine and Rehabilitation, 86*(11), 2177-2183.
Grant, W. P., Sullivan, R., Sonenshine, D. E., Adam, M., Slusser, J. H., Carson, K. A., et al. (1997). Electron microscopic investigation of the effects of diabetes mellitus on the Achilles tendon. *The Journal of Foot and Ankle Surgery, 36*(4), 272-278.
Gregg, E. W., Beckles, G. L., Williamson, D. F., Leveille, S. G., Langlois, J. A., Engelgau, M. M., et al. (2000). Diabetes and physical disability among older US adults. *Diabetes Care*, *23*(9), 1272-1277.
Gutierrez, E. M., Helber, M. D., Dealva, D., Ashton-Miller, J. A., & Richardson, J. K. (2001). Mild diabetic neuropathy affects ankle motor function. *Clinical Biomechanics, 16*(6), 522-528.
Hajrasouliha, A. R., Tavakoli, S., Esteki, A., Nafisi, S., & Noorolahi-Moghaddam, H. (2005). Abnormal viscoelastic behaviour of passive ankle joint movement in diabetic patients: an early or a late complication? . *Diabetologia, 48*(6), 1225-1228.
Hase, K., & Stein, R. B. (1999). Turning strategies during human walking. *Journal of Neurophysiology, 81*(6), 2914-2922.
Hazime, F. A., Allard, P., Ide, M. R., Siqueira, C. M., Amorim, C. F., & Tanaka, C. (2012). Postural control under visual and proprioceptive perturbations during double and single limb stances: insights for balance training. *Journal of Bodywork and Movement Therapies, 16*(2), 224-229.
Herdman, S. J. (1993). Balance rehabilitation: background, techniques, and usefulness. In G. P. Jacobson, C. W. Newman & J. M. Kartush (Eds.), *Handbook of balance function testing* (pp. 392-406). St Louis: Mosby Year Book.
Higgins, J. P. T., & Altman, D. G. (2008). Assessing risk of bias in included studies. In J. P. T. Higgins & S. Green (Eds.), *Cochrane Handbook for Systematic Reviews of interventions*.
Hilton, T. N., Tuttle, L. J., Bohnert, K. L., Mueller, M. J., & Sinacore, D. R. (2008). Excessive adipose tissue infiltration in skeletal muscle in individuals with obesity, diabetes mellitus, and peripheral neuropathy. *Physical Therapy, 88*(11), 1336-1344.
Hoch, M. C., Staton, G. S., & McKeon, P. O. (2011). Dorsiflexion range of motion significantly influences dynamic balance. . *Journal of Science and Medicine in Sport, 14*(1), 90-92.
Howe, T. E., Rochester, L., Neil, F., Skelton, D. A., & Ballinger, C. (2011). Exercise for improving balance in older people. *Cochrane Database of Systmeatic Reviews*(11).

Hurvitz , E. A., Richardson, J. K., Werner, R. A., Ruhl, A. M., & Dixon, M. R. (2000). Unipedal stance testing as an indicator of fall risk among older outpatients. *Archives of Physical Medicine and Rehabilitation, 81*(5), 587-591.

Ijzerman, T. H., Schaper, N. C., Melai, T., Meijer, K., Willems, P. J., & Savelberg, H. H. (2012). Lower extremity muscle strength is reduced in people with type 2 diabetes, with and without polyneuropathy, and is associated with impaired mobility and reduced quality of life. *Diabetes Research and Clinical Practice, 95*(3), 345-351.

Iversen, M. M., Tell, G. S., Hanestad, B. R., Østbye, T., Graue, M., & Midthjell, K. (2009). History of foot ulcer increases mortality among individuals with diabetes. *Diabetes Care, 32*(12), 2193-2199.

Jones, R., Carter, J., Moore, P., & Wills, A. (2005). A study to determine the reliability of an ankle dorsiflexion weight-bearing device. *Physiotherapy, 91*(4), 242-249.

Jonsson, E., Seiger, A., & Hirschfeld, H. (2004). One-leg stance in healthy young and elderly adults: a measure of postural steadiness? . *Clinical Biomechanics, 19*(7), 688-694.

Jung, D. (2008). Fear of falling in older adults: comprehensive review. *Asian Nursing Research, 2*(4), 214-222.

Kaesler, D. S., Mellifont, R. B., Swete Kelly, P., & Taaffe, D. R. (2007). A novel balance exercise program for postural stability in older adults: a pilot study. *Journal of Bodywork and Movement Therapies, 11*(1), 37-43.

Kemoun, G., Thoumie, P., Boisson, D., & Guieu, J. D. (2002). Ankle dorsiflexion delay can predict falls in the elderly. *Journal of Rehabilitation Medicine, 34*(6), 278-283.

Kerrigan, D. C., Todd, M. K., Croce, U. D., Lipsitz, L. A., & Collins, J. J. (1998). Biomechanical gait alterations independent of speed in the healthy elderly: evidence for specific limiting impairment. *archives of Physical Medicine and Rehabilitation, 79*(3), 317-322.

Kim, C., Hwang, A. R., & Yoo, J. S. (2004). The impact of a stage-matched intervention to promote exercise behaviour in participants with type 2 diabetes. *International Journal of nursing Studies, 41*(8), 833-841.

Kim, C. J., & Kang, D. H. (2006). Utility of a web-based intervention for individuals with type 2 diabetes. *CIN: Computers, Informatic, Nursing, 24*(6), 337-345.

King, D. K., Estabrooks, P. A., Strycker, L. A., Toobert, D. J., Bull, S. S., & Glasgow, R. E. (2006). Outcomes of a multifaceted physical activity regimen as part of a diabetes self-management intervention. . *Annals of Behavioral Medicine, 31*(2), 128-137.

Klaesner, J. W., Commean, P. K., Hastings, M. K., Zou, D., & Mueller, M. J. (2001). Accuracy and reliability testing of a portable soft tissue indentor. *IEEE Transactions on Neural System and Rehabilitation Engineering, 9*(2), 232-240.

Konradsen, L., Ravn, J. B., & Sorensen, A. L. (1993). Proprioception at the ankle: the effect of anaesthetic blockade of ligament receptors. . *Journal of Bone & Surgery-British Volume, 75*(3), 433-436.

Krouskop, T. A., Dougherty, D. R., & Vinson, F. S. (1987). A pulsed Doppler ultrasonic system for making noinvasive measurements of the mechanical properties of soft tissue. *Journal of Rehabilitation Research and Development, 24*(2), 1-8.

Kruse, R. L., Lemaster, J. W., & Madsen, R. W. (2010). Fall and balance outcomes after an intervention to promote leg strengthm balance and walking in people with

diabetic peripheral neuropathy:” Feet First” randomized controlled trial. *Physical Therapy, 90*(11), 1568-1579.
Kwan, R. L., Zheng, Y. P., & Cheing, L. Y. (2010). The effect of aging on the biomechanical properties of plantar soft tissue. *Clinical Biomechanics, 25*(6), 601-605.
Lam, P., Dennis, S. M., Diamond, T. H., & Zwar, N. (2008). Improving glycaemic and BP control in type 2 diabetes: The effectiveness of tai chi. *Australian Family Physician, 37*(10), 884-887.
Lambers, S., van Laethem, C., van Acker, K., & Calders, P. (2008). Influence of combines exercise training on indices of obesity, diabetes and cardiovascular risk in type 2 diabetes patients. *Clinical Rehabilitation*, *22*(6), 483-492.
Larose, J., Sigal, R. J., Boule, N. G., Wells, G. A., Prud'homme, D., Fortier, M. S., et al. (2010). Effect of exercise training on physical fitness in type 2 diabetes mellitus. *Meidcine & Science in Sports & Exercise*, *42*(8), 1439-1447.
Lau, J. C., Li-Tsang, C. W., & Zheng, Y. P. (2005). Application if tissue ultrasound palpation system (TUPS) in objective scar evaluation. *Burns, 31*(4), 445-452.
Launer, L. J., Harris, T., Rumpel, C., & Madans, J. (1994). Body mass index, weight change, and risk of mobility disability in middle-aged and older women. *The Journal of the American Medical Association*, *271*(14), 1093-1098.
Lehtola, S., Koistinen, P., & Luukinen, H. (2006). Falls and injurious falls late in home-dwelling life. *Archives of Gerontology and Geriatrics, 42*(2), 217-224.
Levinger, I., Goodman, C., Hare, D. L., Jerums, G., & Selig, S. (2007). The effect of resistance training on functional capacity and quality of life in individuals with high and low numbers of metabolic risk factors. *Diabetes Care, 30*(9), 2205-2210.
Li, J. X., Xu, D. Q., & Hong, T. (2009). Changes in muscle strength, endurance, and reaction of the lower extremities with Tai Chi intervention. *Journal of Biomechanics, 42*(8), 967-971.
Liu, M., Hsu, W., Lu, T., Chen, H., & Liu, H. (2010). Patients with type II diabetes mellitus display reduced toe-obstacle clearance with altered gait patterns during obstacle-crossing. *Gait & Posture, 31*(1), 93-99.
Lord, S. R., Murray, S. M., Chapman, K., Munro, B., & Tiedemann, A. (2002). Sit-to-stand performance depends on sensation, speed, balance, and psychological status in addition to strength in older people. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 57*(8), M539-543.
MacGilchrist, C., Paul, L., Ellis, B. M., Howe, T. E., Kennon, B., & Godwin, J. (2010). Lower-limb risk factors for falls in people with diabetes mellitus. *Diabetic Medicine, 27*(2), 162-168.
Maiorana, A., O’Driscoll, G., Goodman, C., Taylor, R., & Green, D. (2002). Combined aerobic and resistance exercise improves glycemic control and fitness in type 2 diabetes. *Diabetes Research and Clinical Practice, 56*(2), 115-123.
Mak, A. F., Lie, G. H., & Lee, S. Y. (1994). Biomechanical assessment of below-knee residual limb tissue. *Journal of Rehabilitation Research and Development*, *31*(3), 188-198.
Makishita, H., & Matsunaga, K. (2008). Differences of drivers’ reaction times according to age and mental workload. *Accident Analysis and Prevention, 40*(2), 567-575.

Mathias, S., Nayak, U. S., & Isaacs, B. (1986). Balance in elderly patients: the "Get-Up and Go" Test. *Archives of Physical Medicine and Rehabilitation, 67*(6), 387-389.
Matsuda, P. N., Shumway-Cook, A., & Ciol, M. A. (2010). The effects of a home-based exercise program on physical function in frail older adults. *Journal of Geriatric Physical Therapy, 33*(2), 78-84.
Menz, H. B., Lord, S. R., & Fotzpatrick, R. C. (2004). Walking stability and sensorimotor function in older people with disabetic peripheral neurpathy. *Archives of Physical Medicine and Rehabilitation, 85*(2), 245-252.
Menz, H. B., & Morrison, M. E. (2006). Clinical determinants of plantar forces and pressures during walking in older people. *Gait & Posture, 24*(2), 229-236.
Merza, T., & Tesfaye, S. (2003). The risk factors for diabetic foot ulceration. *The Foot, 13*(3), 125-129.
Michikawa, T., Nishiwaki, Y., Takebayashi, T., & Toyama, Y. (2009). One-leg standing test for elderly populations. *journal of Orthopaedic Science, 14*(5), 675-685.
Miller, D. K., Lui, L. Y., Perry, I. H. M., Kaiser, F. E., & Morley, J. E. (1999). Reported and measured physical functioning in older inner-city diabetic African Americans. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences., 54*(5), M230-M236.
Miller, K. L., Magel, J. R., & Hayes, J. G. (2010). The effects of a home-based exercise program on balance confidence, balance performance, and gait in debilitated, ambulatory community-dwelling older adults: a pilot study. *Journal of Geriatic Physical Therapy, 33*(2), 78-84.
Morrison, S., Colberg, S. R., Mariano, M., Parson, H. K., & Vinik, A. I. (2010). Balance training reduces falls risk in older individuals with type 2 diabetes. *Diabetes Care, 33*(4), 748-750.
Morrison, S., Colberg, S. R., Parson, H. K., & Vinik, A. I. (2012). Relation between risk of falling and postural sway complexity in diabetes. *Gait & Posture, 35*(4), 662-668.
Mueller, M. J., Diamond, J. E., Delitto, A., & Sinacore, D. R. (1989). Insensitivity, limited joint mobilty, and plantar ulcers in patients with diabetes mellitus. *Physical Therapy, 69*(6), 453-459.
Mueller, M. J., Minor, S. D., Schaaf, J. A., Strube, M. J., & Sahrmann, S. A. (1995). Relationship of plantar-flexor peak torque and dorsiflexion range of motion kinetic variables during walking. *Physical Therapy, 75*(8), 684-693.
Mueller, M. J., Zou, D., & Lott, D. J. (2005). "Pressure gradient" as an indicator of plantar skin injury. *Diabetes Care, 28*(12), 2908-2912.
Murray, H. J., Young, M. J., Hollis, S., & Boulton, A. J. (1996). The association between callus formation, high pressure and neuropathy in diabetic foot ulceration. *Diabetic Medicine, 13*(11), 979-982.
Nather, A., Neo, S. H., Chionh, S. B., Liew, S. C., Sim, E. Y., & Chew, J. L. (2008). Assessment of sensory neuropathy in diabetic patients without diabetic foot problems. *Journal of Diabetic Complications, 22*(2), 126-131.
Negri, C., Bacchi, E., Morgante, S., Soave, D., Marques, A., Menghini, E., et al. (2010). Supervised walking groups to increase physical activity in type 2 diabetic patients. *Diabetes Care, 33*(11), 2333-2335.

Ng, T. K., & Cheing, G. L. (2011). *Physical characteristics over the ankle joint predicts the mobility performance for elderly with type II diabetes*. Paper presented at the 13th Hong Kong Diabetes & Cardiovascular Risk Factor-East Meets West Symposium, Hong Kong.

Ng, T. K., Lo, S. K., & Cheing, G. L. (2012). The association between physical characteristics over the ankle joint and the mobility performance of elderly people with type 2 diabetes. *Archives of Physical Medicine and Rehabilitation, Under review*.

Norris, J. A., Granata, K. P., Mitros, M. R., Byrne, E. M., & Marsh, A. P. (2007). Effect of augmented plantarflexion power on preferred walking speed and economy in young and older adults. *Gait & Posture, 25*(4), 620-627.

Orendurff, M. S., Segal, A. D., Berge, J. S., Flick, K. C., Spanier, D., & Klute, G. K. (2006). The kinematics and kinetics of turning: limb asymmetries associated with walking a circular path. *Gait & Posture, 23*(1), 106-111.

Orozco, L. J., Buchleitner, A. M., Gimenez-Perez, G., Roque i Figuls, M., Richter, B., & Mauricio, D. (2008). Exercise or exercise and diet for preventing type 2 diabetes. *Cochrane Database of Systmeatic Reviews*(3).

Orr, R., Tsang, T., Lam, P., Comino, E., & Singh, M. F. (2006). Mobility impairment in type 2 diabetes. *Diabetes Care, 29*(9), 2120-2122.

Ozdirenc, M., Kocak, G., & Guntekin, R. (2004). The acute effects of in-patient physiotherapy program on functional capacity in type II diabetes mellitus. *Diabetes Research and Clinical Practice, 64*(3), 167-172.

Park, S. W., Goodpaster, B. H., Strotmeyer, E. S., de Rekeneire, N., Harris, T. B., Schwartz, A. V., et al. (2006). Decreased muscle strength and quality in older adults with type II diabetes: the health, aging, and body composition study. *Diabetes, 55*(6), 1813-1818.

Park, S. W., Goodpaster, B. H., Strotmeyer, E. S., Kuller, L. H., Broudeau, R., Kammerer, C., et al. (2007). Accelerated loss of skeletal muscle strength in older adults with type 2 diabetes. *Diabetes Care, 30*(6), 1507-1512.

Perry, S. B., Marchetti, G. F., Wagner, S., & Wilton, W. (2006). Predicting caregiver assistance required for sit-to-stand following rehabilitation for acute stroke. *Journal of Neurologic Physical Therapy: JNPT, 30*(1), 2-11.

Petre, M., Erdemir, A., & Cavanagh, P. R. (2008). An MRI-compatible foot loading device for assessment of internal tissue deformation. *Journal of Biomechanics, 41*(2), 470-474.

Podsiadlo, D., & Richardson, S. (1991). The timed "Up & Go": a test of basic functional mobility for frail elderly persons. . *Journal of American Geriatrics Society, 39*(2), 142-148.

Portney, L. G., & Watkins, M. P. (2000). *Foundations of clinical research: application to practice* (2 ed.). New Jersey: Prentice Hall.

Praet, S. F., van Rooij, E. S., Wijtvliet, A., Boonman-de Winter, L. J., Enneking, T., Kuipers, H., et al. (2008). Brisk walking compare with an individualised medical fitness programme for patients with type 2 diabetes: a randomised controlled trial. *Diabetologia, 51*(5), 736-746.

Ramsey, S. D., Newton, K., Blough, D., McCulloch, D. K., Sandhu, N., Reiber, G. E., et al. (1999). Incidence, outcomes, and cost of foot ulcers in patients with diabetes. *Diabetes Care, 22*(3), 382-387.

Redfern, M. S., Yardley, L., & Bronstein, A. M. (2001). Visual influences on balance. *Journal of Anxiety Disorder, 15*(1-2), 81-94.

Reiber, G. E., Vileikyte, L., Boyko, E. J., Aguila, M. D., Smith, D. G., Lavery, L. A., et al. (1999). Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. *Diabetes Care, 22*(1), 157-162.

Reihsner, R., Melling, M., Pfeiler, W., & Menzel, E. J. (2000). Alteration of biomechanical and two-dimensional biomechanical properties of human skin in diabetes mellitus as compared to effects of in vitro non-enzymatic glycation. *Clinical Biomechanics (Bristol, Avon), 15*(5), 379-386.

Reimer, R. C. r., & Wilkstrom, E. A. (2010). Functional fatigue of the hip and ankle musculature cause similar alterations in single leg stance postural control. *Journal of Science and Medicine in Sport, 13*(1), 161-166.

Ribeiro, F., Teixeira, F., Brochado, G., & Oliveira, J. (2009). Impact of low cost strength training of dorsi- and plantarflexors on balance and functional mobility in institutionalized elderly people. *Geriatric and Gerontology International, 9*(1), 75-80.

Richardson, J. K., Sandman, D., & Vela, S. (2001). A focused exercise regimen improves clinical measures of balance in patients with peripheral neuropathy. *Archives of Physical Medicine and Rehabilitation, 82*(2), 205-209.

Rome, K., Webb, P., Unsworth, A., & Haslock, I. (2001). Heel pad stiffness in runners with plantar heel pain. *Clinical Biomechanics, 16*(10), 901-905.

Rosengren, K. S., Rajendran, K., Contakos, J., Chuang, L. L., Peterson, M., Doyle, R., et al. (2007). Changing control strategies during standard assessment using computerized dynamic posturography with older women. . *Gait & Posture, 25*(2), 215-221.

Salsich, G. B., Mueller, M. J., & Sahrmann, S. A. (2000). Passive ankle stiffness in subjects with diabetes and peripheral neuropathy versus and age-matches comparison group. *Physical Therapy, 80*(4), 352-362.

Sayer, A. A., Gilbody, H. J., Dennison, E. M., Phillips, D. I. W., Syddall, H. E., & Cooper, C. (2005). Type 2 diabetes, muscle strength, and impaired physical function. The tip of the iceberg. *Diabetes Care, 28*(10), 2541-2542.

Schneider, K. L., Pagoto, S. L., Handschin, B., Panza, E., Bakke, S., Liu, Q., et al. (2011). Design and methods for a pilot randomized clinical trial involving exercise and behavioral activation to treat comorbid type 2 diabetes and major depressive disorder. *Mental Health and Physical Activity, 4*(1), 13-21.

Schwartz, A. V., Hiller, T. A., Sellmeyer, D. E., Resnick, H. E., Gregg, E., Ensrud, K. E., et al. (2002). Older women with diabetes have a higher risk of falls. *Diabetes Care, 25*(10), 1749-1754.

Scott-Okafor, H. R., Silver, K. K., Parker, J., Almy-Albert, T., & Gardner, A. W. (2001). Lower extremity strength deficits in peripheral arterial occlusive disease patients iwht intermittent claudication. *Angiology, 52*(1), 7-14.

Sefton, J. M., Hicks-Little, C. A., Hubbard, T. J., Clemens, M. G., Yengo, C. M., Koceja, D. M., et al. (2009). Sensorimotor function as a predictor of chronic ankle instability. *Clinical Biomechanics*, *24*(5), 451-458.

Sekir, U., Yildiz, Y., Hazneci, B., Ors, F., & Aydin, T. (2007). Effect of isokinetic training on strength, functionality and proprioception in athletes with functional ankle instability. *Knee Surgery, Sports Traumatology, Arthroscopy, 15*(5), 654-664.

Shumway-Cook, A., Brauer, S., & Woollacott, M. (2000). Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Physical Therapy, 80*(9), 896-903.

Simmons, R. W., Richardson, C., & Deutsch, K. (1997). Limited joint mobility if the ankle in diabetic patients with cutaneous sensory deficit. *Diabetes Research and Clinical Practice, 37*(2), 137-143.

Sleet, D. A., Moffett, D. B., & Stevens, J. (2008). CDC's research portfolio in older adult fall prevention: a review of progress, 1985-2005, and future research directions. *Journal of Safety Research, 39*(3), 259-267.

Smith, K. E., Commean, P. K., Mueller, M. J., Robertson, D. D., Pilgram, T., & Johnson, J. (2000). Assessment of the diabetic foot using spiral computed tomography imaging and plantar pressure measurements: A technical report. *Journal of Rehabilitation Research and Development, 37*(1), 31-40.

Sorensen, K. L., & Hollands, M. A. P., A.E. . (2002). The effects of human ankle muscle vibration on posture and balance during adaptive locomotion. *Experimental Brain Research. , 143*(1), 24-36.

Spink, M. J., Fotoohabadi, M. R., Wee, E., Hill, K. D., Lord, S. R., & Menz, H. B. (2011). Foot and ankle strength, range of motion, posture, and deformity are associated with balance and functional ability in older adults. *Archives of Physical Medicine and Rehabilitation, 92*(1), 68-75.

Steffen, T. M., Hacker, T. A., & Mollinger, L. (2002). Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berh Balance Scale, Timed Up & Go Test and gait speeds. *Physical Therapy, 82*(2), 128-137.

Tessier, D., Menard, J., Fulop, T., Ardilouze, J., Roy, M., Dubuc, N., et al. (2000). Effects of aerobic physical exercise in the elderly with type 2 diabetes mellitus. *Archives of Gerontology and Geriatrics, 31*(2), 121-132.

Thomas, D., Elliott, E. J., & Naughton, G. A. (2009). Exercise for type 2 diabetes mellitus. *Cochrane Database of Systmeatic Reviews*(1).

Thomas, P. K. (1999). Diabetic peripheral neuropathies: their cost to patient and society and the value of knowledge of risk factors for development of intervention. *European Neurology, 41(suppl 1)*, 35-43.

Tiedemann, A., Sherrington, C., Close, J. C., & Lord, S. R. (2011). Exercise and sports science Australia position statement on exercise and falls prevention in older people. *Journal of Science and Medicine in Sport, 14*(6), 489-495.

Tiedemann, A., Sherrington, C., & Lord, S. R. (2005). Physiological and psychological predictors of walking speed in older community-dwelling people. *Gerontology, 51*(6), 390-395.

Tilling, L. M., Darawil, K., & Mary, B. (2006). Falls as a complication of diabetes mellitus in older people. *Journal of Diabetes and Its Complications 20*(3), 158-162.

Tinetti, M. E., Speechley, M., & Ginter, S. F. (1988). Risk factors for falls among elderly people living in the community. *New England Journal of Medicine, 319*(26), 1701-1707.

Tsang, T., Orr, R., Lam, P., Comino, E., & Singh, M. F. (2007). Health benefits of Tai Chi for older patient s with type 2 diabetes: The "Move It for Diabetes Study"- A randomized controlled trial. *Clinical Interventions in Aging, 2*(3), 429-439.

Tsang, W. W., Wong, V. S., Fu, S. N., & Hui-Chan, C. W. (2004). Tai chi improves standing balance control under reduced or conflicting sensory conditions. *Archives of Physical Medicine and Rehabilitation, 85*(1), 129-137.

Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus. (2011). Geneva: World Health Organization.

Vadstrup, E. S., Frolic, A., Perrild, H., Borg, E., & Roder, M. (2009). Lifestyle intervention for type 2 diabetes patients-trial protocol of The Copenhagen type 2 diabetes rehabilitation project. *BMC Public Health, 29*(9), 166.

van Deursen, R. W., & Simoneau, G. G. (1999). Foot and ankle sensory neuropathy, proprioception, and postural stability. *Journal of Orthopaedic & Sports Physical Therapy 29*(12), 718-726.

van Iersel, M. B., Munneke, M., Esselink, R. A., Benraad, C. E., & Olde Rikkert, M. G. (2008). Gait velocity and the timed up and go test were sensitive to changes in mobility in frail elderly patients. *Journal of Clinical Epidemiology, 61*(2), 186-191.

van Sloten, T. T., Savelberg, H. H., Duimel-Peeters, I. G., Meijer, K., Henry, R. M., Stehouwer, C. D., et al. (2011). Peripheral neuropathy, decreased muscle strength and obesity are strongly associated with walking in persons with type 2 diabetes without manifest mobility limitation. *Diabetes Research and Clinical Practice, 91*(1), 32-39.

Vela, S. A., Lavery, L. A., Armstrong, D. G., & Anaim, A. A. (1998). The effect of increased weight on peak pressures: implications for obesity and diabetic foot pathology. *The Journal of foot and ankle surgery: official publication of the American College of Foot and Ankle Surgeons, 37*(5), 416-420.

Vicenzino, B., Branjerdporn, M., Teys, P., & Jordan, K. (2006). Initial changes in posterior talar glide and dorsiflexion of the ankle after mobilization with movement in individuals with recurrent ankle sprain. *Journal of Orthopaedic & Sports Physical Therapy, 36*(7), 464-471.

Visser, M., Pahor, M., Taaffe, D. R., Goodpaster, B. H., Simonsick, E. M., Newman, A. B., et al. (2002). Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly mean and women: the Health ABC Study. *Journal of Gerontology. Series A. Biological Sciences and Medical Sciences., 57*(5), M326-M332.

Weinstock, R. S., Brooks, G., Palmas, W., Morin, P. C., Teresi, J. A., Eimicke, J. P., et al. (2011). Lessened decline in physical activity and impairment of older adults with diabetes with telemedicine and pedometer use: results from IDEATel study. *Age and Ageing, 40*(1), 98-105.

Westlake, K. P., Wu, Y., & Culham, E. G. (2007). Seonsory-specific balance training in older adults: effect on position, movement, and velocity sense at the ankle. *Physical Therapy, 87*(5), 560-568.

Wild, S., Roglic, G., Greenm, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: Estimaties of the year 2000 and projections for 2030. *Diabetes Care, 27*(5), 1047-1053.

Winter, D. A., Patla, A. E., Frank, J. S., & Walt, S. E. (1990). Biomechanical walking pattern changes in the fit and healthy elderly. *Physical Therapy, 70*(6), 340-347.

Zheng, Y., & Mak, A. F. (1999). Effective elastic properties of lower limb soft tissues from manual indentation experiment. *IEEE Transactions on Rehabilitation Engineering, 7*(3), 257-267.

Zheng, Y. P., Choi, Y. K., Wong, K., Chan, S., & Mak, A. F. (2000). Biomechanical assessment of plantar foot tissue in diabetic patients using an ultrasound indentation system. *Ultrasound in Medicine and Biology, 26*(3), 451-456.

Zheng, Y. P., Huang, Y. P., Zhu, Y. P., Wong, M., He, J. F., & Huang, Z. M. (2012). Development of a foot scanner for assessing the mechanical properties of plantar soft tissue under different bodyweight loading in standing. *Medical Engineering & Physics, 34*(4), 506-511.

Zheng, Y. P., Li, Z. M., Choi, A. P., Lu, M. H., & Huang, Q. H. (2006). Ultrasound palpation sensor for tissue thickness and elasticity measurement- Assessment of transverse carpal ligament. *Ultrasonics, 22;44 Suppl1:e*, 313-317.

Zheng, Y. P., & Mak, A. F. (1996). An ultrasound indentation system for biomechanical properties assessment of soft tissues in-vivo. *IEEE Transactions on Biomedical Engineering, 43*(9), 912-918.

Zheng, Y. P., Mak, A. F., & Lue, B. (1999). Objective assessment of limb tissue elasticity: Development of a manual indentation procedure. . *journal of Rehabilitation Research and Development, 36*(2), 71-85.