EFFECT OF AN EXERCISE TRAINING PROGRAMME ON MUSCULAR STRENGTH, ANKLE MOBILITY, BALANCE AND GAIT PATTERNS IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY IN THE LOWER LEGS

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A thesis submitted in fulfilment of the requirements for the degree
Magister Scientiae in Biokinetics,

in the Department of Sport, Recreation, and Exercise Science
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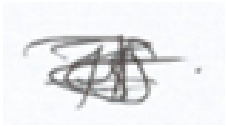
March 2021

DECLARATION

I hereby declare that "Effects of an exercise training programme on muscular strength, ankle mobility, balance and gait patterns in patients with diabetic peripheral neuropathy in the lower legs" is my own work, that it has not been submitted before for any other degree or examination at any other university, and that the sources I have used have been indicated and acknowledged as completed references.



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ABSTRACT

Background: Patients who suffer from diabetic peripheral neuropathy in the leg experience a greater risk of developing gait deviations due to a decrease in strength of the lower extremities, especially the tibialis anterior and triceps surea muscle groups.

Aim: The aim of the study was to determine the effect of an exercise training programme on blood pressure, fasting blood glucose, muscle strength, range of motion, balance and gait pattern deviations in patients with diabetic neuropathies.

Methods: A total of fourteen participants, who had been diagnosed with diabetic peripheral neuropathy or nocturnal allodynia in either one or both extremities, were asked to participate in this study. Participants were purposively selected from two private Podiatry practices based on their signs and symptoms of diabetic neuropathy, age, gender and doctor's clearance to participate in any form of physical activity. Dependent variables included isometric strength of the muscles surrounding the hip, knee and ankle, the range of motion of the ankle in plantarflexion and dorsiflexion using goniometry, an assessment of balance using the stork stand test, and a gait pattern analysis, using the modified Tinetti Gait pattern Assessment Scale.

Study design: The study was a single-blinded, pre-test and post-test experimental study design using a quantitative approach.

Intervention: The researcher (a registered biokineticist) developed a scientifically-based exercise intervention programme to specifically target the entire kinetic chain, and to reduce fall risks, improve quality of life and to assist in developing a standard protocol for patients with DPN. The intervention programme consisted of a combination of ankle, hip and knee rehabilitation, including gait pattern specific rehabilitation. The intervention took place 2-3 times a week for 45 minutes per session and was divided in four categories: Range of motion

exercises, strengthening exercises, balance and proprioception and gait pattern training exercises.

Results: The Mann-Whitney and Wilcoxon Sign Rank Tests were used to evaluate the differences in dependent variables from pre- to post-intervention. The level of significance was set at $p<0.05$. An increase in range of motion only in the left ankle dorsiflexion were observed and an increase in balance time for the left leg were observed in the intervention group after a 10-week follow up assessment. Clinical significance was observed in the intervention group, post-intervention, with a decrease in systolic (-9.09%) and diastolic blood pressure (-13.89%) and a decrease in blood glucose levels (-17.89%), however, an increase in these variables was observed in the control group post-intervention. An increase in plantarflexion, 8% (left) and 8% (right) and dorsiflexion 5.26% (left) and an 11.11% (right) increase in range of motion for both left and right ankles, and balance time for both legs, 200% (left) and 159% (right) was observed in the intervention group post-intervention. Although the muscular strength variables showed a mix of an increase and decrease in strength post-intervention in the intervention group, however a clinically significant decreased amount was observed in the control group post-intervention for the majority of muscular strength variables.

Conclusions: Although not many findings of this study are statistically significant, clinical significance were observed with most of the variables of this study. The findings of this study can assist future researchers in the development of exercise interventions for patients who suffers from DPN.

Keywords: Diabetic autonomic neuropathy, Diabetic nerve pain, Distal polyneuropathy, Hyperglycaemia, Peripheral neuropathy, Pressure Air Biofeedback system.

ACKNOWLEDGEMENTS

Firstly, I would like to express my sincere gratitude and appreciation to my study Supervisor, Prof. S.H. Bassett for her continuous guidance, encouragement and extensive knowledge throughout the course of the study.

Secondly, my special thanks to my study Co-Supervisor, Ms. Nadia Dembskey for her continuous encouragement, valuable suggestions, immense knowledge and patience throughout the course of the study. I appreciate her assistance in getting patient numbers and making her private practice available for data collection in Alberton, Johannesburg.

Also, to Ms. Megan Maddocks who assisted in recruiting patients and making her private practice available for data collection in Sandton, Johannesburg.

At last, thank you to all the participants for their cooperation that made this study possible.

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LIST OF ABBREVIATIONS (as they appear in-text)

AGEs	Advanced Glycation End Products
AR	Aldose Reductase
DM	Diabetes Mellitus
DPN	Diabetic Peripheral Neuropathy
IDF	International Diabetes Federation
PAB	Pressure Air Biofeedback
PKC	Protein Kinase C
ROS	Reactive Oxygen Species

DEFINITIONS

The following definitions/clarification of terminology has been provided for a clearer understanding of the content:

Arthrokinematics – Articulation of joint surfaces (Loudon & Bell, 1996).

Arthrogenic muscle response (ARM) – The ongoing reflex reaction of the surrounding musculature once there has been damage to the joint structures (Sendory, McVey, Cross, Ingersoll & Hertel, 2007).

Diabetic sarcopenia - Sarcopenia as a progressive decrease in muscle mass and muscular strength (Jang, 2016).

Dorsiflexion – Moving the foot towards to shin (Thelen, Schultz, Alexander & Ashton-Miller, 1996).

Hypoxia - A decrease in oxygen availability under physiological stress (Pierson, 2000).

Myo-inositol – Helps with the utilization of insulin (Bruschi et al., 2017; Zuchowska, Rojewska, Prezewlocka & Mika, 2013).

Plantarflexion – Ankle movement towards the ground (Thelen et al., 1996).

Polyneuropathy – Common disorder of the peripheral nervous system (Sommer et al., 2018).

Polyol pathway - The polyol pathway is also known as the sorbitol-aldose reductase pathway. It is a two-step metabolic process where glucose is converted into fructose. During this process, glucose is reduced to sorbitol which is later oxidized into fructose (Bruschi et al., 2017; Zuchowska et al., 2013).

Vasa Nervorum – Blood supply to peripheral nerves (Amenta, Mione & Napoleone, 1983)

CHAPTER 1

INTRODUCTION

1.1. Background

Diabetes mellitus (DM) is a metabolic disorder that affects one's quality of life. It is characterised by hyperglycaemia, hyperlipidaemia and hyper aminoacidemia, as a result of a deficit of the secretion of the β-cells in the pancreas or from peripheral resistance to insulin action, or both (Bruschi et al., 2017; Nagwa, Badr, Shawkya, Fouad & Hamdy, 2010; Ozougwa, Obimba, Belonwu & Unakalamba, 2013). However, DM is a "silent disease" in that glucose levels can be increased for years, with little or no symptoms, before a diagnosis is made (Skyler et al., 2017). Approximately, 2.1% of the world's population suffer from DM (Ozturk, Turkbeyler, Demir, Bilici & Kepekei, 2018), which currently affects over 420 million people worldwide (Hingorani et al., 2016; International Diabetes Federation [IDF], 2015). The prevalence of DM is still increasing rapidly each year (Ozougwa et al., 2013). As a result, DM can have a major impact on one's quality of life due to high risk complications that may be either chronic or acute (Bruschi et al., 2017; Sartor et al., 2012; Singh, Kishore & Kaur, 2014). Chronic implications of DM can be associated with neuropathic changes that affect the longest nerve axons at their proximal end, known as diabetic peripheral neuropathy (DPN) (Bruschi et al., 2017; Suda, Gomes, Butugan & Sacco, 2016).

Since DM frequently results in peripheral neuropathies, the end result is associated with reduced muscle strength and balance, gait impairment and decreased ankle stability (El-Refay & Ali, 2014; Katoulis et al., 1997). Aerobic and resistance training is of great benefit to DM patients, as it is an effective way to control blood glucose levels and enhance insulin action up to 72 hours (Gangwar, 2015). These parameters need to be targeted specifically in any rehabilitation programme designed for people with diabetic peripheral neuropathy.

1.2. Statement of the Problem

Diabetic neuropathy can appear in the early onset of diabetes (Danjo, Danjo, Sawada, Uchida & Nakamura, 2018). According to Yagihashi, Mizukami and Sugimoto, (2011) there are several risk factors associated with the progression of DPN, such as the glycated haemoglobin levels, which leads to the increased risk of the development of DPN, including poor blood glucose control, hypertension, hyperlipidaemia, smoking and the duration of diabetes mellitus. Elevated blood glucose levels lead to small nerve fibre involvement, which can result in sharp shooting pain and dysesthesia (Bril, Breiner, Perkins & Zochodne, 2018).

High glucose levels in the blood are associated with decreased muscle strength due to a decrease in the glucose uptake by the muscle, which also contributes to postural sway (Mustapa, Justine, Mustafah, Jamil & Manaf, 2016). During diabetic neuropathy, muscles can be affected either singly or symmetrically as well as one muscle group at a time or several different muscle groups at a time (Hillson, 2017).

Thus, DPN changes related to the lower limbs may vary and lead to altered gait biomechanics as a result of reduced ankle range of motion, a decrease in muscular strength in the muscles of the ankle joint as well as a decrease in efficient lower extremity kinematics (El-Refay & Ali, 2014; Kluding et al., 2017). Lower extremity injuries can be caused by various factors such as an increase in body mass and altered hip biomechanics. Lower extremity malalignment is often caused by altered foot mechanics and lower extremity stiffness (Neal at al., 2014). Bone mineral density (BMD) has been shown to be decreased in the calcaneus in DPN patients (Wrobel & Najafi, 2010). According to Wrobel and Najafi (2010) BMD in the calcaneus is 16% lower in the foot with a deformity compared to the foot without a deformity.

1.3. Aims and Objectives

The aim of this study was to investigate the effect of an exercise training programme intervention on blood pressure, fasting blood glucose, muscular strength, range of motion, balance and gait patterns in people with peripheral diabetic neuropathy in the lower legs. A secondary aim was to monitor any changes in blood pressure and blood glucose levels throughout the intervention and to develop a new of parameters to assist clinicians in the treatment of DPN.

The main objectives of this study were to:

1. evaluate the effect of an exercise training programme on clinical variables (systolic and diastolic blood pressure and blood glucose) in patients with peripheral diabetic neuropathy in the lower legs.
2. evaluate the effect of an exercise training programme on muscular strength in patients with peripheral diabetic neuropathy in the lower legs.
3. evaluate the effect of an exercise training programme on range of motion in patients with peripheral diabetic neuropathy in the lower legs.
4. evaluate the effect of an exercise training programme on balance in patients with peripheral diabetic neuropathy in the lower legs.
5. evaluate the effect of an exercise training programme on gait patterns in patients with peripheral diabetic neuropathy in the lower legs.

1.4. Hypotheses

It was hypothesised that:

1. clinical variables (systolic and diastolic blood pressure and blood glucose) levels in patients with peripheral diabetic neuropathy in the lower legs would decrease as a result of an exercise training programme.

2. muscular strength in patients with peripheral diabetic neuropathy in the lower legs would increase as a result of an exercise training programme.
3. range of motion in patients with peripheral diabetic neuropathy in the lower legs would increase as a result of an exercise training programme.
4. balance time in patients with peripheral diabetic neuropathy in the lower legs would increase as a result of an exercise training programme.
5. gait patterns in patients with diabetic peripheral neuropathy in the lower legs would improve as a result of an exercise training programme.

1.5. Significance of the Study

In patients with DM, the pathophysiological changes that take place result in an imbalance between the degeneration and the regeneration of nerve fibres. All peripheral nerves are affected by diabetic neuropathies, which subsequently affect pain fibres, motor neurons and the autonomic nervous system (Zuchowska, Rojewska, Prezewlocka & Mika, 2013). This involves degeneration of the neurons and the axons, a decrease in nerve fibre size and demyelination of nerve fibres (Cancelliere, 2016; Vuckovic-Rebrina, Barada & Smiricic-Duvnjak, 2013). Altered muscle function subsequently occurs and neural origins are affected (McLeod, Gribble & Pietrosimone, 2015). Structural changes within the connective tissue also occur in patients with DM, such as increased collagen type III, loss of fascicular organization, increased cross-linking and breakdown in collagen fibrils (Nagwa et al., 2010).

Glucose intolerance contributes to chronic axonal neuropathy and small fibres are first affected. Tissue ischemia of peripheral nerves can be caused by the inhibition of nitric oxide-mediated vasodilation in DM patients (Duarte, 2017). Damage to small fibres in the early onset of DM leads to early impairment of pain and temperature sensations (Duarte, 2017). Diabetic sarcopenia is one of the main musculoskeletal complications in patients with diabetic peripheral neuropathy with upper and lower body muscular weakness being

demonstrated in DM patients, but lower extremity muscular weakness was more evident (Abadi, Salahzadeh, Rezaei, Oskouei & Azghani, 2017; Nenkova, Stewart, Potterton & Becker, 2009). These muscular strength changes result in impaired gait patterns in DPN patients (Nenkova et al., 2009).

Proper assessments and intervention programmes will guide clinicians to identify physical characteristics where improvements are required (Williams et al., 2016). It is important for clinicians to understand the effect of DPN on muscular strength, balance and gait to be able to prescribe adequate rehabilitation protocols to improve the quality of life of DPN patients (Camargo et al., 2015). According to El-Refay and Ali (2014), patients who suffer from DPN should follow a rehabilitation-based exercise programme to strengthen lower limb muscles with a progressive increase in resistance (El-Refay & Ali, 2014). Streckmann et al. (2014) and Gangwar (2015) suggest that DPN patients should participate in an exercise intervention to benefit from the effect of exercise on the metabolic factors such as glycemic control and insulin sensitivity. Exercise has also been shown to improve neuromuscular control in patients with diabetic peripheral neuropathy (Brazeau, Rabasa-Lhoret, Strychar & Mircescu, 2008; Streckmann et al., 2014).

CHAPTER 2

LITERATURE REVIEW

2.1. Introduction

The prevalence of DPN increases each year and has become one of the most leading causes of disability in diabetic patients. According to the literature, the researcher developed a new set of parameters to assist clinicians in the assessment and treatment of DPN as there are no current research protocols available to assist clinicians in the assessment of DPN.

2.2. Diabetes Mellitus

Diabetes mellitus is a metabolic disease that is characterized by an increase in blood glucose concentration as a result of either insufficient insulin production, insulin resistance or both (Zuchowska et al., 2013). There are two main types of DM, Type I, also known as insulin dependent diabetes mellitus, and Type II, known as non-insulin dependent diabetes (IDF, 2015; Ozougwu et al., 2013).

2.2.1. Type I diabetes mellitus

Type I DM is an autoimmune reaction of the islet cells of the pancreas in which the β-cells reduce or stop producing insulin (Gupta, Sharma & Sharma, 2015; Ozougwu et al., 2013). It was originally called juvenile diabetes because it was mainly diagnosed in young children aged four or five years, or in the early teens; however, it is now known that type I DM as it can affect people of all ages. The onset of type I DM occurs once the end stage of the β-cells occurs (Ozougwa et al., 2013).

2.2.2. Type II diabetes mellitus

Type II DM is a progressive metabolic disease with progressive chronic complications due to the severity/duration of diabetes (Leibowitz, Kaiser & Ceras, 2011). Type II DM is caused by a decreased sensitivity of target tissues to insulin with older individuals at higher risk for its development (IDF, 2015; Lee & Halter, 2017; Olokoba et al., 2012; Ozougwa et al., 2013). The insulin-responsive glucose transporter protein, GLUT4, transport glucose into skeletal and cardiac muscle and adipose tissue (Kanzaki, 2006). In the absence/decrease in insulin available, the remainder of GLUT4 is stored in small intracellular vesicles, also known as GLUT4 storage vesicles (GSVs) and insulin responsive vesicles (IRVs) (Stockli, Fazakerley & James, 2011) (Figure 2.1).

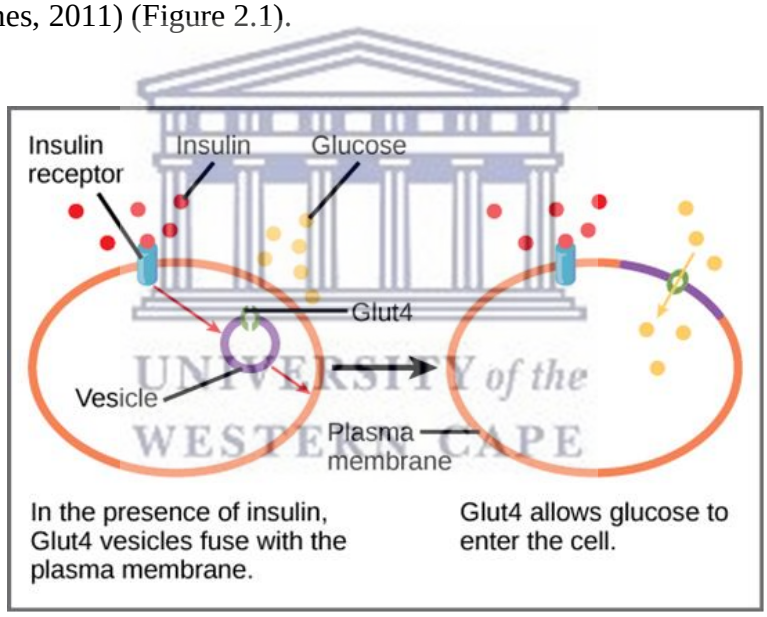


Figure 2.1: Insulin-mediated GLUT4 translocation
(Roach & Harel, 2019)

As with type I Diabetes, the net result is an increase in blood glucose concentration due to a decreasing uptake and utilization of glucose by the cells in the body as well as an increase in utilisation of fats and proteins for energy production (Ozougwa et al., 2013). The effect of an increase in insulin resistance on glucose metabolism is to prevent or decrease the uptake and utilisation of glucose by the cells in the body, except for the cells of the brain.

With type II DM, there is a progressive deterioration of metabolic factors that lead to a progressive decrease of β-cells in the pancreas. A decrease in β-cells is associated with a decrease of the function, number of β-cells and/or both. In type II DM, there are structural abnormalities in islets cells, and a decrease in β-cells (Leibowitz et al., 2011). According to Leibowitz et al. (2011) there is approximately a 50-60% decrease in β-cell mass, dependent on the severity and duration of DM, in type II DM regardless of appropriate and adequate lifestyle modifications/changes. β -cell mass is dependent on the duration of diabetes. With an increase in hyperglycaemia and the duration of DM leads to a decline/decrease in β-cell mass (Leibowitz et al., 2011). Insulin resistance and β-cell dysfunction leads to type II diabetes mellitus. Impaired insulin secretion results in β-cell dysfunction (Cerf, 2013).

Increased blood fatty acid levels contribute to insulin resistance as well as the deterioration of β-cell function (Singh et al., 2014). Type II DM patients develop hyperglycaemia due to an imbalance of glucose production and glucose intake and an increase in the breakdown of fat (Lee & Halter, 2017; Olokoba et al., 2012; Gupta et al., 2015). Skyler et al. (2017) and Olokoba et al. (2012) say that type II DM occurs when the β-cells cannot secrete enough insulin due to an increased demand of insulin due to the ectopic fat deposition in the liver and muscles. Accumulation of fat in the pancreas contributes to a decline in β-cell function, inflammation of islet cells and a decrease in the β-cells (Skyler et al., 2017). Thus, hyperglycaemia is a result of both tissue sensitivity and β-cell insulin secretion capacity (Lee & Halter, 2017).

Factors such as lifestyle play a role in the development of type II diabetes mellitus. Preventative measures such as lifestyle modifications, dietary modifications and controlling and managing weight can be followed to prevent type II DM in patients. Preventative measures can also be adjusted and tailored to improve quality of life for DM patients (Olokoba et al., 2012).

2.3. Diabetic Peripheral Neuropathy

Diabetic peripheral neuropathy (DPN) is one of the main complications of DM and can be classified as a decrease in sensation and proprioception in the distal extremities (Azhary, Farooq, Bhanushali, Majid & Kassab, 2010). Diabetic neuropathy is a result of nerve damage caused by uncontrolled high blood glucose levels and is a common complication of DM, affecting up to 50% of patients suffering from both types of diabetes (Gangwar, 2015; Nagwa et al., 2010). Iqbal et al. (2018) refer to diabetic neuropathy as "a collection of clinically diverse disorders affecting the nervous system with differing anatomic features, clinical courses and phenotypes". The prevalence of DPN ranges from 7% within the first year of the onset of DM to 50% within 25 years of its onset (Yagihashi et al., 2011). Azhary et al. (2010) state that DPN occurs in 8% of patients aged 55 years and older, hence a large part of the diabetic population is made up of geriatrics (Azhary et al., 2010). According to the Centers of Disease Control and Prevention, approximately 26.9% of geriatrics are older than 65 years and suffers from type II diabetes mellitus (Gates & Walker, 2014).

The Toronto consensus panel recently defined DPN as, "a symmetrical length-dependent sensorimotor polyneuropathy attributed to metabolic and micro vessel alterations, resulting from chronic hyperglycaemia and cardiovascular risk co-varieties" (Petropoulos et al., 2016; Singh et al., 2014). Jambert et al. (2011) define neuropathic pain as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system". Various risks add to the development of diabetic neuropathy such as the duration of DM, ischemia of the peripheral nerves, glycaemic variability and poor glycaemic control (Bruschi et al., 2017; Cancelliere, 2016; Suda et al., 2016; Singh et al., 2014). This condition refers to peripheral nerve dysfunction and can be classified according to nerve distribution; including polyneuropathy, mononeuropathy and mononeuropathy multiplex.

Symptoms of DPN may consist of atypical pain, numbness, pins and needles and/or hot and burning sensations (Hamed & Monem, 2018; Petropoulos et al., 2016; Singh et al., 2014; Suda et al., 2016) with patients often experiencing more pain and discomfort at night. Symptoms can be classified into sensory symptoms, such as vibratory and tactile sensitivity, prickling/pain sensations and motor symptoms, such as motor dysfunction (Suda et al., 2016). Signs and symptoms of DPN start in the toes and move proximally, once the symptoms are established in the lower limbs, the upper limbs are affected with sensory loss in a "glove and stocking" pattern (Camargo et al., 2015; Singh et al., 2014). Camargo et al. (2014) add by saying that, due to the sensory-motor system being affected, soft tissue damage occurs, there is a decrease in muscular strength, changes in foot structure, altered gait biomechanics and a decrease in balance and proprioception. Postural control is also affected by DPN, which leads to an increased risk of falling. As DM progresses, DPN patients will experience symptomatic muscle weakness (Camargo et al., 2015; Singh et al., 2014).

2.3.1. Pathophysiology of diabetic peripheral neuropathy

Being a pathology of the nervous system, peripheral neuropathy affects gait patterns in diabetic patients due to a decrease in efferent peripheral sensory information as well as a decrease in the cortical centers involved in processing this sensory information (Courtemanche et al., 1996; Maksimovic et al., 2016). Do Nascimento, Pupe and Cavalcanti, (2016) and Pop-Busui et al. (2017) added by saying that "diabetic neuropathies are a group of heterogeneous conditions that affect different parts of the nervous system and present with a diverse group of clinical manifestations". The Toronto Diabetic Neuropathy Expert group (Iqbal et al., 2018) classified DPN as: 1) confirmed DPN (abnormal nerve conduction), 2) probable DPN (patients experience two or more symptoms) and 3) possible DPN (patients experience symptoms such as a decrease in sensation or a decrease in distal sensation).

Yagihashi et al. (2011) explain in detail how hyperglycaemia leads to peripheral nerve injury during diabetic peripheral neuropathy. The perineurium covers the peripheral nerves and trans-perineurial arterioles penetrate into the endoneurium to supply the peripheral nerves. Blood supply to the peripheral nerves is limited, which compromises autoregulation that in turn leads to ischemia of the peripheral nerves. Endoneurial micro vessels are connected in the inner surface with endothelial cells. The endoneurial tissue is affected when the endoneurial micro vessels leak. During DM, the innervation of the epineurial micro vessels are involved, which results in impaired blood supply in diabetic nerves, leading to diabetic peripheral neuropathy.

Furthermore, the neural cell body is small and the axonal neurites are long. Distal axons are too weak to be able to support themselves to transport nutrients. During DPN, it is the degeneration of distal and sensory nerve fibres that is affected which leads to endoneurial micro-angiopathy. Microvascular injury of the predominant axon is a leading cause of diabetic peripheral neuropathy. Nerve injury is a result of axonal injury, hyperglycaemia, insulin resistance and endothelial injury (Singh et al., 2014). Patients with DPN may experience sensory changes in their feet, which leads to gait pattern abnormalities and improper pressure distribution through their feet; as well as a longer stance phase and shorter stride length when walking (Petrofsky, Macnider, Navarro & Lee, 2005). With DPN, the peroneal nerve that supplies the tibialis anterior muscle is usually the first affected muscle, which contributes to a lack of sensorial and kinaesthetic information from the ankle (El-Refay & Ali, 2014). Muscle weakness and atrophy leads to a decrease in ankle reflexes and a decreased sensation of the distal extremities (Azhary et al., 2010). Since DPN is a microvascular complication, patients have a higher risk of falling due to a lack of postural control and gait stability (Mustapa et al., 2016; Petrofsky et al., 2005).

In diabetics, the pathophysiological changes that take place result in an imbalance between the degeneration and the regeneration of the nerve fibres. In terms of anatomy, peripheral nerves are made up of bundles of long neuronal axons, each wrapped with a myelin sheath, containing Schwann cells, that is divided by Nodes of Ranvier.

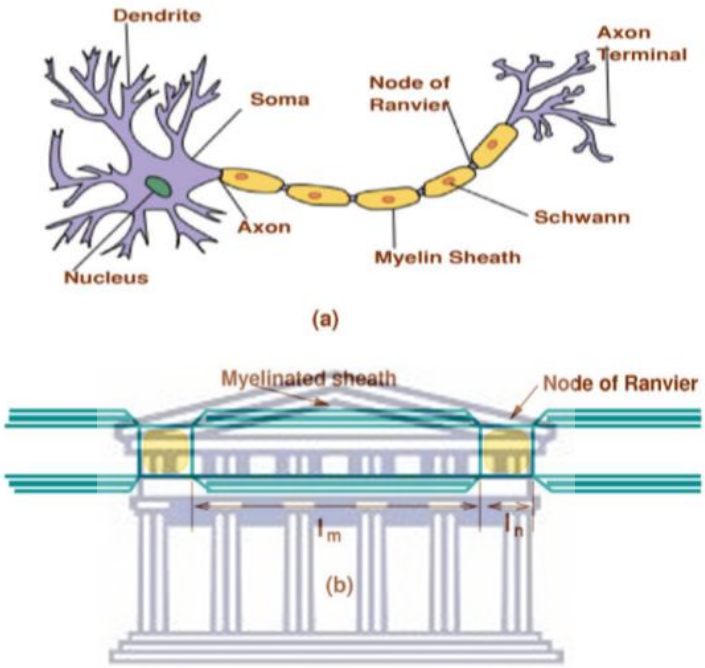


Figure 2.2: Anatomy of peripheral nerves
(Kim, Davidson, Rohrle, Soboleva & Pullen, 2007)

Peripheral nerves are responsible for different functions such as motor, sensory and autonomic functions (Azhary et al., 2010). All peripheral nerves are affected by diabetic neuropathies, which subsequently affect pain fibres, motor neurons and the autonomic nervous system (Zuchowska et al., 2013). This includes degeneration of the neurons and the axons, a decrease in nerve fibre size and demyelination of nerve fibres (Vuckovic-Rebrina, et al., 2013). As a result, altered muscle function occurs and neural origins are affected. A phenomenon known as arthrogenic muscle response (McLeod, Gribble & Pietrosimone, 2015) is characterized by abnormal inhibition of the neural drive to the uninjured muscular surroundings (McLeod et al., 2015). Structural changes within the connective tissue also

occur in patients with DM, such as increased collagen type III, loss of fascicular organization, increased cross-linking and breakdown in collagen fibrils (Nagwa et al., 2010). According to Sorensen, Trenell, Siddall and Yue, (2008), there are various studies that have investigated the central nervous system after peripheral nerve injuries have been diagnosed, which show structural and biomechanical changes.

Diabetic neuropathy is also a complication of the development of free radicals, oxidants and metabolic factors, known collectively as oxidative stress. Chronic hyperglycaemia can lead to microvascular cell damage and hypoxia in various ways, such as via the polyol pathway through generation of reactive oxygen species (ROS) as well as by nitrogen (Bruschi et al., 2017). Cell damage can also be caused by the accumulation of advanced glycation end-products (AGE) which results in cell damage and death (Bruschi et al., 2017; Zuchowska et al., 2013). A depletion of myo-inositol is also one of the main causes of diabetic neuropathy (Bruschi et al., 2017; Zuchowska et al., 2013). Various pathogenic mechanisms, such as increased cytokine release and inadequate activation of protein kinase C (PKC) pathways, may also result in diabetic neuropathy by directly damaging nerve cells or indirectly damaging the vasa nervorum (do Nascimento et al., 2016; Vuckovic-Rebrina et al., 2013). Cancelliere (2016), Maekawa et al. (2001) and Singh et al. (2014) and add by saying that the development of DPN can be divided into four pathways: polyol pathway, non-enzymatic glycation of proteins resulting in AGE, activation of PKC and increased hexosamine pathway flux (Figure 2.3.) (Yang, Fang, Xiang & Yang, 2019).

An increased polyol flux, which is regulated by aldose reductase (AR), contributes to the development of DPN in diabetes mellitus (Feldman, 2003; Yagihashi et al., 2011). Parasoglou, Rao and Slade (2017) agree and add by saying that an increased polyol flux, AGE, PKC and oxidative stress are associated with metabolic derangements. During the polyol pathway (first mechanism) the enzyme, aldose reductase plays an important role. This

enzyme decreases toxic aldehydes when the glucose concentration in the cells becomes increasingly high. Aldose converts glucose into sorbitol, which is then oxidized into fructose (Cancelliere, 2016; Negi, Kumar, Joshi & Sharma, 2011).

Advanced glycation end products (AGE) damage cells in four various mechanisms where the endothelial cells are involved and intracellular proteins are modified. In the second mechanism, AGE diffuses out of the cell and extracellular matrix molecules, changing the correspondence between the matrix and the cell involved, which leads to cellular dysfunction. This can be seen at the cross linking of collagen as well as the tendon and ligament pathology, which takes place during diabetic peripheral neuropathy. The third mechanism is when AGE products diffuse from the cell and changes the proteins in the blood such as albumin. The production and release of inflammatory cytokines and growth factors are a result of the active AGE products, which in turn, lead to vascular pathology (Cancelliere, 2016). Protein kinase-C (PKC) activation is responsible when hyperglycaemia increases the synthesis of diacylglycerol that is responsible for activation of the protein PKC pathway and resultant changes in Schwann cell metabolism (Cancelliere, 2016). The final pathway during DPN is known as the hexosamine pathway during which changes to gene expression take place (Cancelliere, 2016).

2.4 Prevalence of Diabetic Peripheral Neuropathy

The world is currently experiencing an increase in the prevalence of diabetes mellitus (Ganu, Fletcher & Caleb, 2016). In both urban and rural areas of the world with 64% of those affected living in urban areas and 36% in rural areas (Ganu et al., 2016). Regions such as Sub-Saharan Africa have recently experienced an increase in the prevalence of diabetes mellitus (Ganu et al., 2016).

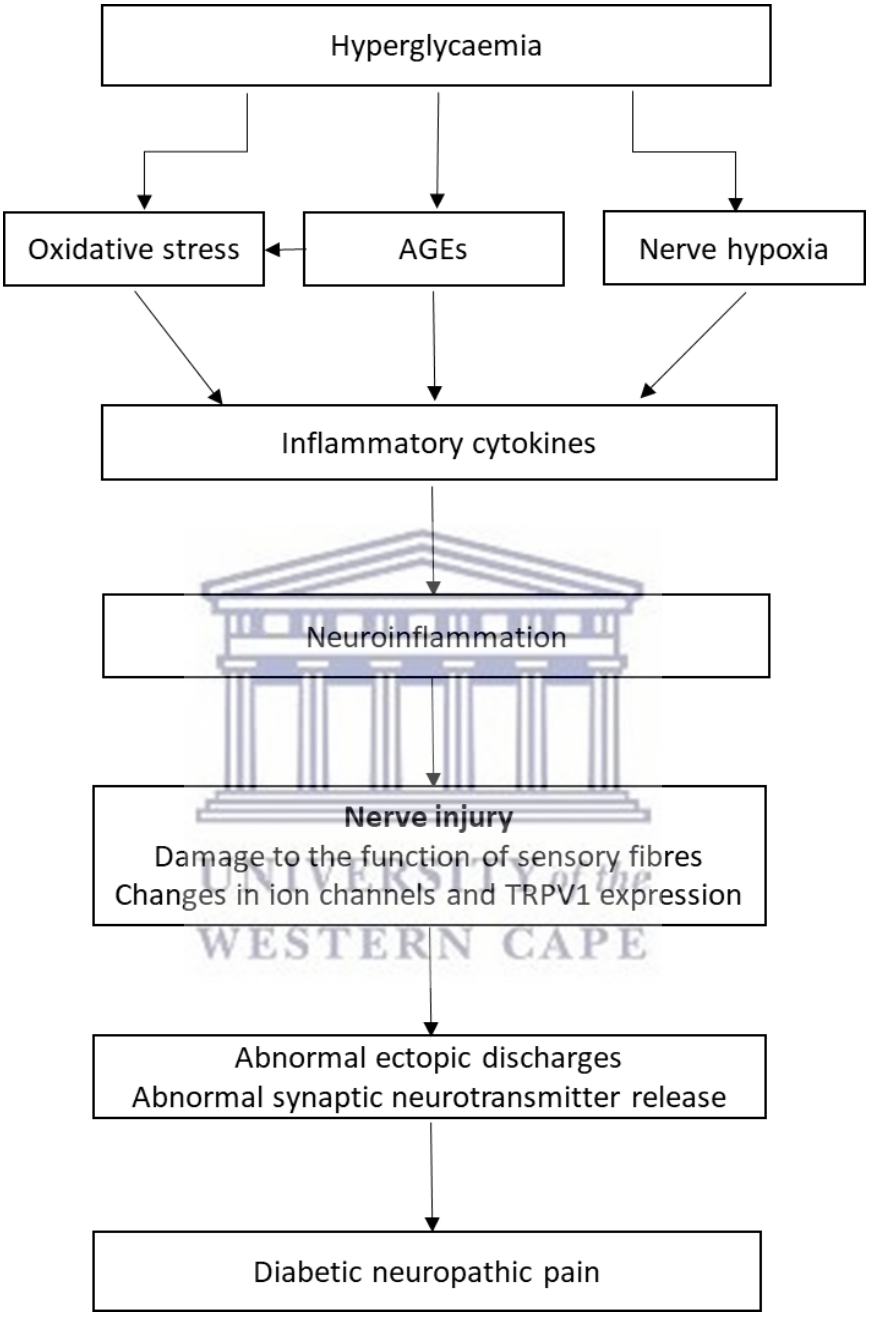


Figure 2.3: Pathogenesis of diabetic peripheral neuropathy
(Yang et al., 2019)

In 2010, it was estimated that more than 21 million people in Africa would be living with type II DM, but the estimate is now 23.9 million (Ganu et al., 2016). The International Diabetes Federation (2015) noted that the number of people with type II diabetes in Sub-Saharan Africa is expected to increase from 14.2 million in 2015 to 34.2 million by 2040. Further it has been estimated by the World Health Organization (WHO) that in 2030, type II DM will overtake all other non-communicable diseases (NCDs) and will be one of the leading causes of mortality in Africa (Ganu et al., 2016). Thus, people living in Africa are amongst the highest percentage living with DM, and have the highest risk of developing other chronic complications (Ganu et al., 2016). According to Petropoulos et al. (2016), the prevalence of DM in the Middle East and North Africa regions was 12.5% and would increase to 14.3% in the year 2030, which would be the highest in the world. In South Africa, the most common form of DM is type II with less than 10% reported cases being type I. In an audit conducted in 1997, of 300 people with DM in Cape Town, 27% had diabetic neuropathy (Levitt, Bradshaw, Zwarenstein, Bawa & Maphumolo, 1997). However, the current prevalence of DM in South Africa is unknown (Jacovides et al., 2014). They further note that the IDF estimated that 7.04% (3.5 million) of the total population in South Africa will have DM and over 1.5 million will have undiagnosed diabetes mellitus by 2025. Thus, it appears that a large proportion of individuals in South Africa may be susceptible to diabetic peripheral neuropathy and that more research needs to be conducted in this area. Jacovides et al. (2014) state that "DPN is inadequately treated in South Africa" and a course of action must be implemented to improve its diagnosis and management.

2.5 Sarcopenia

A diverse variety of functional disabilities and metabolic imbalances occur due to a decrease in muscle mass and strength, also known as sarcopenia (Camargo et al., 2015; Jang, 2016),

which is a chronic complication of diabetes mellitus (Shu, Matarese & Santulli, 2019). Thus, diabetic sarcopenia is associated with systematic insulin resistance, which is related to mobility disorders and is associated with an increased fall risk in DM patients (Pani, Cavallucci & Bartoccioni, 2016). Thus, DPN leads to diabetic sarcopenia, which leads to a decrease in muscle activation and a decrease in myofascial structures (Camargo et al., 2015).

Furthermore, diabetic sarcopenia can develop in combination with obesity. An increased adiposity can impair muscle response to insulin due to an increased release of saturated fatty acids (Pani et al., 2016). Myopathies and other musculoskeletal complications are associated with DM, which decreases one's quality of life. Myopathies are characterized by muscle weakness, decreased muscle mass and a decreased physical activity participation level (Santos, Silva, Albuquerque, Oliveira & Caiaffo, 2016). As a result of a decrease of muscle mass and muscle strength, degeneration of the sarcoplasmic proteins occurs and there is a decrease in muscle activation rates. Also, the axons from these muscle fibres are reinnervated from the nearby motor units, known as axonal sprouting (Ferreira et al., 2017), that causes an increase in muscle fibre density.

Patients with DM experience a change in muscle fibre types, especially type II muscle fibres. Type I muscle fibres are sensitive and experience an increase in intracellular calcium concentration (Suda et al., 2016). Patients with DM may experience premature fatigue and a decrease in exercise tolerance due to the change in type I and type II muscle fibre types (Suda et al., 2016).

2.5.1 Effect of insulin on nerve innervation

A decrease in the number of motor neurons due to high glucose levels in patients with DM leads to diabetic neuropathy and the prevalence of sarcopenia in diabetes mellitus increases (Jang, 2016). Degeneration of the nerves affect sensory, motor and autonomic components

of the peripheral nerves and results in a decrease in muscular strength of the foot and ankle (El-Refay & Ali, 2014). Any strength deficit in the tibialis anterior muscle affects the ankle joint and results in atrophy of the intrinsic foot muscles and a concomitant decrease in static and dynamic balance, which is largely responsible for gait deviations in diabetic patients (Nagwa et al., 2010; Sartor et al., 2012; Sartor et al., 2014). Patients with DPN experience a delay/prolongation and a decrease in the activation during the same stance phase in the tibialis anterior muscle and an increase in plantar loading due to a decrease in dorsiflexion and an increase passive ankle stiffness (Suda et al., 2016). Abnormal ankle loading in DM patients could lead to the development in foot ulcers, leading to an increased rate in amputations seen in DM patients. Fifty percent of lower limb amputations in DM patients are consequences of foot ulcers/charcot foot (Rao, Saltzman & Yack, 2006). Autonomic fibre involvement can occur either during DPN or during isolation (Low et al., 2004).

2.5.2 Effect of insulin on skeletal muscle

Insulin is a catabolic hormone that stimulates protein synthesis, resulting in muscle growth. When there is a deficit in insulin signalling, there is a reduction in insulin synthesis. A decrease in insulin sensitivity and regulation of glucose is a result thereof (Umegaki, 2015). Sarcopenia is strongly linked to metabolic impairments and in diabetic sarcopenia, a significant decrease in muscle mass, especially in the lower extremities, can be seen (Jang, 2016). Diabetic sarcopenia leads to an increase in visceral and intermuscular fat (Jang, 2016). Functional disability and limited range of motion is associated with DPN patients (Umegaki, 2015). Diabetic peripheral neuropathy can also be associated with a decrease in functional movement, a decrease in quality of life and a decrease in the ability to perform activities of daily living (Jambart et al., 2011). Multiple factors can be associated with diabetic sarcopenia, such as hyperglycaemia, insulin resistance, and inflammatory cytokines as well as the endocrine changes, which all contribute to its acceleration (Jang, 2016;

Umegaki, 2015). As a result of an increase in the systemic inflammatory cytokines, there is a negative effect on the muscle mass, strength and physical fitness of patients with diabetes mellitus (Jang, 2016). Advanced glycation end products (AGEs), also known as proteins or lipids which become glycated when exposed to sugars, increase and accumulate in skeletal muscle and cartilage, which results in an increase in muscular stiffness in DM patients (Jang, 2016; Negi et al., 2011; Singh et al., 2014). Peripheral neuropathy leads to metatarsophalangeal joint (MTPJ) deformity, which leads to deterioration of the foot and ankle musculature (Cheuy, Hastings, Commean & Meuller, 2016). The first MTPJ mobility/range of motion decreases in DPN patients (Wrobel & Najafi, 2010). According to Wrobel and Najafi (2010), patients who suffer from DPN have a decreased range of motion in their ankle. Hyperextension of the MTPJ occurs in DPN patients due to an imbalance between the decreased strength of the intrinsic foot muscles and the stronger extrinsic toe extensors, such as the extensor digitorum longus (Cheuy et al., 2016).

Impaired glucose regulation affects metabolic muscle function, which subsequently affects mitochondrial muscle function towards insulin due to insulin resistance. A significant decrease in muscular strength and function is a result of mitochondrial muscle dysfunction (Hewston & Deshpande, 2015). Hip alterations during walking occur due to a decrease in strength in the plantar flexion muscle group. Patients with DPN experience a decrease in movement during the late stance phase of gait. Due to the strength deficit, the patient will adapt a “hip strategy” (El-Refay & Ali, 2014; Nagwa et al., 2010; Sacco et al., 2015), where the leg is pulled forward using the hip flexors instead of using the plantar flexor muscles to push forward (ankle strategy). This phenomenon is also known as the “slowness strategy” (El-Refay & Ali, 2014; Nagwa et al., 2010; Sacco et al., 2015).

2.6 Muscle Strength

In the human body, muscle plays a vital role in movement and in the performance of daily activities (Jang, 2016). Muscle is not just responsible for movement but muscle is a major site for the storage of glucose in the human body and insulin is regulated by the insulin receptors in skeletal muscle (Umegaki, 2015), thus playing a vital role in the regulation of blood glucose levels (Han et al., 2018). Shu et al. (2019) noted that DM patients experience musculoskeletal disorders as well as morphological changes in both slow and fast twitch muscle fibres as a result of a skeletal muscle insulin resistance deficit as well as hyperinsulinemia. Patients who suffer from DPN have an increased amount of intramuscular non-contractile tissue and an increase in intramuscular tissue, which is correlated to insulin resistance and results in a decrease in the distal musculature of the triceps surea, quadriceps femoris, and hamstring and adductor muscle groups (Almurdhi et al., 2016). Muscle strength deviations present in DPN patients vary from the total amount of muscle volume present (Almurdhi et al., 2016). Patients who suffer from DM show a decrease in the diameter of the gastrocnemius type I and II muscle fibres, which results in a decrease in torque and muscle atrophy (Ferreira et al., 2017). A decrease in muscle mass indicates a decreased amount of insulin responsive target tissue, resulting in an increased development of insulin resistance, metabolic syndrome, obesity and hypertension in patients with DM (Shu et al., 2019). Thus, DM leads to metabolic and inflammatory changes that result in a decrease in muscle mass and muscle strength (Ferreira et al., 2017; Shu et al., 2019).

2.7 Gait pattern biomechanics

The decrease in muscular strength, and therefore balance, also leads to gait abnormalities (Nagwa et al., 2010; Najafi, Bharara, Talal & Amstrong, 2012). Gait patterns in diabetes mellitus patients can be severely affected, and they may present with a decreased walking

speed, shorter stride length and/or reduced mobility of the trunk and limbs. There will be an increased muscular effort to maintain balance as a result of muscular deficiencies that are present in patients with diabetic peripheral neuropathy (Brown, Handsaker, Bowling, Boulton & Reeves, 2015; Hillson, 2017; Najafi et al., 2012; Wrobel and Najafi, 2010). Wrobel and Najafi (2010) add by saying that patients who suffer from DPN also often have resultant gait instability.

Distal musculature around the foot and ankle is primarily affected by peripheral neuropathy (Azhary et al., 2010; Nagwa et al., 2010). Longstanding hyperglycaemia of the connective tissue leads to an increase in joint and muscle stiffness (Rao et al., 2006). An increase in joint and muscle stiffness, altered joint biomechanics, and altered gait result in prolonged and excessive weight bearing under the metatarsal heads (Rao et al., 2006). The peroneal nerve, which plays a big role in ankle and foot control during heel strike while walking, is commonly affected, leading to a decline in muscular strength of the tibialis anterior and triceps surea muscle groups. This ultimately results in gait deviations. There is also a decrease in plantar flexion, which contributes to alterations of the hip during walking, resulting in the hip flexors pulling the hip forward during plantar flexion instead of the hip being pushed forward by the foot (Nagwa et al., 2010). Structural changes within the connective tissue also occur, such as increased collagen type III, loss of fascicular organization, increased cross-linking and breakdown in collagen fibrils (Nagwa et al., 2010). These changes are partially responsible for the decrease in ankle mobility. Any impairment will alter movement of the limbs and add additional pressure distribution through the foot, thus having a negative effect on gait (Brown et al., 2015). The gait of people with DM is often characterized by a decrease in speed, increased double stance time and decreased single stance time (de Souza Fortaleza et al., 2014). This is commonly seen when the difficulty in walking increases, such as on irregular surfaces (El-Refay & Ali, 2014). Peripheral

neuropathy leads to a decrease in gait velocity, decreased cadence, decreased stride length, increased stance time and an increase in step-to-step variability (Hoch et al., 2014; Sacco et al., 2015).

A person's gait can be associated with quality of life and overall health and well-being (Wrobel & Najafi, 2010). To be able to maintain an effective quality of life, one should be able to maintain the optimal gait cycle while walking through complex environments and to adapt one's gait cycle with various demands during this period. Sensory input, adaptations and muscle patterns and output are required for one to perform tasks. To be able to perform a full gait cycle, one needs fully functioning bones and joints and the desired muscular strength (Wrobel & Najafi, 2010).

Within the anatomy of the ankle and foot, there is also soft tissue involved that will affect any biomechanical analysis, as well as the foot-ground interface. Biomechanics of gait patterns can be affected by the sole, gait velocity and the internal muscle activation with activity (Wrobel & Najafi, 2010), which would affect the average steps taken by day. Patients who suffer from diabetic neuropathy experience a decrease in ankle plantar- and dorsiflexion as well as a decrease in ankle power output. Co-contractions of the agonist and antagonist muscle groups are also present at the ankle and knee joints during the stance phase (Hoch et al., 2014; Meuller, Minor, Sahrmann, Schaaf & Strube, 1994; Sacco et al., 2015; Wrobel & Najafi, 2010). According to Nagwa et al. (2010) ankle mobility and the strength of the muscle supporting the ankle is affected by DM, which is one of the leading causes of gait abnormalities in these patients (El-Refay & Ali, 2014), thus a higher incidence of injuries during walking (Katoulis et al., 1997; Nagwa et al., 2010). A reduction in the maximal ankle torque can be seen in DM patients, due to the axonal reinnervation and the decrease of muscle fibre/mass (Suda et al., 2016). Diabetic patients experience an accelerated decreased muscle mass and strength over time, which leads to a higher risk of

functional disability and a decrease in mobility (Kalyani, Metter, Egan, Golden & Ferrucci, 2015).

Walking is part of our daily living activities (Pirker & Katzenschlager, 2017). Various systems such as the nervous, musculoskeletal and cardiorespiratory systems are involved. Gait patterns are influenced by various factors such as age, living circumstances, one's balance and proprioception as well as health status of the patients. Gait pattern impairments can therefore affect one's quality of life and can either be caused by neurological, orthopedic and medical conditions (Pirker & Katzenschlager, 2017). In the geriatric population, gait pattern impairments are mainly caused by a decrease in the proprioceptive function such as in polyneuropathy and frontal gait disorders such as hip and knee osteoarthritis (Pirker & Katzenschlager, 2017).

Sawacha, Guarneri, Avogaro and Cobelli (2010) identified specific gait pattern parameters in DPN patients such as shorter stride length, decreased walking speed and altered biomechanics of the lower limb and trunk mobility. According to Sawacha et al. (2010) various authors have found that alterations in gait patterns are present, and therefore best analysed in the sagittal plane.

Gait patterns can be characterized by loading and unloading of the lower limbs while specific neurological, muscular and skeletal pathologies can be characterized by various gait pattern deviations (Baker, Esquenazi, Benedetti & Desloovere, 2016; Chambers & Sutherland, 2002). Gait pattern assessments are an important clinical tool to use to ensure adequate rehabilitation protocols are followed during the rehabilitation process (Zimbelman et al., 2012). Gait pattern assessments such as the Tinetti Gait Scale (TGS) provide gait kinematics and kinetics of muscle activation to the clinician (Zimbelman et al., 2012). The TGS is widely used in clinical settings and is recommended by the American Physical Therapy

Association (APTA) for the assessing of gait and gait patterns (Zimbelman et al., 2012). The TGS is a credible tool and assists clinicians to identify the changes in gait patterns in response to gait pattern training interventions (Zimbelman et al., 2012).

2.7.1 Normal gait pattern

Pirker and Katzenschlager (2017) describe the normal gait pattern as follows: the individual raises one leg by flexing the hip and the knee; the contralateral leg and trunk muscles support the weight-bearing leg and moves/ shifts the center of gravity forward; the heel is placed on the ground and body weight is shifted to the sole of the foot towards the toes and the opposite leg is then lifted and moved forward until heel strike, which occurs during the mid-stance phase.

2.7.2 Steppage gait pattern

A steppage gait pattern occurs when the patient lifts the leg higher during the swing phase than in a normal gait pattern. With the steppage gait pattern, the patient plantar flexor muscles (tibialis posterior, peroneus longus, peroneus brevis, flexor hallucis longus and flexor digitorium longus) are unable to flex the foot, resulting in the need to lift the leg higher in order to raise the toes off the floor and prevent stumbling/tripping up (Pirker & Katzenschlager, 2017).

2.7.3 Shuffling gait pattern

A shuffling gait pattern is characterised by a slow gait with a decrease in step length, a decrease base of support, rounded shoulders, decreased lumbar curve and a forward head posture. During the shuffling gait pattern, the feet are not lifted as high as normal, which results in the shuffling of feet (Pirker & Katzenschlager, 2017).

2.8 Alterations in Balance and Proprioception

Van Deursen and Simonau (1999) describe balance as being controlled by various systems including the somatosensory, visual and vestibular systems. These systems control feedback for posture and for various muscles, joints and cutaneous mechanoreceptors, and work together to produce sensations of joint position and movement. During balance, postural orientation is important and a number of various proprioceptors play a key role including muscle spindles, Golgi tendon organs, and superficial and deep cutaneous afferents (Ulus, Akyol, Tander, Bilgici, & Kuru, 2012).

Due to progressive and long-term hyperglycaemia, deterioration of sensory nerve fibres in the somatosensory system (provide information regarding body position) take place during diabetic peripheral neuropathy. Patients who suffer from DPN experience decreased stability during static and dynamic conditions (Sawacha et al., 2010). The sensory fibres which affect DPN include 1a afferents from the muscle spindles (muscle spindles are responsible for changes taking place in muscle length), 1b afferents from the Golgi tendon organs (which sense change in muscle tension) and the cutaneous mechanoreceptors (which provide information about changes in pressure sensation) (Hewston & Deshpande, 2015; Parasoglou, et al., 2017). As a result, there is a decrease in lower-limb somatosensation in DPN, which decreases the ability to detect balance impairments and increases fall risks (Hewston & Deshpande, 2015). Due to myofascial structural changes in DPN patients, altered gait biomechanics and performance can occur (Camargo et al., 2015). Neural input from mechanoreceptors in the joints, muscles, tendons and associated tissue also play a vital role in terms of proprioception of the joint and limb position (Ulus et al., 2012). Mechanical insufficiencies include laxity, articular synovial changes, degenerative changes and arthrokinematic restrictions (Petrofsky et al., 2005).

Progressive and long-term hyperglycaemia also affects the circulatory system, which can result in diabetic retinopathy, and changes in the visual system lead to balance impairments in DPN patients (Hewston & Deshpande, 2015). The increased amount of inflammation and decreased sensitivity of the metabolic vasculature in the inner ear in diabetics results in functional and structural changes that reduce the quality of vestibular information. This leads to a decrease in head stability and inability to maintain an upright posture (Hewston & Deshpande, 2015). Patients with type I and II diabetes experience balance impairments that precede sensory loss to the feet (Petrofsky et al., 2005). These factors may contribute to the development of diabetic foot ulcers or charcot foot (Danjo et al., 2018).

A decrease in lower extremity proprioception is common in DPN patients (Grewal et al., 2013). Alterations in sensory input due to ankle instability can also be associated with deficits in postural control. This occurs when there is damage to ligamentous and capsular tissues and is due to changes in the arthrokinematics (Hoch et al., 2014). Postural instability is significantly associated in patients with diabetic peripheral neuropathy (Brown et al., 2015). For DPN patients, it is therefore of utmost importance to maintain gait stability (de Souza Fortaleza et al., 2014).

Due to the loss of gait stability, there is usually a decrease in neuromuscular control of the distal joints, which sometimes presents as a decrease in ankle joint range of motion (El-Refay & Ali, 2014). People who suffer from peripheral neuropathy show decreased mobility and stability while standing and during dynamic movement (Sawacha et al., 2012). Thus, motor dysfunction such as muscle weakness, diabetic sarcopenia, decreased joint flexibility and range of motion affect body movements in diabetic peripheral neuropathy (Almurdhi et al., 2016).

2.9 Exercise Training

As a result of long-term physical activity, mitochondrial density, insulin sensitivity and oxidative enzymes increase. Also, blood vessel reactivity, lung function and maximal cardiac output increase (Colberg et al., 2016). Shu et al. (2019) state that exercise training improves mitochondrial function as well as improved insulin sensitivity. Exercise training improves and increases muscle mass, decreases blood pressure and improves glucose tolerance (Shu et al., 2019).

During exercise, the active muscle uses stored glycogen for energy. When the muscle stores start to deplete, the insulin dependent transporter, known as Glu T4 or GLUT4, conducts glucose into the muscle cell from the bloodstream (Figure 2.4). During exercise, the blood glucose levels steadily fall as well as pancreatic insulin production, allowing the release of glucose from the liver glycogen stores (Hillson, 2017; Gangwar, 2015).

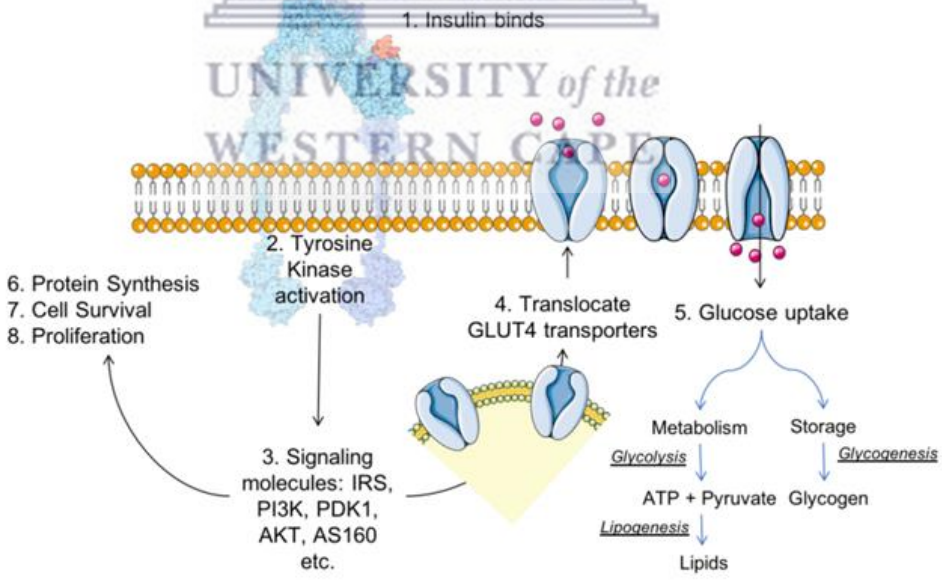


Figure 2.4: Insulin re-uptake

(Shu et al., 2019)

Structural remodeling of the skeletal muscle as well as the glucose uptake in the muscle during exercise leads to an improvement of glucose homeostasis. Due to the higher metabolic rates of glucose metabolism as a result of exercise training adaptations, glycaemic control improves (Tokmakidis, Zois, Volaklis, Kosta & Touvra, 2004). There is also a decrease in insulin resistance, an increase in muscle mass and bone density as well as a decrease in diabetic sarcopenia (Sigal et al., 2018). Figure 2.2 describes the pathophysiology of DPN and the effect of exercise on DPN (Parasoglou et al., 2017).

It is known that regular physical activity improves insulin sensitivity, and that both aerobic and resistance training improve glycaemic levels (Colberg et al., 2016; Gangwar, 2015; Sigal et al., 2018). Resistance training should be done for at least two sessions per week. The American Diabetes Association recommends physical activity of at least 150 minutes per week, over a three-day period, of moderate intensity for individuals who suffers from diabetes mellitus (Lee & Halter, 2017).

Pan and Bai (2014) state that geriatrics with DPN have an increased risk factor of falls due to impaired balance. They further state that with an appropriate balance training programme it could decrease the risk of falls. Static and dynamic balance in DPN patients are affected by factors such as a decrease in lower extremity muscular strength and range of motion (Pan & Bai, 2014). Lower extremity resistance training improves muscle mass, decrease sarcopenia and increase static and dynamic postural balance (Pan & Bai, 2014). They experience decreased ankle dorsiflexors and external rotators, thus, ankle plantar-and dorsiflexion rehabilitation (muscular strength training and range of motion/flexibility training) with gradual progression of the rehabilitation exercises improves muscular strength of the foot and ankle as well as gait pattern abilities and balance significantly (Pan & Bai, 2014).

A combination of lower limb muscle strengthening, balance and proprioceptive rehabilitation, improves range of motion, balance, muscular strength and glycated haemoglobin in older patients with diabetic peripheral neuropathy (Pan & Bai, 2014). Low-intensity exercise improves/enhances vascular and metabolic pathways, which decreases painful neuropathic symptoms and improve quality of life (Johnson & Takemoto, 2019).

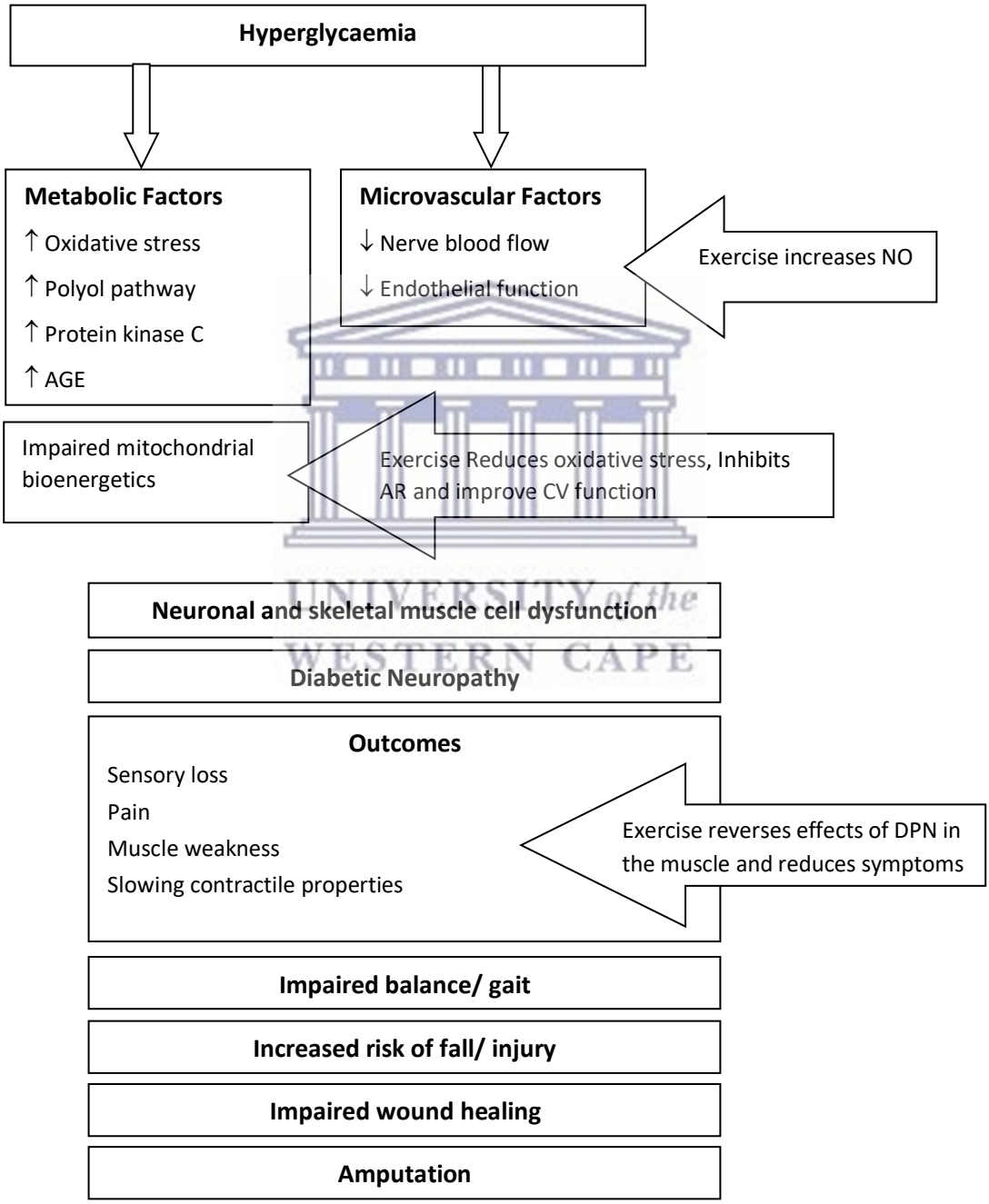


Figure 2.5: Pathophysiology of DPN and the effect of exercise on DPN *(Parasoglou et al., 2017)*

2.9.1 Muscular strength training

Muscular strength plays an important role in activities of daily living (Kwon et al., 2010). Strength training has been shown to decrease the effects of diabetic sarcopenia, increase inter- and intramuscular coordination and neural control, and increase stability and improve gait in patients with diabetic peripheral neuropathy (Streckmann et al., 2014). Increasing muscular strength of the anterior and posterior compartment of the lower leg decreases the risk of developing drop foot, which reduces the risk of falls in patients who suffer from diabetic peripheral neuropathy (Huang, Chen, Lin & Lee, 2014). Muscular strength training improves blood glucose control, insulin sensitivity and muscle function such as muscle force and muscle fibre size (Tan, Li & Wang, 2012). Furthermore, muscle strength and muscle mass have been shown to increase with resistance training, which slows down diabetic sarcopenia and improves insulin sensitivity (Colberg et al., 2016). Resistance exercise training improves metabolic adaptations such as glycaemic control and insulin uptake. Muscle mitochondrial density and oxidative capacity increases with muscular strength training (Pesta, Goncalves, Madiraju, Strasser & Sparks, 2017). Skeletal muscle is responsible for approximately 80% of insulin-mediated glucose uptake. Insulin uptake in skeletal muscle is severely reduced in patient with diabetes. Muscular strength training improves muscle mass, strength and assists with muscle hypertrophy and neuromuscular remodelling (Pesta et al., 2017). Esteghamati, Hassabi, Halabchi and Bagheri (2008) agree and add that muscular strength training improves quality of life, decrease body mass and increase bone mineral density.

2.9.2 Range of motion training/Flexibility training

Patients who suffer from DPN have a decrease joint mobility due to the AGE's that accumulate in the soft tissue of the feet, specifically in the skin, tendons, joints, bones,

collagen and fat pads (Wrobel & Najafi, 2010; Kluding et al., 2017). They experience a decrease in lower limb mobility/flexibility such as decreased ankle mobility (Boyd, Nee & Smoot, 2017). This can manifest in a significant increase in plantar aponeurosis as well as a thicker flexor hallucis longus (FHL) tendon. Having a decrease in flexibility, increases their risk for related morbidity and mortality (Boyd et al., 2017). Herroitt, Colberg and Pearson (2004) add to this by saying that flexibility training is of great benefit for individuals with DM due to a decrease in joint mobility and glycation of joint structures. Range of motion/flexibility training decreases blood glucose levels in patients with diabetes (Nelson, Kokkenhem & Arnall, 2011). Improved joint range of motion in these structures decreases pain and discomfort and decreases any risk of re-injury and injury (Esteghamati et al., 2008).

2.9.3 Balance and proprioceptive training

Diabetic peripheral neuropathy causes a great impairment in sensation in the lower extremities in patients, leading to a decrease in balance and control during activities of daily living. A decrease in balance and proprioception is caused by impaired proprioception, movement-strategy, bio-mechanical structural disorders as well as orientation (Akbari, Jafari, Moshashaee & Forugh, 2012). Incorporating balance, neuromuscular and proprioceptive training in an intervention programme improves the ability to maintain body position and enhances proprioceptive sensibility, increases afferent pathways and improves joint movement sensation (Huang et al., 2014). When balance improves, a result of training, lower limb injuries are usually reduced due to implementation of sensorimotor and neuromuscular coordination (Danjo et al., 2018). Balance and proprioceptive exercise rehabilitation are an important tool to use and incorporate in the prevention of falls in geriatrics. Balance and proprioceptive training contribute to the improvement of gait speed, stride length and cadence. In combination with other exercise intervention strategies/modalities, balance and proprioceptive exercise interventions shows as greater

improvement in functional ability in DPN patients (Ahmad, Hussain, Singla, Verma & Ali, 2017). A progressive balance and proprioceptive training programme are of long-term benefit for DPN patients, because it improves stability in the anterior-posterior compartments (Akbari et al., 2012).

2.9.4 Gait pattern training

Decreased proprioception during walking leads to slower gait speed and greater stride variability, resulting in an increased risk for falling (D'Silva, Lin, Staecker, Whitney & Kluding, 2016). Rehab and Saleh (2019) state that 39% of DPN patients have an increase of up to 10 seconds during unilateral leg stance. Alterations in gait patterns are associated with decreased ankle proprioception. To maintain a proper gait pattern, one must be able to maintain an upright posture (Pirker & Katzenschlager, 2017). A number of strategies can be employed to decrease gait deviations, decrease the risk of re-injury and enhance/improve dynamic postural stability in patients with diabetic peripheral neuropathy. These include: increasing range of motion of the ankle and trunk; lengthening the extensor and flexor hallucis longus and increasing proprioception and balance (Huang et al., 2014; Williams et al., 2016). Improvement in ankle stability, leads to improved gait pattern abnormalities in DPN patients (Rehab & Saleh, 2019).

As seen in the literature above, proper clinical evaluation and low intensity exercise training is a safer way to decrease the physiological effects of diabetic peripheral neuropathy. For the purpose of the study, the researcher used the Pressure Air Biofeedback system (PAB), an isometric measuring tool, for both study groups to evaluate isometric muscle strength and a scientifically based exercise training program for the intervention group. Thus, the aim of the research project was to explore the effectiveness of the PAB for measurements of the ankle- plantar and dorsiflexion and of a scientifically based exercise training program on

muscular strength, ankle mobility, balance and gait patterns in the treatment of DPN, and to establish a new set of clinical objective measurements for the effective and safe treatment thereof.

CHAPTER 3

METHODS AND MATERIALS

3.1. Introduction

As previously stated DPN is one of the leading causes of morbidity and mortality worldwide. The purpose of this research study was to evaluate the effectiveness of an exercise protocol that was developed for people with DPN and was different from the standard clinical protocol commonly used today. This chapter describes the research design, sampling, procedures and statistical analyses utilized to test the proposed hypotheses detailed in Chapter 1.

3.2. Research Design

The research design was a single-blinded, pre-test post-test experimental study using a quantitative approach. A single-blinded study was chosen as only the researcher knew which treatment the participants would receive, as this would have led to spurious results. The study design was chosen to evaluate muscular strength and flexibility of the ankle joint, balance and gait patterns to determine if an exercise intervention was effective treatment for patients who suffer from diabetic peripheral neuropathy in the lower leg (McCuster & Gunaydin, 2015) (Figure 3.1).

3.3. Study Setting

Participants were recruited from two private Podiatry practices, because they were an accessible source of data for the researcher (Kumar, 2014). The testing equipment was set up in both private practices for the purpose of this study. Performing this study in a clinical setting ensured that participants were assessed under the supervision of a biokineticist, who monitored the participants' glycaemic state during all exercise sessions.

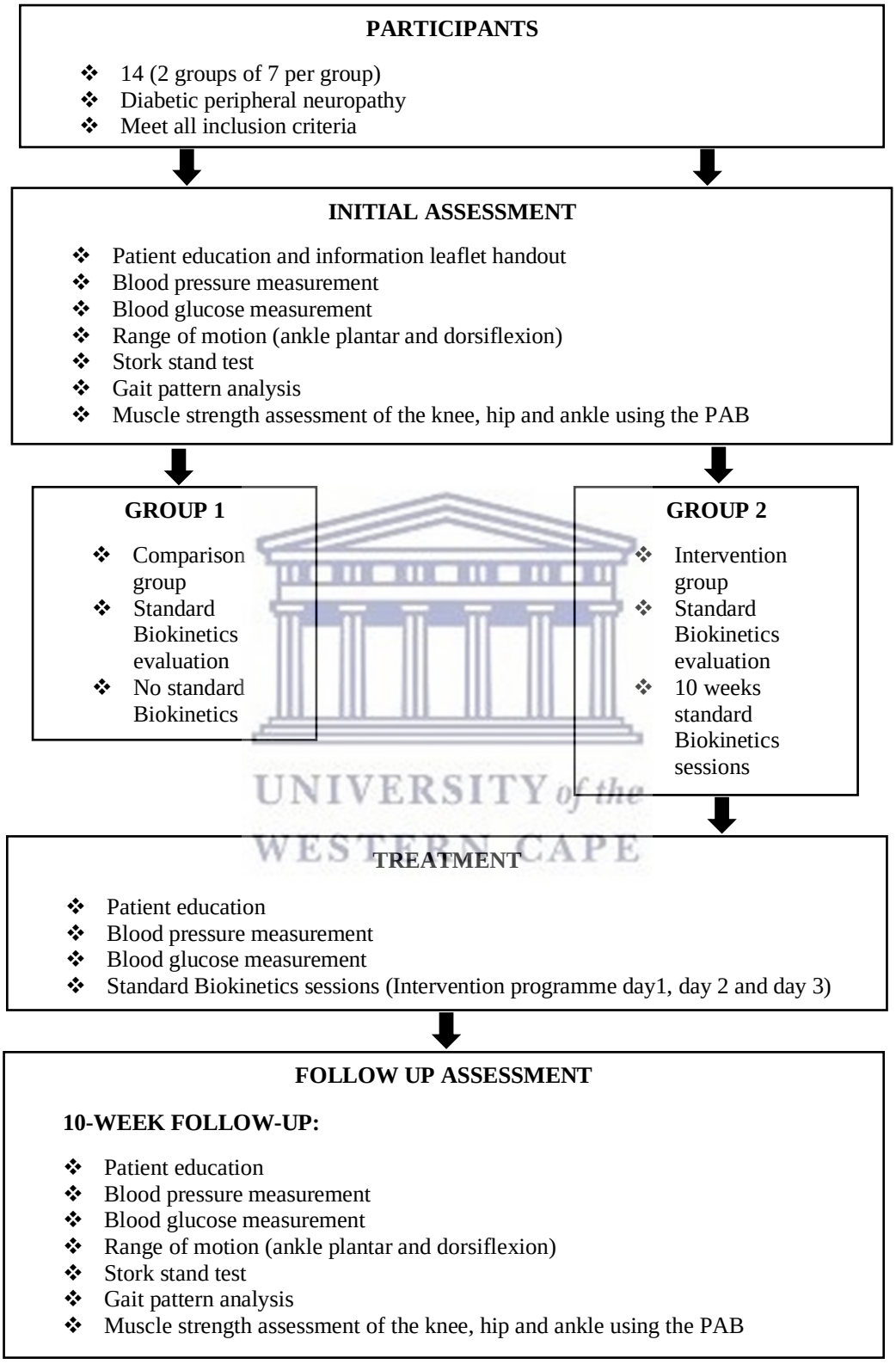


Figure 3.1: Study design flow diagram

3.4. Population and Sampling

Patient files in two Podiatry practices (see permission letter in Appendix A) were accessed to determine DM status and those with a confirmed diagnosis of DPN were recruited to be part of the study. Participants were purposely selected based on a previous diagnosis, by a doctor or Registered Podiatrist, of diabetic peripheral sensory neuropathy in one or both lower limbs. Potential participants were contacted by the Podiatrists and the study was explained to them. If they then chose to accept the invitation to participate in the study, only then did the Podiatrist put them in contact with the researcher.

The inclusion and exclusion criteria for the study were as follows:

Inclusion criteria:

- Diabetic peripheral neuropathy in one or both lower limbs
- Any age
- Male or female
- Any level of physical activity
- A pre-test health risk evaluation was conducted by the doctor before a medical release was issued.

Exclusion criteria:

- A current fracture(s) in the lower limb.
- Any participant who suffered from foot ulcers.

Those who volunteered for the study and met the inclusion criteria were given an information letter (Appendix B) describing the purpose of the study as well as the procedures of the study. If the participants agreed to participate, they were asked to sign a consent form (Appendix C), after which they became part of the research study. They were all required to acquire a clearance letter to participate in any form of physical activity from their doctor before being accepted into the study. The final study sample consisted of 14 participants,

aged 18-80 years. As DPN is a longstanding chronic condition, the age range is appropriate for this study.

3.5. Research Procedures

All 14 participants underwent pre- and post-intervention testing which consisted of: range of motion of the ankle in plantar- and dorsiflexion, through goniometry, a balance test using the stork stand test, isometric strength assessment of the muscles surrounding the hip (gluteus maximus, gluteus medius and gluteus minimus, piriformis, adductor magnus and the long head of the biceps femoris), knee (vastus lateralis, vastus medialis, vastus intermedius and rectus femoris) and ankle [the tibialis anterior, extensor hallicus longus, extensor digitorum longus and the peroneus tertius (ankle plantarflexion), and tibialis posterior, peroneus longus, peroneus brevis, flexor hallucis longus and the flexor digitorium longus (ankle dorsiflexion) muscles] joints using a pressure air biofeedback system, and gait pattern analysis. They were then randomly divided into an intervention group and a comparison group. The process of randomization was based on previous diagnosis, of diabetic peripheral sensory neuropathy in one or both lower limbs, participants symptom severity and clinical assessment done by die Registered Podiatrist. The intervention group (Group 2) received a 10-week training programme specifically designed for people with diabetic neuropathy, and the comparison group (Group 1) received standard biokinetics training sessions for 10 weeks. At the end of the study, the intervention training programme was offered to the comparison group, so that they too could benefit from the study.

3.5.1. Range of motion

Ankle plantar and dorsiflexion were assessed for ankle range of motion. The participant was asked to sit upright on a plinth, with legs straight and both ankles slightly elevated over a rolled towel. For plantarflexion, the researcher placed the fulcrum of the goniometer over the lateral malleolus with the proximal arm being placed along the fibula using the head of

the fibula for reference. The researcher aligned the distal arm parallel to the midline of the 5th metatarsal then directed the participant to point their toes, extending the ankle, and the angle of plantarflexion was measured in degrees. Each measurement was conducted three times and the mean ROM will was determined. For dorsiflexion, the researcher placed the fulcrum of the goniometer at the centre of the lateral malleolus with the proximal arm along the fibula, using the head of the fibula for reference, and aligned the distal arm parallel to the midline of the 5th metatarsal. The researcher directed the participant to pull their toes back as far as possible, flexing the ankle, and ankle dorsiflexion was measured in degrees. Each measurement was conducted three times and the mean was used as their final ROM score (Appendix E). The examiner used constant positions by stabilising the lower leg, proximal to the ankle being measured, to avoid any movements that could hinder the measurement. A goniometer suitable to measure the ankle joint was used to get the correct measurements. The participant was asked to use the same amount of force to move the ankle with each measurement to obtain successive measurements. According to Gajdosik and Bohannon (1987), the validity and reliability (r=0.58) of goniometry have been established; however, these vary for different joints, specific to the action, regional structure and function of the specific joint.

3.5.2. Balance

The stork stand test was utilised to measure static balance. A static test was used as a dynamic test would have led to an increase risk of injury and/or pain and discomfort. The participants performed the stork stand test on both legs with their shoes removed and with their hands on their hips. The non-supporting foot was placed against the inside knee of the supporting leg, as far up to the shin as possible if they could not place their foot on the knee. The time started when the heel was raised from the floor and stopped when either hand came off the hips, the supporting foot moved in any direction or when the non-supporting foot lost contact with

the knee/ shin. The amount of time that the participant was able to stand on one leg was measured in seconds (Appendix E). Panta, Arulsingh, Raj, Sinha and Rahman, (2015) indicated that the stork stand test is a valid and reliable (r=0.567~0.646) clinical test to perform to measure static balance.

3.5.3. Muscle strength

The Pressure Air Biofeedback System® (PAB) was used to measure muscular function. This device measures the force applied to an air bladder located inside the product. The device enables to clinician to test maximum isometric strength as well as fatigue performance patterns of the muscles. The duration of the test can be altered depending on the criterion being assessed. Specific movements, such as hip extension, knee extension and ankle-plantar- and dorsiflexion were conducted. These tests are designed to measure the gluteal muscle group, piriformis, adductor magnus and the long head of the biceps femoris (hip), the quadriceps femoris muscle group (knee), the tibialis anterior, extensor hallicus longus, extensor digitorum longus and the peroneus tertius (ankle plantarflexion), and tibialis posterior, peroneus longus, peroneus brevis, flexor hallucis longus and the flexor digitorium longus (ankle dorsiflexion) muscles (Appendix F). The validity of the PAB® in measuring isometric strength has been established by Pienaar and Barnard (2017) and reliability (r=0.997) by Azevedo et al. (2013) and Pienaar and Barnard (2017).

3.5.4. Gait pattern analysis

The modified Tinetti Gait pattern Assessment Scale was used to measure the participants' gait patterns (Kegelmeyer, Kloos, Thomas & Kostyk, 2007). The participants were asked to walk on a treadmill, at a constant speed at which they felt comfortable, with their arms by their sides. Whilst they were walking, the researcher observed their gait pattern from the front, back, left and right sides. The researcher recorded each participant's gait pattern/cycle

on video, under the supervision of a registered Podiatrist, to be able to discuss the findings with each participant. Hand-held digital videography, with a 40 mega-pixel lens, was taken of the gait patterns during the initial and 10-week evaluations and analysed results were recorded on the assessment sheet.

A registered podiatrist diagnosed each participant's gait pattern according to the modified Tinetti Gait Assessment Tool (Appendix G). The researcher looked at normal plantar- and dorsiflexion during the gait analysis. By conducting a gait pattern analysis, the researcher was able to indicate body movement and muscle activity and identify abnormal gait patterns. The gait pattern analysis was recorded and used to identify gait pattern abnormalities. Each participants' gait pattern was calculated as a score out of ten (10). Gait patterns were further divided into three categories, according the score obtained from the modified Tinetti Gait pattern Assessment Tool, with a score assigned to each such item as: 3 = normal (9-10/10), 3 = high/steppage (4-8/10) and 1 = shuffle gait (1-3/10). Gait pattern analysis has been shown to be a valid and reliable test to determine gait deviations and walking patterns in patients with DPN, in order to determine gait biomechanics and gait training to reduce lower limb injuries (Meuller et al., 1994). The Modified Tinetti Gait pattern Assessment Scale is a reliable and valid (r=0.53) gait pattern assessment tool to use to identify fall risks in patients with diabetic peripheral neuropathy (Kegelmeyer et al., 2007). Kim (2009) and Kopke and Meyer (2006) agreed and added by saying that the Tinetti Gait Assessment Tool assists clinicians to clinically assessment to assess a patient's, balance and functional gait pattern in geriatric population and patients with DPN.

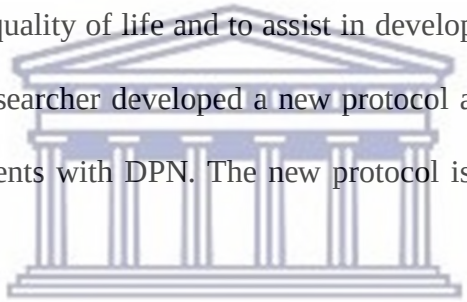
3.6. Reliability

Reliability involves ensuring that results are consistent over time and that these results can be reproduced when using a similar methodology (Taherdoost, 2016). To ensure reliability,

the same equipment was used throughout the study and a standardised procedure was used for each measurement. The researcher was the only one to conduct any tests, thus eliminating any inter-rater reliability issues and, being an experienced biokineticist, intra-rater reliability was enhanced.

3.7. Exercise Intervention

The researcher (registered biokineticist) has developed standard intervention programmes for patients with chronic conditions, such as DPN gradually over the past three (3) years. For the purpose of this study, the researcher developed a scientifically-based exercise intervention programme to specifically target the entire kinetic chain, and to hopefully reduce fall risks, improve quality of life and to assist in developing a standard protocol for patients with DPN. The researcher developed a new protocol as there is a lack of current research protocols for patients with DPN. The new protocol is easily accessible and cost effective.



The intervention group received the newly devised exercise programme (Appendix I) that was based on ankle, hip and knee rehabilitation, including gait pattern specific rehabilitation, and designed by a registered biokineticist. The control group received the same biokinetics exercises designed by the researcher (registered biokineticist) for the purpose of this study. The intervention took place 2-3 times a week for 45 minutes per session and was divided in four categories: Range of motion exercises, strengthening exercises, balance and proprioception and gait pattern training exercises. The intervention programme was divided into three sessions for clear indication of what was expected on each day. The intervention programme was done under strict supervision of the researcher (registered biokineticist), and all three programmes had to be done in the week. Progression of exercises was determined

and adjusted according to each participant's individual progress. Where progression was needed, an increase in repetitions and intensity was made accordingly.

3.7.1. Blood pressure

An aneroid blood pressure cuff and stethoscope were used to measure the participants' blood pressure before, during and after exercise to ensure the participant was not hypo- or hypertensive. Hypo- and/or hypertension is an absolute indication to terminate any exercise training (Pescatella, Arena, Riebe & Thompson, 2013; Sharman & LaGerche, 2014; Riebe, Ehrman, Liguori, & Magal, 2018). The participant was asked to take a seat with their feet flat on the floor and legs uncrossed. The reading was recorded in millimetres of mercury (mmHg) and any false or abnormal measurements were noted (Appendix E). The participant was informed about the results, which were explained and discussed immediately. Barker, Hediger, Katz and Bowers (1984) and Pickering et al. (2005) stated that manual measurements of blood pressure are valid and reliable (r=>0.65) for clinicians to use to classify each patient according to blood pressure-related risk factors and to assist with management and treatment according to risk stratification.

3.7.2. Blood glucose

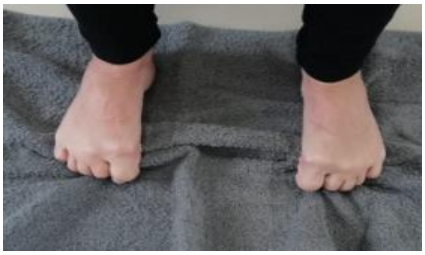
A Contour Plus® blood glucose monitoring system was used the measure the participants' blood glucose levels. Blood glucose was measured before, during and after exercise to monitor the participant's glycaemic state (Appendix E). Blood glucose was measured 5 minutes before the exercise session took place, 5 minutes after the first set of exercises and 5 minutes after the session was completed. Hypo- and/or hypoglycaemia is an absolute indication to terminate any form of exercise training (Colberg, Hernandez & Srahza, 2013; Pescatella et al., 2013). The clinician strictly followed the universal health precautions (Appendix H) for drawing blood (Broussard & Kahwaji, 2019) and used medical gloves at

all times during the procedure. The index finger was used to take the blood sample and an alcohol swab was used to clean the area. A single-use lancet was used to draw blood and was disposed of in a sharp's container. The blood was applied to the testing strip according to the manufacturer's specifications and an alcohol swab or gauze was placed around the test site, with a clinician monitoring for any excess bleeding. The reading was measured in millimoles per litre ($mmol \cdot L^{-1}$) and recorded on the data sheet. The participant was informed about the results, which were explained and discussed immediately. The used equipment was disposed of in line with hospital or health care policies. Testing blood glucose before, during and after exercise provides data for the patient as well as for the clinician to prevent the patient from going into hypo- or hyperglycaemia (Ginsberg, 2007).

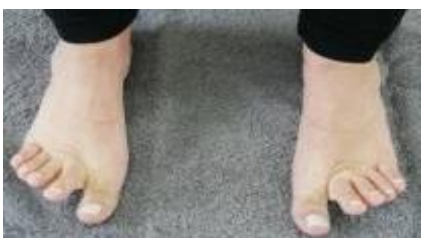
3.7.3. Muscular strength training

Muscular strength training has been shown to decrease the rate of diabetic sarcopenia (Abadi et al., 2017). Muscular strength rehabilitation exercises improve overall muscular strength and endurance and assist with activities of daily living (Streckmann et al., 2014). The researcher, an experienced biokineticist, compiled a list of low intensity muscular strength training exercises as part of the rehabilitation protocol to treat DPN patients.

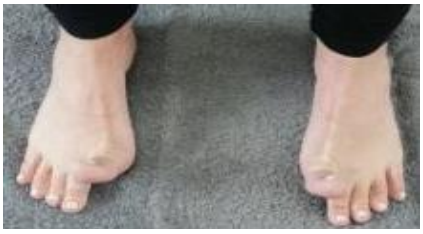
Towel Crunches: The participant was instructed to keep the heels on the ground, whilst simultaneously crunch the towel by using her toes.



Toe Extensors: The participant was asked to keep the heels on the ground, whilst simultaneously pushing the halluces down and lifting the other four metatarsals/lesser digits up.



Toe Flexors: The participant was asked to keep the heels on the ground, whilst simultaneously pushing the four metatarsals/lesser digits down and lifting her halluces up.



Dorsiflexion: The participant was asked to keep the knee straight and pull the toes up and dorsiflex the ankle as far as possible, pulling against the resistance of the theraband.

Plantarflexion: The participant was asked to keep the knee straight and push the toes down and plantarflex the ankle as far as possible, pushing against the resistance of the theraband.

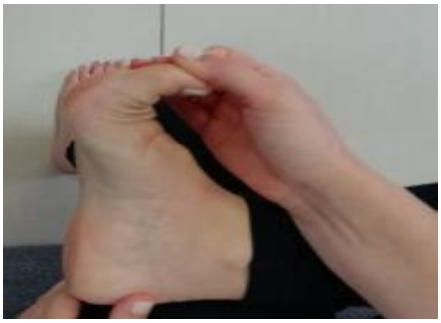
Standing calf raises with a myofascial ball: The participant was asked to go up on her toes into a calf raise and slowly back down again into plantarflexion.

¼ Squat side stepping with a resistance band: The participant was asked to walk side-ways in a quarter squat position.

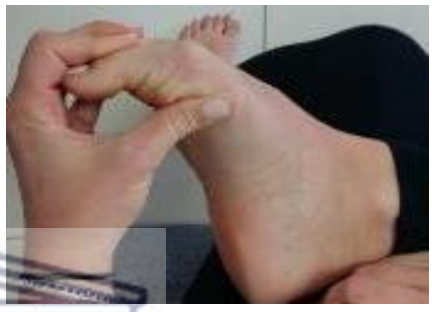
3.7.4. Range of motion training/Flexibility training

Static range of motion/flexibility training is frequently used to increase joint mobility and flexibility (Huang et al., 2014; Pan & Bai, 2014; Shu et al., 2019; Williams et al., 2016). Range of motion/flexibility rehabilitation exercises have been shown to improve blood flow and decrease the risk of any injury (Huang et al., 2014; Pan & Bai, 2014; Shu et al., 2019; Williams et al., 2016). The researcher compiled a list of low intensity static and passive stretches as part of the rehabilitation protocol to treat DPN patients.

Toe Extensors Stretch, with Gluteal Stretch (seated): The participant was seated in an upright position on the chair with one leg in the figure-of-four position, in order to stretch the gluteal medialis muscle. One hand was placed on the first metatarsal and slight pressure applied in order to stretch the MTPJ. This allowed for stretching of the toe extensors.



Toe Flexors Stretch, with Gluteal Stretch (seated): The participant was seated upright in an upright position on the chair with one leg in the figure-of-four position, in order to stretch the gluteal medialis muscle. One hand was placed on the first metatarsal and slight pressure applied in order to stretch the MTPJ. This allowed for stretching of the toe flexors.



Gastrocnemius Stretch: The participant was asked to stand in an upright position with one foot slightly to the front and the other at the back. The front knee needed to be slightly bent and the back knee straight until the gastrocnemius stretches.

Soleus Stretch: The participant was asked to stand in an upright position with the foot slightly to the front and the other at the back. The front knee needed to be slightly bent as well as the back with weight slightly shift to the back leg until the soleus stretches.

Standing Rotation: The participant was asked to stand with back against the wall, feet slightly to the front and the knees bent at thirty degrees with the back slightly pushed back. The participant was instructed to lift the arms up to a ninety-degree bent at the elbow, parallel to the ground. The participant felt the pectoralis major stretches as well as an increase in thoracic mobility.

T-Spine Mobility: The participant was asked to stand next to the wall with the leg closest to the wall slightly more to the front and the other leg slightly more to the back. With both arms straight out parallel to the ground the participant was asked to rotate the arm away from the arm/hand closest to the wall. By rotating the participant was instructed to look at the other hand as it rotates. The participant felt an increase in thoracic rotation as well as the pectoral girdle stretches

90 Degree T-Spine Mobility, with Hamstring Stretch: The participant was asked to stand in an upright position behind a chair with a backrest, and placing the hands on the backrest; once done, the participant was asked to push chest down to the ground as far as possible and slightly bend the knees to a thirty-degree bend, to stretch the hamstrings.

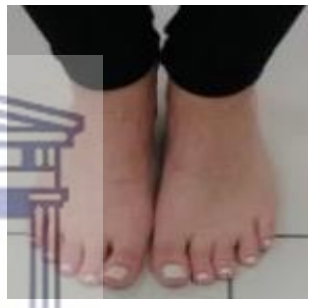
Pectoralis Major Stretch: The participant was instructed to stand in a doorway, with one arm closest to the wall in a ninety-degree position against the wall with the elbow next to the wall and the leg closest to the wall slightly to the front to decrease thoracic rotation and rotation on the spine especially the lower back. From that position, the participant was instructed to rotate away from the wall to feel the pectoralis major stretching.

Pectoralis Minor Stretch: The participant was instructed to stand in a doorway, with one arm closest to the wall in a forty-five-degree position against the wall with the elbow next to the wall and the leg closest to the wall slightly to the front to decrease thoracic rotation and rotation on the spine especially the lower back. From that position, the participant was instructed to rotate away from the wall to feel the pectoralis minor stretching.

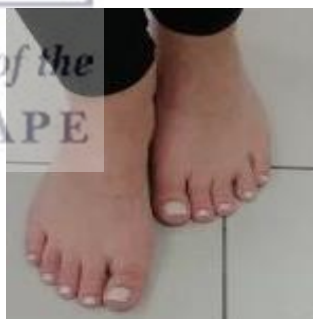
3.7.5. Balance and proprioceptive training

It is known that balance and proprioceptive training decreases fall risk in DPN patients (Huang et al., 2014; Pan & Bai, 2014; Shu et al., 2019; Williams et al., 2016), improve postural stability (Huang et al., 2014; Pan & Bai, 2014; Shu et al., 2019; Williams et al., 2016), and assist in movement patterns (Johnson & Takemoto, 2019). For the purpose of the study, the researcher implemented balance and proprioceptive rehabilitation exercises as part of the DPN protocol to increase balance time and decrease fall risk and any associated injuries.

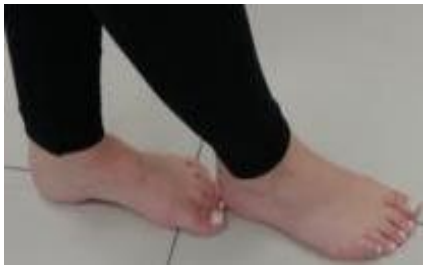
Double Leg Stance (eyes open) and Double Leg Stance (eyes closed): The participant stood in an upright position with both feet together and arms by the sides, eyes open and then to increase the difficulty of the exercise by closing the eyes.



Parallel Balance (eyes open) and Parallel Balance (eyes closed): The participant was instructed to stand in a upright position with arms by the sides with one foot placed in the mid-foot of the other foot, and was then asked to keep eyes open for the duration of the exercise and eyes closed to increase the intensity of the exercise.



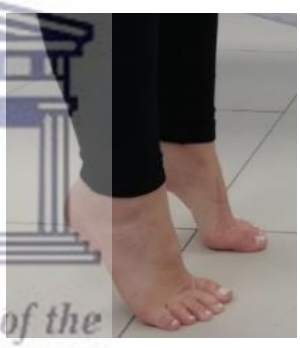
Tandem Balance (eyes open) and Tandem Balance (eyes closed): The participant was instructed to stand in an upright position with arms by the sides, with one foot placed in front of the other in a tandem position, with eyes open for the duration of the exercise and closed to increase the intensity of the exercise.



Single Leg Balance (eyes open) and Single Leg Balance (eyes closed): The participant was instructed to stand in an upright position with hands on the hips, lifting one foot up, holding a static position for the duration of the exercise, with eyes open or closed, depending on the intensity (and patient comfort level) of the exercise.

Single Leg Balance with Weight Shifting: The participant was instructed to stand on one leg in an upright position, bending one leg at thirty degrees and placed a small dumbbell in the contralateral hand. For the duration of the exercise, the participant held a static position by shifting the weight from one hand to another.

Toes Standing (eyes open) and Toes Standing (eyes closed): The participant was instructed to stand in an upright position with hands on the hips, shifting body weight over onto the toes and lifting the heels off the ground, holding the static position, once done the participant was instructed to close the eyes to increase the intensity of the exercise.



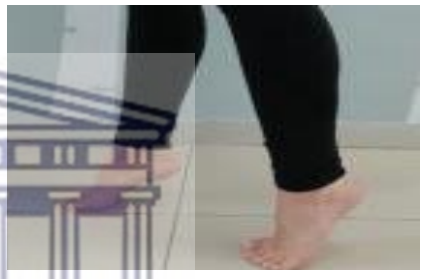
Heels Standing (eyes open) and Heels standing (eyes closed): The participant was instructed to stand in an upright position with hands on the hips, shifting body weight over onto the heels and lifting the toes off the ground and holding the static position, once done the participant was instructed to close the eyes to increase the intensity of the exercise.

3.7.6. Gait pattern training

Gait pattern training enhances movement patterns and improves activities of daily living (Jambert et al., 2011) and assists with kinematics and kinetics of the kinetic chain, enhancing and decreasing fall risks in DPN patients (Pan & Bai, 2014).

Heel Walking: The participant was instructed to stand in an upright position and shift the weight over to the heels. Once done, the participant was instructed to walk on the heels

Toe Walking: The participant was instructed to stand in an upright position and shift the weight over to the toes. Once done, the participant was instructed to walk on the toes



3.8. Statistical Analyses

Descriptive statistics in the form of means and standard deviations were used to describe the data. Mann-Whitney and Wilcoxon Sign Rank Tests were used to compare clinical variables of blood glucose and blood pressure, as well as muscle strength, range of motion of the ankle, balance and gait pattern deviations from pre- to post-intervention in both groups. The level of significance was set at $p<0.05$.

3.9. Ethics Considerations

The study protocol was approved by the institution's Biomedical Research Ethics Committee (Ethics number: BM19/7/12) before any recruitment began (Appendix D). Permission was received from the two practices concerned, to approach their clients to volunteer to

participate in this study. Participants received an information leaflet and a consent form prior to the recruitment process of the study took place. Recruitment was strictly voluntary and participants had the right to withdraw without penalty. Before signing the consent form, volunteers were assured that they had the right to withdraw from the study at any time without any penalties.

It was ensured that all participants' rights were protected and that ethics principles were followed at all times throughout the study, as follows:

The right to anonymity and confidentiality:

- Participants were treated with integrity. No personal details were shared with any other participant.
- Details of the participants remained anonymous through the use of alpha-numeric codes instead of their names.
- To maintain confidentiality, participants' original details were kept in a locked cabinet and/or on a password-protected computer.
- When the findings of the study are published or presented at research conferences, all personal information declared by the participant will be excluded.
- Consent to be photographed and videoed was obtained from each participant and will only be utilised in dissemination of the results, with all faces obscured.
- The researcher saved the photographs and videos on a computer that was password protected.
- Only the researcher, supervisor and co-supervisor had access to personal information of the participants.

Right to privacy

- No data were collected without the participant's consent.
- Treatment sessions were privately booked and conducted in a private space.

Right to self-determination

- Participants were fully informed about the study prior to their inclusion.
- Participation was voluntarily.
- Participants had the right to withdraw at any time without penalty.
- Participants were not deceived in any way throughout the research study. Assessment results were given to the participant throughout the course of the study and results were discussed and explained.

Right to fair treatment

- Based on the ethics principle of justice, each person was treated fairly and received accordingly what was duly explained to him/her at the outset.
- Information about what the participation and the study entailed was provided in written form and the participant was given the chance to ask any questions of the researcher.
- Selection of participants and treatment was based on fair inclusion and exclusion criteria.
- The control group were informed that they could participate in the intervention after the study was complete if they wished.

Right to protection from discomfort and harm

- Based on the principle of beneficence: do good and do not harm. Any risks associated with the study were reduced by exercising in a safe and clean environment. Blood pressure and blood glucose were taken before, during and after to prevent hypo- and hypertension, and hypo-and hypertension. By measuring blood glucose, universal precautions were followed to ensure safety for both parties.

CHAPTER 4

RESULTS AND DATA ANALYSIS

4.1. Introduction

Low-intensity exercise training has been under investigation for the effective treatment of diabetic peripheral neuropathy (Colberg et al., 2016; Shu et al., 2019). In this chapter, the findings are presented for tests of muscular strength, range of motion, balance and gait patterns from pre- to post-intervention in both groups. The objectives of this study were to determine whether there was any effect as a result of an exercise training programme on these individual variables in patients with DPN in the lower legs.

These data were compiled in a Microsoft Excel® 2016 spreadsheet, before being imported to the STATA version 15.2 for analysis. Non-parametric tests were used in the analysis because the range of motion, balance, muscular strength and gait patterns parameters were measured on a continuous scale and the study had 14 participants in total. This was appropriate because the data were skewed, i.e. was not normally distributed (Hahm, 2016). The Mann Whitney test was therefore used to determine the median differences between the intervention and the comparison group for the pre-and post-intervention measures. Moreover, the Mann Whitney test was also used to determine any significant changes in blood pressure, blood glucose, range of motion, balance, muscular strength and gait patterns at baseline (pre-intervention) and after a 10-week follow-up (post-intervention) between the intervention and the control group. Lastly, the Wilcoxon Sign rank test was used to determine the within-group difference through matching the pre-intervention and the post-intervention variables. The percentage change of the parameters from the baseline to after the intervention was calculated:

$$\left[\frac{\text{Postvalue-Prevalue}}{\text{Prevalue}} \times 100\right]$$

Since this study involved a commitment by participants for 10 weeks, participants sometimes missed scheduled appointments. For such scenarios, the group mean value was used to replace the missing entries to maintain the sample size. The level of statistical significance was set at $p<0.05$.

4.2. Participant Demographics

All participants who presented with diabetic peripheral neuropathy in the lower legs, who presented at the two private practices in Alberton and Sandton were welcome to partake in the study. The majority of participants (12) hailed from the private practice in Alberton, (Johannesburg) and the remainder (2) were from Sandton (Johannesburg). Demographic data indicates that fourteen participants took part in this study, of which 7 were female and 7 were male. Gender, activity level, age, and duration of DM (Table 4.1).

Table 4.1 Participant demographics

Variables	**N**	**Female**	**Male**
Gender			
Control	7	5	2
Intervention	7	2	5
Activity level	14	Inactive	

		Minimum	**Maximum**	**Mean**	**Standard Deviation**
Age (years)					
Control	7	45	77	66	10.52
Intervention	7	20	76	60	19.33
Duration of DM (years)					
Control	7	2	30	13.29	10.03
Intervention	7	2	36	16	11.82

The participants in this study were 50% female and 50% male, who had a broad age range from 20-77 years, however the mean age was not significantly different between the groups.

Similarly, there was no significant difference between the duration of having DM. All of the participants were sedentary and living an inactive lifestyle.

4.3. Between Group Comparisons

4.3.1. Pre-Intervention: Control vs Intervention Group

The study was conducted with 14 participants, seven in the intervention group, which was engaged in the intervention programme, and seven in the control group. The results for the statistical comparison of all parameters between the two groups at pre-intervention are shown in Table 4.2. At week 1 (pre-intervention), participants from both groups underwent the same clinical assessments in measuring blood glucose levels and blood pressure.

Comparing the median differences for the clinical parameters between the two groups at the pre-intervention stage, the median differences were not statistically significant. However, the blood glucose was higher for the intervention group (9.5 $mmol \cdot L^{-1}$) compared to the control group (7.4 $mmol \cdot L^{-1}$) at the pre-intervention stage. However, the median systolic blood pressure was higher in the intervention group compared to the control group (132 mmHg for the intervention group and 128 mmHg for the control group) at the pre-intervention stage. In contrast, the median diastolic blood pressure was higher for the control group compared to the intervention group (80 mmHg and 72 mmHg for the intervention group) at pre-intervention stage.

Table 4.2 Between group comparisons of clinical variables at pre-intervention

	Pre-intervention		
Clinical Variables	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Blood glucose ($mmol \cdot L^{-1}$)	7.4 (6.5-8.3)	9.5 (5.4-14.3)	0.565
Systolic Blood Pressure (mmHg)	128 (122-132)	132 (122-142)	0.367
Diastolic Blood Pressure (mmHg)	80 (70-82)	72 (62-80)	0.396

The results indicate that there was no statistically significant difference in the range of motion parameters (plantarflexion and dorsiflexion) at the week 1. The median range of motion plantarflexion left was higher in the control group (65°) compared to the intervention group (57°) while the median range of motion plantarflexion right was higher in the intervention group (65°) compared to the control group (62°) at week 1 (pre-intervention stage). The median range of motion dorsiflexion left was equal (19°) for both the control and the intervention group while the median range of motion dorsiflexion right was higher for the control group (24°) compared to the intervention group (18°) at pre-intervention stage.

Table 4.3 Between group comparisons of range of motion at pre-intervention.

	Pre-intervention		
Range of motion (degrees)	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Plantarflexion Left	65 (57-71)	57 (55-68)	0.607
Plantarflexion Right	62 (41-75)	65 (52-69)	0.949
Dorsiflexion Left	19 (13-27)	19 (12-27)	0.796
Dorsiflexion Right	24 (9-33)	18 (8-31)	0.654

The median stork stand times (right and left) were longer for the control group (17 seconds and 11 seconds) compared to the intervention group (7 seconds and 9 seconds).

Table 4.4 Between group comparisons of balance times at pre-intervention

	Pre-intervention		
Balance (seconds)	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Stork Stand Left	17 (8-75)	7 (3-12)	0.029 *
Stork Stand Right	11 (8-69)	9 (3-10)	0.248

** significant at p<0.05*

At week 1 participants from both groups underwent the same assessments in measuring their muscular strength of the hip, knee and ankle, Table 4.5. At week 1 (pre-intervention stage), majority of the assessed parameters (7/8 or 87.5%) were not significantly different between the control group and the intervention group.

The median right knee extension muscular strength value was higher for the control group (9.3 kg) compared to the intervention group (5.4 kg) while the median left knee extension muscular strength value was higher for the intervention group (16.9 kg) compared to the control group (7.9 kg) at week 1 (pre-intervention stage). The median left plantarflexion muscular strength value was higher for the intervention group (5.1 kg) compared to the control group (4.8 kg) at week 1. Similarly, at the pre-intervention stage, the left dorsiflexion and right dorsiflexion muscular strength values for the control group (5.6 kg and 4.3 kg) were higher compared to the intervention group (3.5 kg and 2.9 kg) respectively. The left hip extension muscular strength value was higher for the control group (4.8kg) compared to the intervention group (3.8 kg) at week 1 (pre-intervention stage). In contrast, the right hip extension muscular strength value was higher for the intervention group (4.8kg) compared to the control group (3.6 kg) at week 1. There was a strong significant difference in the median right plantarflexion muscular strength value between the control and the intervention group at pre-intervention stage (p=0.018). The median right plantarflexion muscular strength

value was higher for the control group (9.1kg) compared to the intervention group (4.7kg) at baseline.

Table 4.5 Between group comparisons of muscular strength at pre- intervention

	Pre-intervention		
Muscular strength (kg)	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Left Knee Extension	7.9 (7.7-10.9)	16.9 (4.2-19.9)	0.337
Right Knee Extension	9.3 (6.5-11.3)	5.4 (4.2-21.8)	0.371
Left Plantarflexion	4.8 (1.9-9.3)	5.1 (3.9-18.7)	0.277
Right Plantarflexion	9.1 (5.9-9.3)	4.7 (2.6-5.4)	0.018 *
Left Dorsiflexion	5.6 (2.9-9.3)	3.5 (2.8-4.2)	0.291
Right Dorsiflexion	4.3 (2.4-5.1)	2.9 (2.3-3.3)	0.405
Left Hip Extension	4.8 (2.4-6.2)	3.8 (2.6-6.1)	0.701
Right Hip Extension	3.6 (2.9-7.8)	4.8 (2.4-7.1)	0.797

** significant at p<0.05*

At week 1 participants from both groups underwent the same clinical assessments in measuring their gait patterns. The gait pattern was not statistically significant different between the two groups at the pre-intervention assessments. At week 1 (pre-intervention), there were more participants with gait pattern category 2 in the control group (43%) compared to the 29% in the intervention group. In contrast, there were more participants in with gait pattern category 3 while those in the category 3 in the intervention group (71.4%) compared to the control group (57.1%) at week 1.

Table 4.6 Between group comparisons of gait patterns variables at pre-intervention

	Pre-intervention		
Gait Patterns	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
2 [n(%)] 3[n(%)]	3(42.86%) 4(57.14%)	2(28.57%) 5(71.43%)	0.5770

4.3.2. Post-Intervention: Control vs Intervention Group

The results for the statistical comparison of all parameters between the two groups at pre-intervention are shown in Table 4.7. At week 10 (post-intervention), participants from both groups underwent the same clinical assessments in measuring blood pressure and blood glucose levels.

After the 10-weeks of intervention there were no significant differences between the groups as a result of the intervention, except for diastolic pressure, which significantly lower for the intervention group. Similarly, the blood glucose median value was higher for the control group (10.2 mmol·L^{-1}) compared to the intervention group (7.8 mmol·L^{-1}) at the post-intervention stage. There was a statistically significant difference (p=0.017) between the median post-intervention diastolic blood pressure values between the two groups. The control group had a higher median diastolic blood pressure value of 72 mmHg compared to 62 mmHg in the intervention group.

Table 4.7 Between group comparisons of clinical variables at post-intervention

	Post-intervention		
Clinical Variables	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Blood glucose ($mmol \cdot L^{-1}$)	10.2 (7.6-13.2)	7.8 (7.2-9.2)	0.200
Systolic Blood Pressure (mmHg)	122 (120-122)	120 (112-124)	0.607
Diastolic Blood Pressure (mmHg)	72 (72-74)	62 (60-62)	0.017 *

** significant at $p<0.05$*

The range of motion parameters were also compared between the control and the intervention groups at week 10 (post-intervention), (Table 4.8). At week 10 (post-intervention stage), the results indicate that there was no statistical significance between the median range of motion plantarflexion left; and the median range of motion dorsiflexion left and right (Table 4.8). However, the median range of motion plantarflexion left was higher for the intervention group (64.3°) compared to the control group (62°). Similarly, the median range of motion dorsiflexion left was slightly higher for the intervention group (20°) compared to the control group (19°) while the median range of motion dorsiflexion right was higher for the control group (25°) compared to the intervention group (20°) at week 10 (post-intervention stage). Only the plantarflexion range of motion (right) showed a statistically significant median difference between the two groups after exercise for the intervention group (p=0.025). The intervention group had a higher median value of 70.2° compared to the control group with a value of 60°.

Table 4.8 Between group comparisons of range of motion at post-intervention.

	Post-intervention		
Range of motion (degrees)	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Plantarflexion Left	62 (56.4-68)	64 (63-65)	0.177
Plantarflexion Right	60 (58.2-65)	70 (68-73)	0.025 *
Dorsiflexion Left	19 (17-24.8)	20 (15-26)	0.898
Dorsiflexion Right	25 (18-27.4)	20 (18-24)	0.335

** significant at p<0.05*

Post-intervention, participants from both groups underwent the same Stork Stand balance assessment (Table 4.9). The median stork stand times (right and left) were longer for the control group (17 seconds and 11 seconds) compared to the intervention group (7 seconds and 9 seconds). None of these differences were statistically significant between the two groups, however, the median stork stand balances (left and right) were higher for the control group (30.2 seconds and 43.4 seconds) compared to the interventions group (21 seconds and 23.3 seconds) at the post-intervention stage.

Table 4.9 Between group comparisons of balance times at post-intervention

	Post-intervention		
Balance (seconds)	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Left leg	30.2 (5-67)	21 (6-27.5)	0.949
Right leg	43.4 (7-72)	23.3 (6-31)	0.337

At week 10 participants the isometric muscular strength of the hip, knee and ankle were measured (Table 4.10). Of the eight parameters that assessed muscular strength, only two were statistically significant between the control and the intervention group. The median left and right plantarflexion muscular strength values were similar between the control and the intervention group at 6.8 kg (left) and 6.6 kg (right) for the control group, compared to 6.5 kg (left) and 6.7 kg (right) for the intervention group. The right knee extension median value was higher for the intervention group was 15.1 kg compared to the control group of 8.8 kg. In contrast, there was a significant difference (p=0.025) for left knee extension, which was higher for the intervention group (15.1 kg) than the control group (9.7 kg).

The left hip extension muscular strength at week 10 was slightly higher for the intervention group (3.4 kg) compared to the control group (3.1 kg). Similarly, the right hip extension muscular strength at week 10 was higher for the intervention group (5.9 kg) compared to the control group (4.6 kg) and this parameter showed a marginal significant difference between the two groups (p=0.083). The right dorsiflexion was higher for the control group (2.8 kg) compared to the intervention group (2.4kg) while the left dorsiflexion was higher for the control group (3.3 kg) compared to the intervention group (2.4 kg) at week 10. There was a significant difference in the left dorsiflexion muscular strength between the two groups at week 10 (p=0.034).

Table 4.10 Between group comparisons of muscular strength at post-intervention

	Post-intervention		
Muscular strength (kg)	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
Left Knee Extension	9.7 (8.3-10.9)	15.1 (13.9-18.1)	0.025 *
Right Knee Extension	8.78 (8.3-9.5)	15.1 (7.1-19.9)	0.110
Left Plantarflexion	6.8 (5.1-6.8)	6.5 (3.4-9.5)	0.949
Right Plantarflexion	6.6 (4.9-6.6)	6.7 (4.8-10.5)	0.564
Left Dorsiflexion	3.3 (3.1-3.4)	2.4 (2.2-2.7)	0.034 *
Right Dorsiflexion	2.8 (2.2-3.1)	2.4 (2.2-2.9)	0.653
Left Hip Extension	3.07 (2.9-4.9)	3.4 (2.8-4.2)	0.521
Right Hip Extension	4.6 (3.5-4.6)	5.9 (4.8-6.9)	0.083

** significant at p<0.05*

At week 10 participants from both groups underwent the same clinical assessments in measuring their gait patterns. The gait pattern was not statistically significant different between the two groups at post-intervention assessments (Table4.11). As per clinical observations of gait patterns, the researches recorded improvements in gait patterns in the intervention group after the 10-week follow up assessment. At week 10 (post-intervention), there were more participants with gait pattern category 2 in the control group (43%) compared to the 29% in the intervention group.

In contrast, there were more participants in the intervention group compared to the control group (57.1%) at week 1. The same proportion distribution of gait pattern between the two groups was also observed at week 10; hence, the gait pattern remains the same during the whole follow-up period.

Table 4.11 Between group comparisons of gait patterns at post-intervention

	Post-intervention		
Gait Patterns	**Control Median (IQR)**	**Intervention Median (IQR)**	***p*-value**
2 [n(%)] 3[n(%)]	3(42.86%) 4(57.14%)	2(28.57%) 5(71.43%)	0.5770

4.4. Within Group Comparisons from Pre- and Post-Intervention

4.4.1. Control Group

In comparing clinical variables, i.e. blood glucose levels and blood pressure in the control group. Interestingly, there was a 38% significant (p=0.018) increase in blood glucose levels within the control group from 7.4 mmol·L^{-1} at week 1 to 10.2 mmol·L^{-1} at week 10. The median systolic blood pressure in the control group decreased significantly (p=0.017), by approximately 5%, from week 1 week 10 (Table 4.12). The median diastolic blood pressure for this group also decreased, by 10%, from week 1 to week 10 but this was not statistically significant.

Table 4.12 Comparison of clinical variables within the control group

Clinical variables	**Pre-intervention Median (IQR)**	**Post-intervention Median (IQR)**	**% Change**	***p*-value**
Blood Glucose (mmol·L^{-1})	7.4 (6.5-8.3)	10.2 (7.6-13.2)	38%	0.018 *
Systolic Blood Pressure (mmHg)	128 (122-132)	122 (120-122)	-5%	0.017 *
Diastolic Blood Pressure (mmHg)	80 (70-82)	72 (72-74)	-10%	0.866

** significant at p<0.05*

Range of motion in the ankle for plantar and dorsiflexion did not change significantly in the control group from pre- to post-intervention (Table 4.13). There was a 5% decrease in left and right plantarflexion and a 4% decrease in dorsiflexion of the right ankle over this time, but no change for the left ankle, which remained constant at 19° from week 1 to week 10.

The median right dorsiflexion showed an improvement in the control group. The median right dorsiflexion increased by approximately 4% from 24° at week 1 to 25° at week 10.

Table 4.13 Comparison of range of motion within the control group

Range of motion (degrees)	**Pre-intervention Median (IQR)**	**Post-intervention Median (IQR)**	**% Change**	***p*-value**
Plantarflexion Left	65 (57-71)	62 (56.4-68)	-4.6%	0.735
Plantarflexion Right	62 (41-75)	60 (58.2-65)	-3.2%	0.800
Dorsiflexion Left	19 (13-27)	19 (17-24.8)	0	0.866
Dorsiflexion Right	24 (9-33)	25 (18-27.4)	4.2%	0.398

There was no statistically significant change in the median left and right leg stork stand balances for the control group after the 10-week follow-up (Table 4.14). However, the median balance time on the left leg increased by 78%, which, although large, it was non-significant, while the right median stork stand balance increased by 30% over the same period.

Table 4.14 Comparison of balance times within the control group

Balance (seconds)	**Pre-study Median (IQR)**	**Post-study Median (IQR)**	**% Change**	***p*-value**
Left leg	17 (8-75)	30.2 (5-67)	78%	0.612
Right leg	11 (8-69)	43.4 (7-72)	291%	0.128

There were no significant differences for muscular strength of the knee, ankle nor hip joint for the control group from week 1 to week 10 (Table 4.15). There was a 23% and 3% change in left and right knee extension strength respectively.

Table 4.15 Comparison of muscular strength within for the control group

Muscular strength (kg)	Pre-study Median (IQR)	Post-study Median (IQR)	% Change	*p*-value
Left Knee Extension	7.9 (7.7-10.9)	9.7 (8.3-10.9)	22.8%	0.672
Right Knee Extension	9.3 (6.5-11.3)	8.8 (8.3-9.5)	-3.0%	0.445
Left Plantarflexion	4.8 (1.9-9.3)	6.8 (5.1-6.8)	41.7%	0.311
Right Plantarflexion	9.1 (5.9-9.3)	6.6 (4.9-6.6)	-27.5%	0.128
Left Dorsiflexion	5.6 (2.9-9.3)	3.3 (3.1-3.4)	-41.1%	0.225
Right Dorsiflexion	4.3 (2.4-5.1)	2.8 (2.2-3.1)	-34.9%	0.398
Left Hip Extension	4.8 (2.4-6.2)	3.1 (2.9-4.9)	-36.0%	0.465
Right Hip Extension	3.6 (2.9-7.8)	4.6 (3.5-4.6)	27.8%	0.799

For strength during plantarflexion, a 41.7% increase was seen in the right ankle from week 1 to week 10 for the control group, while the same variable decreased by approximately 27% in the right ankle. Dorsiflexion ankle strength decreased by 41% on the left and 35% for the right. In terms of left hip extension, strength also decreased by 36% while right hip extension improvement by almost 28% over the 10-week intervention.

Lastly, no statistically significant differences were observed in gait patterns for the control group over the 10-week intervention period (Table 4.16).

Table 4.16 Comparison of gait pattern variables within the control group

Gait Patterns	Pre-intervention Median (IQR)	Post-intervention Median (IQR)	% Change	*p*-value
2 [n(%)] 3[n(%)]	3(42.86%) 4(57.14%)	3(42.86%) 4(57.14%)	0 0	1.000

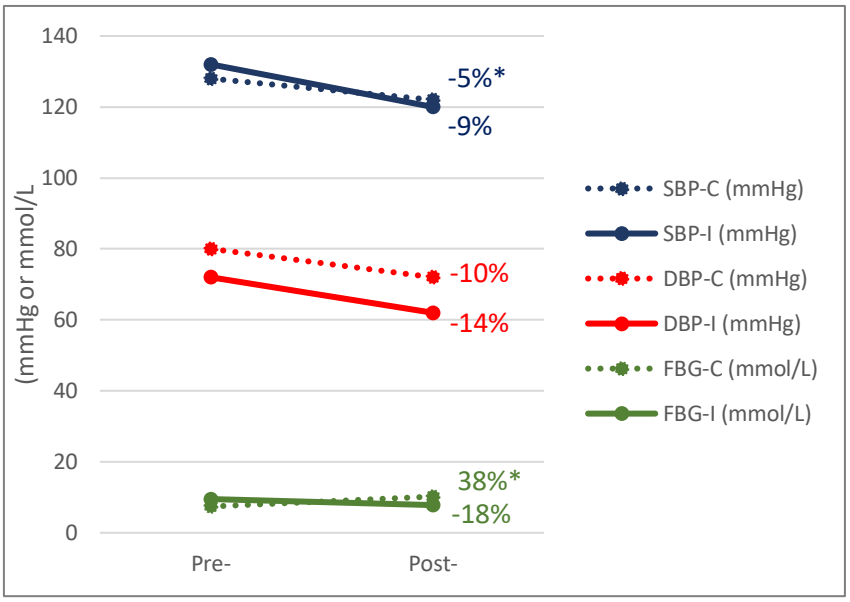
4.4.2. Intervention Group

Regarding the comparison of from pre- to post-intervention within the intervention group, there were no statistically significant differences for any of the clinical variables in the intervention group (Table 4.17). Although there were no statistically significant differences for blood glucose levels and blood pressure, the results indicate that there was a 9% decrease in median systolic blood pressure in the intervention group after a 10-week intervention programme while the median diastolic pressure decreased by approximately 14% during this time. Similarly, the median blood glucose decreased by 18% in the intervention group. The clinical parameters in the intervention group showed the anticipated direction of results after exercise.

Table 4.17 Comparison of clinical variables within the intervention group

Clinical variables	**Pre-intervention Median (IQR)**	**Post-intervention Median (IQR)**	**% Change**	***p*-value**
Blood Glucose ($mmol \cdot L^{-1}$)	9.5 (5.4-14.3)	7.8 (7.2-9.2)	-18%	0.612
Systolic Blood Pressure (mmHg)	132 (122-142)	120 (112-124)	-9%	0.102
Diastolic Blood Pressure (mmHg)	72 (62-80)	62 (60-62)	-14%	0.062

These trends for both groups are depicted graphically in Figure 4.1, where it can be seen that all variables decreased for both groups over the 10-week intervention, except for blood glucose levels in the control group, which went up during this time.



Key: C=control; I=intervention; SBP=systolic blood pressure; DPB=Diastolic Blood pressure; FBG=fasting blood glucose; * significant at $p<0.05$

Figure 4.1. Clinical variable comparisons

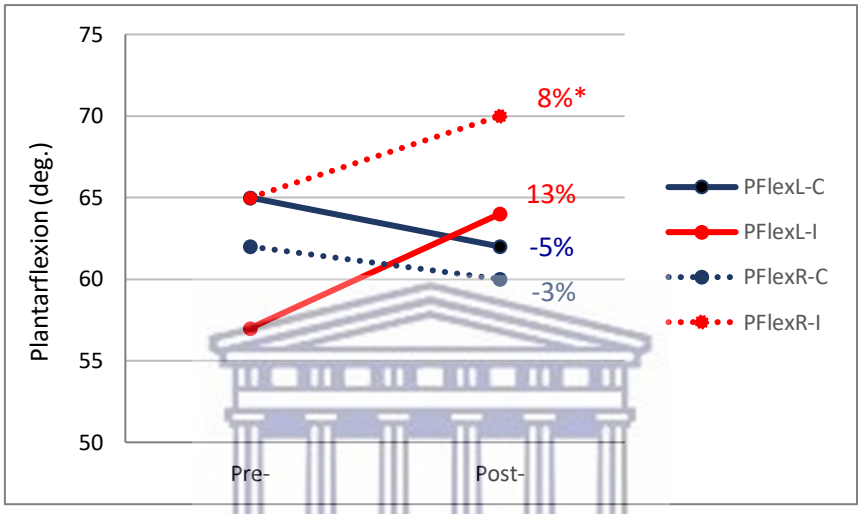
Within the intervention group, range of motion in the ankle for plantar and dorsiflexion improved from week 1 to week 10, with flexibility variables increasing for all variables (Table 4.18). There was a significant (p=0.02) increase in right plantarflexion (8%) post-intervention, but the 13% increase seen in median left plantarflexion was not significant. The median left dorsiflexion increased by 5% while the there was an 11% improvement in the intervention group.

Table 4.18 Comparison of range of motion within the intervention group

Range of motion (degrees)	**Pre-intervention Median (IQR)**	**Post-intervention Median (IQR)**	**% Change**	***p*-value**
ROM Plantarflexion Left	57 (55-68)	64 (63-65)	12.8%	0.203
ROM Plantarflexion Right	65 (52-69)	70 (68-73)	8.0%	0.022 *
ROM Dorsiflexion Left	19 (12-27)	20 (15-26)	5.3%	0.735
ROM Dorsiflexion Right	18 (8-31)	20 (18-24)	11.1%	0.553

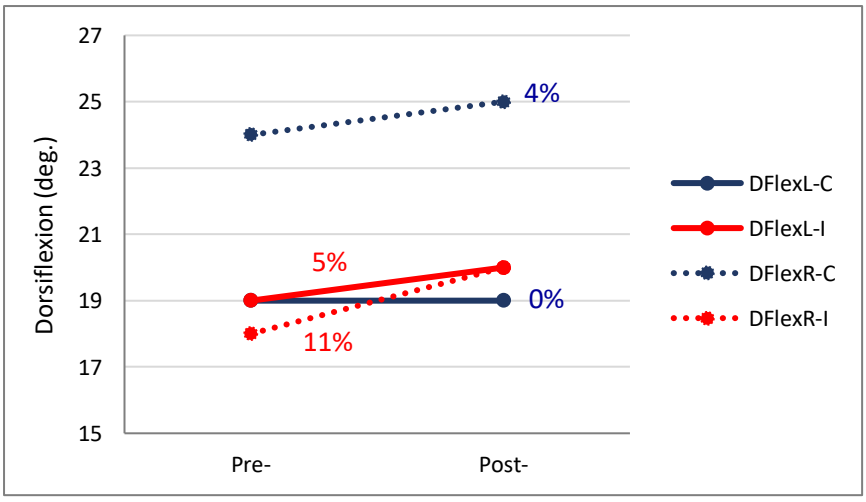
** significant at p<0.05*

The percent changes in ROM for both groups are presented in Figures 4.2 and 4.3 below. This clearly shows the increases in ankle plantarflexion ROM for the intervention group, whereas ROM decreased for the control group. This trend was not so clear in terms of dorsiflexion, with an increase in ROM in both the control and intervention group after a 10-week follow up.



Key: C=control; I=intervention; PFlexL=Plantarflexion Left; PFlexR=Plantarflexion Right; * significant at $p<0.05$

Figure 4.2. Left and right ankle plantarflexion comparisons



Key: C=control; I=intervention; DFlexL=Dorsiflexion Left; DFlexR=Dorsiflexion Right

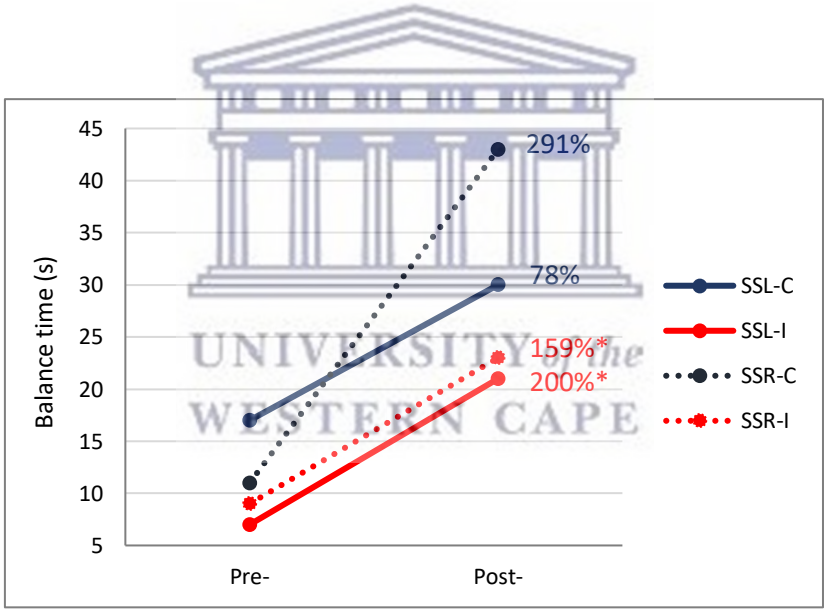
Figure 4.3. Left and right ankle dorsiflexion comparisons

For the intervention group, there were large changes in balance time for both left and right legs (Table 4.19). Statistically significant (p=0.018) increases were seen in both left (200%) and right (159%) legs from pre- to post-intervention. Trends for both groups are presented in Figure 4.4.

Table 4.19 Comparison of balance times within the intervention group

Balance (seconds)	**Pre-intervention Median (IQR)**	**Post-intervention Median (IQR)**	**% Change**	***p*-value**
Left leg	7 (3-12)	21 (6-27.5)	200%	0.018 *
Right leg	9 (3-10)	23 (6-31)	159%	0.018 *

** significant at p<0.05*



Key: C=control; I=intervention; SSL=Stork Stand Left; SSR=Stork Stand Right;
*=significant at p<0.05

Figure 4.4. Stork stand balance variables

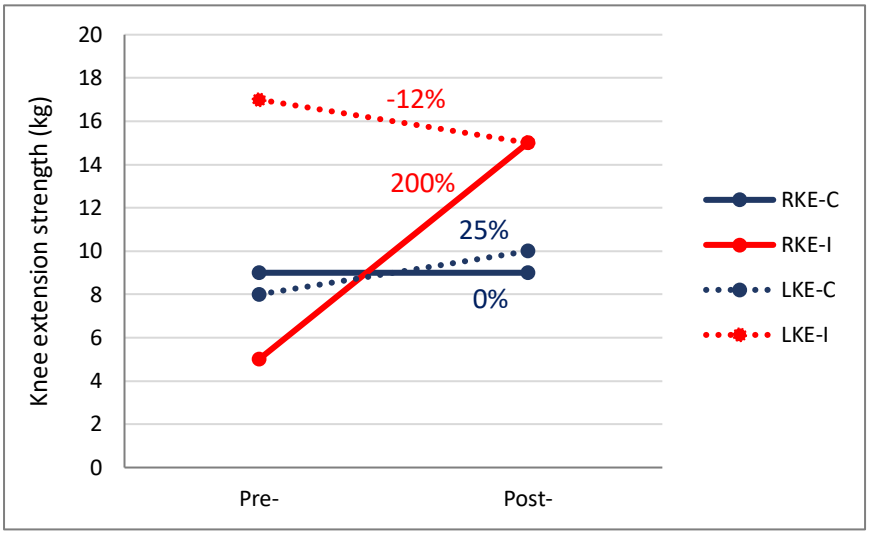
Similarly, there were no significant changes within the intervention group, for muscular strength at the knee, ankle and hip joints from week 1 to week 10 (Table 4.20).

A 10.7% decrease in knee extension strength was noted for the right knee over the intervention period, however right knee extension strength increased by nearly 180% from

nearly 5.5kg at week 1 to 15kg at week 10 in the intervention group, however this large change was not statistically significant. Plantarflexion strength for the left ankle increased by 27.5% at week 10, while the right plantarflexion strength increased by 31.4% over the same period. Both left and right ankle dorsiflexion strength decreased by 31.4% and 17.2% respectively. Left hip extension strength also decreased by 10.5% from week 1 to week 10, while the right hip extension strength increased by 23% over the same period. Trends for strength variables for both groups are presented in Figures 4.5-4.8.

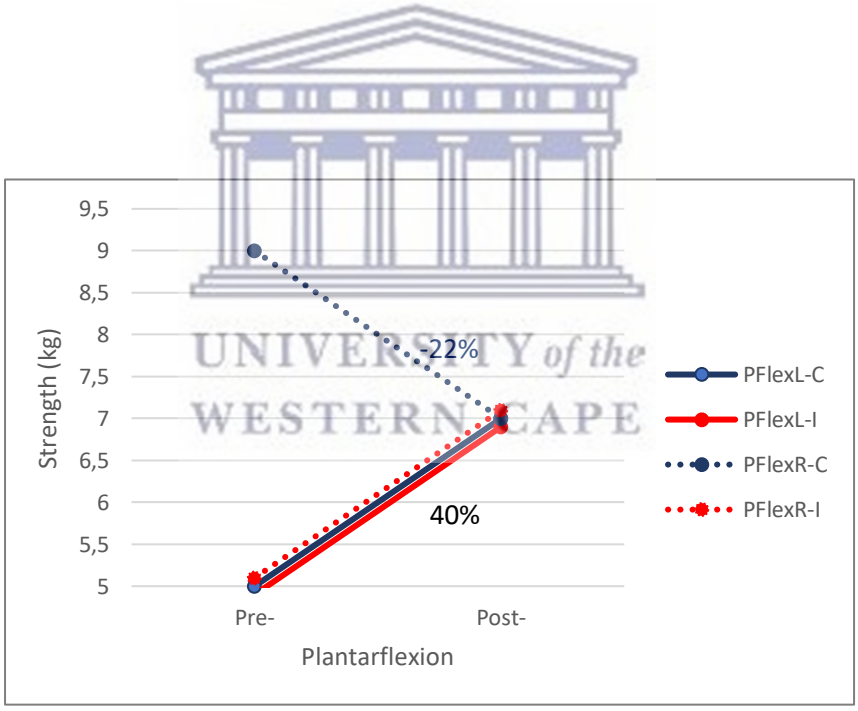
Table 4.20 Comparison of muscular strength for the intervention group

Muscular strength (kg)	**Pre-intervention Median (IQR)**	**Post-intervention Median (IQR)**	**% Change**	***p*-value**
Left Knee Extension	16.9 (4.2-19.9)	15.1 (13.9-18.1)	-10.7%	0.398
Right Knee Extension	5.4 (4.2-21.8)	15.1 (7.1-19.9)	179.6%	0.237
Left Plantarflexion	5.1 (3.9-18.7)	6.5 (3.4-9.5)	27.5%	0.735
Right Plantarflexion	4.7 (2.6-5.4)	6.7 (4.8-10.5)	31.4%	0.063
Left Dorsiflexion	3.5 (2.8-4.2)	2.4 (2.2-2.7)	-31.4%	0.128
Right Dorsiflexion	2.9 (2.3-3.3)	2.4 (2.2-2.9)	-17.2%	0.344
Left Hip Extension	3.8 (2.6-6.1)	3.4 (2.8-4.2)	-10.5%	0.173
Right Hip Extension	4.8 (2.4-7.1)	5.9 (4.8-6.9)	22.9%	0.176



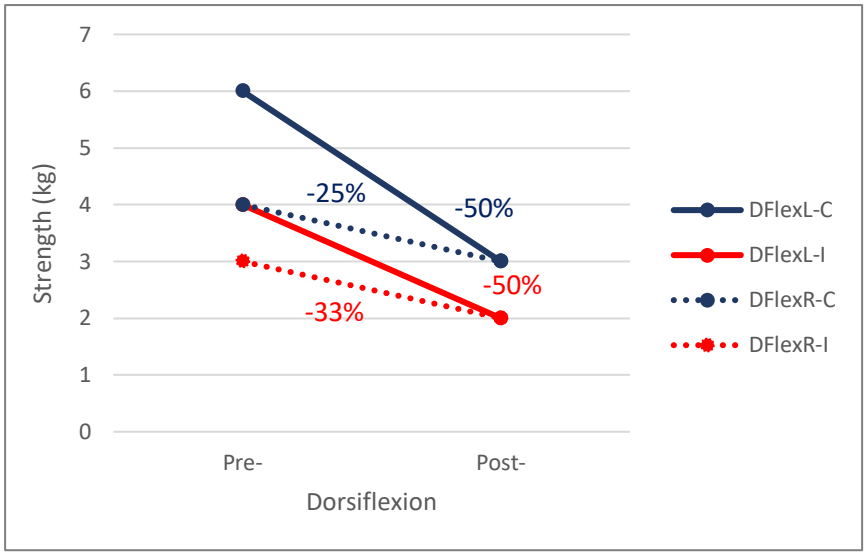
Key: C=control; I=intervention; LKE=Left Knee Extension; RKE=Right Knee Extension

Figure 4.5. Knee extension strength



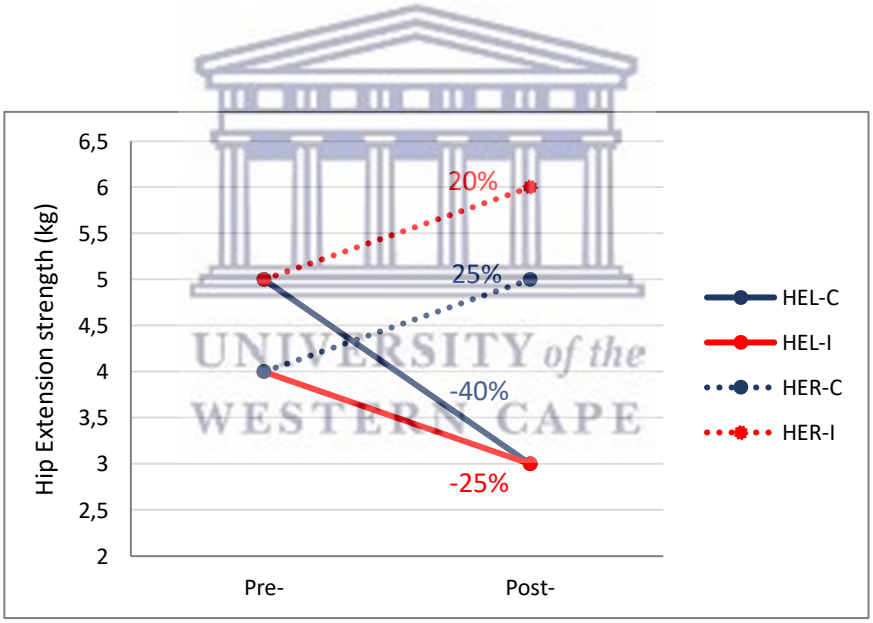
Key: C=control; I=intervention; PFlexL=Plantarflexion Left; PFlexR=Plantarflexion Right

Figure 4.6. Ankle plantarflexion strength



Key: C=control; I=intervention; DFlexL=Dorsiflexion Left; DFlexR=Dorsiflexion Right

Figure 4.7. Ankle dorsiflexion strength



Key: C=control; I=intervention; HEL=Hip Extension Left; HER=Hip Extension Right

Figure 4.8. Hip extension strength

Lastly, no statistically significant differences were observed in gait patterns for either the control group or the intervention group over the 10-week intervention period (Table 4.21).

Table 4.21 Comparison of gait pattern variables for the intervention group

Gait Patterns	Pre-intervention Median (IQR)	Post-intervention Median (IQR)	% Change	*p*-value
2 [n(%)]	2(28.57%)	2(28.57%)	0	1.000
3[n(%)]	5(71.43%)	5(71.43%)	0	

4.5. Summary of findings

A cross evaluation was used to assess the effects of the exercise intervention on these participants based on the changes in measured variables from week 1 to week 10. The expected change for the Intervention group and observed changes for both groups are shown in Table 4.22.

Table 4.22 Summary of the expected and observed changes from pre- to post-intervention

Variable	Expected change post-intervention (Intervention Group)	Observed change	
		Control Group	Intervention Group
Blood Glucose (mmol·L^{-1})	↓	↑ (37.84%) *	↓ (-17.89%)
Systolic Blood Pressure (mmHg)	↓	↓ (-4.69%) *	↓ (-9.09%)
Diastolic Blood Pressure (mmHg)	↓	↓ (-10.0%)	↓ (-13.89%)
ROM - Plantarflexion (deg)			
Left Ankle	↑	↓ (-4.62%)	↑ (12.81%)
Right Ankle	↑	↓ (-3.23%)	↑ (8%) *
ROM Dorsiflexion (deg)			
Left Ankle	↑	↔	↑ (5.26%)
Right Ankle	↑	↑ (4.17%)	↑ (11.11%)
Stork Stand (seconds):			
Left Leg	↑	↑ (77.65%)	↑ (200%) *
Right Leg	↑	↑ (2.95%)	↑ (159%) *
Strength in extension (kg):			
Left Knee	↑	↑ (22.78%)	↓ (-10.65%)
Right Knee	↑	↑ (2.95%)	↑ (179.63%)
Strength in plantarflexion (kg)			
Left Ankle	↑	↑ (41.67%)	↑ (27.45%)
Right Ankle	↑	↓ (-27.47%)	↑ (31. 37%)
Strength in dorsiflexion (kg)			
Left Ankle	↑	↓ (-41.07%)	↓ (-31.43%)
Right Ankle	↑	↓ (-34.88%)	↓ (-17.24%)
Strength in extension (kg)			
Left Hip	↑	↓ (-36.04%)	↓ (-10.53%)
Right Hip	↑	↑ (27.78%)	↑ (22.92%)
Gait pattern	↑	↔	↔

Key = ↑ Increased; ↓ Decreased; ↔ Unchanged; *=*significant at p<0.05*;

Hypothesis 1

H_1 Clinical variables (systolic and diastolic blood pressure and blood glucose) levels in patients with peripheral diabetic neuropathy in the lower legs would decrease as a result of an exercise training programme.

The findings of the study do not support this hypothesis. No significant differences were observed as a result of the intervention but the decrease in systolic and diastolic blood pressure and blood glucose levels for the participants in the intervention group may be considered clinically significant.

Hypothesis 2

H_2 Range of motion in patients with peripheral diabetic neuropathy in the lower legs would increase as a result of an exercise training programme.

The findings of the study do not support this hypothesis. In most of the ROM variables, no significant differences were observed as a result of the intervention, but a significant difference was observed in the intervention group for dorsiflexion of the left ankle. It is clear that ROM increased in the intervention group after a 10-week intervention programme which may be clinically significant.

Hypothesis 3

H_3 Balance in patients with peripheral diabetic neuropathy in the lower legs would increase as a result of an exercise training programme.

Although no significant values were observed it is evident that balance time improved as a result of the intervention programme, which may be clinically significant.

Hypothesis 4

H_4 Muscular strength in patients with peripheral diabetic neuropathy in the lower legs would increase as a result of an exercise training programme.

Although no significant values were observed it is evident that muscular strenght improved as a result of the intervention programme, which may be clinically significant.

Hypothesis 5

H_5 Gait patterns in patients with diabetic peripheral neuropathy in the lower legs would improve as a result of an exercise training programme.

The findings of the study do not support the hypothesis. No significant differences were observed as a result of the intervention but it was clear that more specific gait pattern training should be implemented in follow up research.

CHAPTER 5

DISCUSSION

5.1. Introduction

In the present study, the effects of an exercise training programme on muscular strength, ankle mobility, balance and gait patterns in patients with diabetic peripheral neuropathy in the lower legs were investigated. The research study protocol involved two groups (control and intervention) and a structured self-designed intervention training programme. All the participants received a clinical biokinetics evaluation pre- and post-intervention, regardless of group allocation. Patients in the intervention group received biokinetics exercise training sessions with a registered biokineticist for the duration of the 10-weeks. Patients from both groups were evaluated for muscular strength, range of motion/flexibility, balance and gait pattern and provided with the necessary biokinetics equipment for them to continue exercising after the study was completed.

The participants demographic details were taken in week 1, which included their age, gender duration of diabetes mellitus and physical activity level. There were 14 participants, seven females and seven males, all of whom indicated they were sedentary, and there was no significant difference between the groups in terms of mean age. In the previous chapters, it is evident that the prevalence of diabetic peripheral neuropathy increases each year with the duration of both types of diabetes (Ganu, Fletcher & Calerb, 2016; IDF, 2015) and age (Azhary et al., 2010; Gates & Walker, 2014).

5.2. Between Groups Comparisons

At week 1 (pre-intervention) participants from both groups were assessed on the same clinical and fitness measures consisting of blood glucose levels, blood pressure, ROM of the ankle, balance and isometric muscular strength of the hip, knee and ankle joints as well as a

gait pattern analysis. All the participants presented with high blood glucose levels and diastolic and systolic blood pressure at week 1, which was an expected clinical feature of DPN patients, that may be due to an increase in peripheral resistance, unhealthy and inactive lifestyles, and/or a clinical representation of diabetic sarcopenia (Cerf, 2013; Leibowitz et al., 2011; Olokoba et al., 2012).

There were no statistically significant differences in any of the variables for ROM, balance, strength or gait, except for right ankle strength in plantarflexion and balance time on the left leg. The control group had significantly higher median values for both variables. Numerous researchers have reported an increase in the buildup of advance glycation end products (AGEs) in muscles, tendons, skin, ligaments and joints with DPN, leading to a decrease in range of motion and flexibility (Bruschi et al., 2017; Jang, 2016; Singh et al., 2014; Zuchowska et al., 2013). Similarly, as age increases, single leg balance time decreases, as well as sensation in the lower limbs and proprioception (Azhary et al., 2010), resulting in an increase in fall risk and lower levels of physical activity (Camargo et al., 2014; Mustapa et al., 2016; Olokoba et al., 2012; Pani, Cavallucci & Bartoccioni, 2016; Petrofsky et al., 2005). However, despite the two significant differences, they were significant only at the $p<0.05$ level and not $p<0.01$. Therefore, it can be considered that, overall, both groups were essentially similar at baseline.

After the 10-week intervention period, there were no significant differences noted between the two groups for all variables except diastolic blood pressure, where the control group showed a 10mmHg higher reading compared to the intervention group. Exercise has been shown to decrease blood pressure (Nadi, Bambaeichi & Marandi, 2019; Shu et al., 2019; Suda et al., 2016) and a decrease in activity level follows a decrease in blood vessel reactivity and heart function (Colberg et al., 2016). This helps to explain why diastolic blood pressure increased: Due to an increase resistance and cardiac output, as a result of increased heart rate

from being sedentary. Thus, although the results from numerous variables were better in the intervention group post-test, a closer examination of the within group comparisons is warranted.

At the post-intervention stage, none of the median stork stand balances for both left and right legs were statistically significant between the two groups. The median range of motion plantarflexion of the left ankle was higher in the control group compared to the intervention group while the median range of motion plantarflexion right was higher in the intervention group compared to the control group at pre-intervention stage. Participants in both groups presented with a decrease range of motion/flexibility in plantar- and dorsiflexion in the ankle. Participants from both groups underwent the same assessments in measuring their single leg balance for both left and right leg. At the pre-intervention stage, no significant difference in the right median stork stand between the control and the intervention group were observed; however, there was a significant difference in the median stork stand balance for the left leg between the control and the intervention group. A decrease in balance (single leg stance time) were observed in all the participants at pre-intervention in both groups. A 5% decrease in plantarflexion of the left ankle and a 3% decrease in the right ankle being recorded. There was no change in dorsiflexion of the left ankle, but right ankle plantarflexion improved significantly. It is known that AGEs in the cartilage and skeletal muscle result in increased muscular stiffness and decrease in joint range of motion (Goldin et al., 2016; Jang, 2016; Negi et al., 2011; Singh et al., 2014), which could explain the general loss of ankle flexibility in the control group.

In terms of isometric muscular strength, all variables were higher in the intervention group compared to the control group at week 10 except ankle strength, which was lower. In fact, the strength of the left ankle in dorsiflexion was significantly lower for the intervention group post-test, but left knee extension strength was significantly higher. Muscular strength

training leads to an increase in muscular strength, endurance and hypertrophy (Nadi et al., 2019). Metabolic adaptions also occur during muscular strength training, such as improved sensitivity to insulin and glycaemic control (Nadi et al., 2019). Cauze et al. (2005) looked at the effect of strength training on muscular strength and metabolic control on patients with diabetes, and demonstrated a significant decrease in glycosylated haemoglobin, blood glucose levels as well as insulin resistance. However, those who participated in the endurance exercise intervention showed no significant changes in their blood glucose and insulin levels. This supports the researcher for developing and implementing low intensity muscular strengthening exercises into the intervention training programme for this research study.

Exercise intervention programmes that aim to improve flexibility, lower extremity muscular strength and balance reduce the risk of falls in DPN patients and are considered to be an important part of any exercise intervention programme (Kruse et al., 2010; Venkataraman et al., 2019). Further, those who suffer from DPN have approximately 30-50% decrease in ankle and knee power output that is correlated with the duration and severity of diabetic peripheral neuropathy (Abadi et al., 2017). Changes in lower limbs lead to altered biomechanics due to a decrease in ankle range of motion and lower extremity kinematics (El-Refay & Ali, 2014; Kluding et al., 2017; Neal at al., 2014). Developing, implementing and using a structured exercise intervention training programme consisting of muscular strength, ROM/flexibility, balance and gait pattern exercises for this study, improves functional movements, muscular strength of the ankle, increased knee range of motion and static balance, (Venkataraman et al., 2019).

As a result of diabetic sarcopenia, gait patterns are severely compromised in DPN patients. In this study, participants from both groups presented clinically with alterations in gait patterns and presented with the “slowness strategy”, that supports previous research (Azhary

et al., 2010; El-Refay & Ali, 2014; Nagwa et al., 2010; Sacco et al., 2015). However, with the gait analysis performed in this study, no statistical differences were observed between the two groups at pre-intervention; thus, the two groups were essentially similar at pre- and post-intervention.

5.3. Within Group Comparisons from Pre- to Post-Intervention

5.3.1. Control Group

In terms of clinical variables, blood glucose levels increased significantly in the control group during this time (by 38%). This is an alarming, although not unexpected, increase in only 10 weeks, and could be due to a variety of factors, including participants not presenting in a fasting state or changes in stress and/or wellness, both of which were not evaluated. Also, an increase in blood glucose may be the result of the participants in this group being non-compliant and not following a balanced diet/nutritional guideline to manage and control their blood glucose levels. This result follows research that has shown that participants with DPN, who do not participate in any physical activity or rehabilitative programmes, have steadily increasing blood glucose levels (Goldin et al., 2016; Jang, 2016; Negi et al., 2011; Singh et al., 2014). A published study by Park (2015) determined the effects of passive/static stretches on glucose levels in diabetic patients and showed no change in glycated haemoglobin levels after an 8-week intervention, which is contrary to the findings of this study, however, Park's training programme consisted only of stretches.

A statistically significant 5% decrease in systolic blood pressure and a 10% non-significant increase in diastolic blood pressure were observed in the control group over the course of the intervention period. This may have been a result of 'white coat syndrome' and participants were more comfortable with the biokineticist at post-intervention and knew what the assessments involved. Systolic blood pressure is one of the main clinical variables that a

practitioner should target and evaluate as part of the treatment of diabetic peripheral neuropathy (de Boer et al., 2017).

There were no statistically significant improvements in ROM after 10-weeks. At the 10-week post-intervention stage, the researcher observed no statistical significance between the median range of motion for left ankle plantarflexion, and the median range of motion for left and right dorsiflexion. However, the median range of motion for left plantarflexion was higher for the intervention group compared to the control group. Similarly, the median range of motion for left ankle dorsiflexion was slightly higher for the intervention group compared to the control group while the median range of motion for right ankle dorsiflexion was higher for the control group compared to the intervention group at the 10-week follow up assessment. Only the right ankle plantarflexion range of motion showed a statistically significant median difference between the two groups after the 10-week follow up assessment for the intervention group.

There was no statistical significance in the stork stand balance scores for either leg after a 10-week follow up assessment for the control group, although balance time increased for both legs, indicating that their balance was impaired. Similarly, there were no significant changes in isometric strength of the hip, knee or ankle in the control group over the 10-weeks. Overall, knee strength increased by an average of 13%, ankle strength decreased by about 12% and there was essentially no change in hip strength. Goldsmith, Lidtke and Shott (2002) concluded that range of motion intervention exercises reduces peak plantar pressure in DM patients which reduces the risk of foot ulcerations in DPN patients. An increase in muscle mass and fibre size assist with insulin responsive target tissue to regulate blood glucose levels, resulting in a decrease in the development of insulin resistance (Shu et al., 2019). As a result, a decrease in muscular mass and muscle strength is evident in DPN

patients in this study, leading to an alteration in kinetics and kinematics (Camargo et al., 2014; Jang, 2016; Singh et al., 2014).

When looking at the kinetic chain, functional movement patterns and slings, such as the posterior longitudinal sling changes in patients with diabetic peripheral neuropathy (DPN), and DPN patients has to compromise and adapt to a new movement patterns to generate movement (Hoch et al., 2014; Nenkova et al., 2009; Sacco et al., 2015). The posterior longitudinal sling involves an increased muscle activation pattern of the latissimus dorsi, gluteal muscle group, hip flexors and knee flexors on the dominant side of the individual resulting in a decrease of muscle activation of the hip extensors, knee extensors and ankle plantar- and dorsiflexors. Patients who suffer from type II DM have a significant decrease in proximal and distal musculature and muscular strength due to an increase amount/volume of intramuscular fat present in the distal musculature (Almurdhi et al., 2016). Thus, although there was an overall decrease in ankle strength, there was an increase in muscular strength of both knees in the control group and an increase in left hip strength but a decrease in right hip in extension. This is contrary to the findings of Almurdhi et al. (2016) who conducted a study with type II DM patients who were matched with healthy patients. The authors concluded that patients with type II DM had significantly decreased muscular volume of both knee flexors and extensors compared with healthy individuals. It could well be that the participants in the current study experienced an increase in sarcopenia through increased AGEs in the cartilage, skin, tendons and skeletal muscles, leading to the overall decrease seen in muscle strength of the lower extremities.

Gait patterns remained the same and no improvements were observed after the 10-week follow up assessment, although there was a change in clinically observed gait patterns. The modified Tinetti gait pattern assessment was used to measure gait patterns in this study. No changes were observed in after the intervention, which could be due to insufficient specific

gait pattern rehabilitation exercises prescribed in the intervention programme or the duration of the intervention period only being 10-weeks. It could also be that the gait pattern assessment utilised was not sensitive enough to small changes in gait over the 10 week intervention period.

5.3.2. Intervention Group

In comparing the intervention group from pre- to post-testing, it is clear that blood glucose levels in the intervention group decreased, although not significantly. The decrease was 18%, which can be considered to be clinically significant, however, as any drop in blood glucose levels is desirable in people with DM. This decrease in blood glucose levels can be attributed to an increase in muscular strength. The storage of blood glucose and insulin is regulated by skeletal muscle leading to a decrease in blood glucose levels as muscular size progressively increases (Umegaki, 2015), specifically in areas such as the distal musculature of the triceps surea, quadriceps femoris, hamstrings and adductor muscle groups (Almurdhi et al., 2016). These results support the findings of other researchers in that exercise has been shown to positively affect blood glucose homeostasis, which improves due to structural remodelling of skeletal muscle as a result of the exercise intervention (Abadi et al., 2017; Duclos et al., 2013; Nadi, Bambaeichi & Marandi, 2019; Park, 2015; Shu et al., 2019; Streckmann et al., 2014; Tokmakidis et al., 2004). Elgayer et al. (2019) concluded that passive and active stretches have a positive effect on blood glucose levels and functional capacity in patients with DPN. My research supports the study of Elgayer et al. (2019) to implement passive/active stretches as part of an exercise intervention to treat DPN patients in improving ROM of the ankle and maintaining blood glucose levels. Passive/static stretches are an intervention modality that has been shown to successfully reduce blood glucose levels in DM patients (Solomen, Shakya, Agarwal, & Aaron, 2015).

There was a non-significant 9% decrease in systolic blood pressure and a 14% decrease in diastolic blood pressure for the intervention group during the 10 weeks, which was expected. It is also known that muscular strength/resistance training reduces systolic blood pressure (Nadi, Bambaeichi & Marandi, 2019; Shu et al., 2019). Any form of physical activity increases and improves blood vessel reactivity and heart function (Colberg et al., 2016), hence blood pressure is a factor of total peripheral resistance and cardiac output. A decrease in blood pressure can also result in a decrease in fatigue levels, an increase in exercise tolerance and adaptations and changes in type I and II muscle fibre types (Suda et al., 2016).

Both plantarflexion and dorsiflexion increased in the intervention group after the 10-week follow up assessment. An overall increase of approximately 9% in ankle flexion was noted, but none of the changes were statistically significant. An increase in range of motion can be attributed to a decrease in AGEs, causing a decreased muscle stiffness and increased joint mobility, thus flexibility. Furthermore, increased ankle mobility and flexibility improves balance and activities of daily living in patients with DPN (El-Kader, 2018). The results of this study support these findings with a significant 200% increase in left leg balance time and a non-significant 159% increase for the right leg. It is known that incorporating balance and proprioceptive exercise training into an exercise intervention for DPN patients decreases fall risks and any associated co-morbidities (Almurdhi et al., 2016). These authors stated that prevention exercise training is of utmost importance when working with DPN patients due to their decreased distal musculature and blood flow supply. Cheuy et al. (2016) demonstrated that an increase in intrinsic foot muscle and extrinsic toe extensor strength lead to increased balance and coordination in patients with DPN.

Changes in isometric muscular strength were variable in the intervention group, but none were significant. Right leg isometric strength in knee extension increased by 180%, while the left knee decreased by 11%. Similarly, right hip strength increased by 23% yet decreased

by 10.5% in the left hip. Ankle strength in plantarflexion increased for both legs yet for dorsiflexion, strength decreased. This could be due to an increase in muscular strength and muscle fibre size and muscle stiffness due to the exercise intervention specifically targeting distal musculature. As stated previously, there is currently no published research available on isometric muscular strength testing using the PAB, with previous research having looked mainly at either concentric or isokinetic muscular strength testing of the hip, knee and ankle (Abadi, Salahzadeh, Rezaei, Oskouei & Azghani, 2017). Previous research done by Martinelli et al. (2013) evaluated isometric ankle strength and the effect on gait patterns. They used an electronic baropodometry treadmill to measure the spatio-temporal parameters of gait. They found that patients with DPN experience impaired gait patterns with a smaller stride length and decreased speed and increased stance time, resulting in a decrease in muscular strength of the plantar- and dorsiflexors and decreased range of motion in dorsiflexion and increased range of motion in plantarflexion.

Changes in ankle mobility and strength can assist with improvements in gait patterns. The PAB is a newly developed objective measuring tool but does not allow the participants to be in a moving state but more in a static position. It allows measurements of strength in a specific range of motion of the joint being tested where the participant is able to produce force without discomfort. Research conducted by Allen et al. (2013) measured functioning motor units of the limb muscle not specific to hip, knee and ankle. They noted that, by using the PAB as a measuring tool to assess isometric muscular strength of a joint in a specific range of motion where the participants are most comfortable, allows improvement in muscular strength of the specific joint when developing an intervention programme for patients with DPN. Thus, using the PAB as an objective measurement to assess isometric muscular strength allows the clinician to evaluate the patient's maximum muscular strength

within the patient's ROM capacity and the ability to produce sufficient strength in the various joints in particular movement patterns.

Gait patterns remained the same throughout the 10-week follow-up period in the intervention group. Various methods to improve gait patterns, lower extremity muscular strength and endurance exercise training on DPN patients can be used and implemented (Salsabili, Bahrpeyma & Esteki, 2016). Salsabili et al. (2016) encourage the researcher to design and develop more specific gait pattern training interventions using functional exercise training to improve gait patterns in DPN patients for any future research studies. Increased muscular strength leads to a decrease in muscular deficiencies resulting in improved gait pattern abilities, biomechanics and kinetics (Brown et al., 2015; Hillson, 2017; Najafi et al., 2012; Wrobel & Najafi, 2010). As per clinical observations of gait patterns, the researcher noted improvements in gait patterns in the intervention group after the 10-week follow up assessment. Although no statistical change was observed in gait patterns after the 10-week intervention follow up, gradual progression of improvement can be accountable to the clinical improvement in gait pattern abilities seen in the participants in the intervention group. Although it was emphasised to the participants that their gait patterns would not change completely after the 10-week intervention, but a combination of strengthening, balance and proprioceptive rehabilitation will improve their gait patterns and decrease fall risk, leading to improved quality of life (Pan & Bai, 2014).

With carefully selected exercises consisting of low-intensity activities to assist with the improvements in the vascular and metabolic pathways, exercise interventions will decrease nocturnal allodynia (pain to light touch) and increase quality of life (Johnson & Takemoto, 2019). With that being said, an improvement in all aspects, including increased muscular strength, decreased diabetic sarcopenia, increased joint flexibility and mobility and by

decreasing the DPN signs and symptoms, a carefully prescribed rehabilitation programme for those with DPN will enhance and improve their quality of life.

Although only a few statistically significant increases/decreases were noted in this study as a result of the exercise intervention, a clinically positive change was noted in all the measured variables. A possible reason is that improvement in clinical and fitness variables is not only dependent upon changes in muscle mass but also on alterations and improvements in range of motion/joint flexibility, lifestyle changes and modifications and an increase in activity level. All these take time and perhaps a 10-week exercise programme was not long enough for the adaptations to be large enough to show significant changes. There were definite trends in the right direction in terms of adaptations in the intervention group, and had the study continued for a few more weeks, perhaps significant changes would have been seen. Venkataraman et al. (2019) designed the exercise intervention based on the following aspects of DPN, such as, decrease muscle strength in the lower extremities, decreased ankle ROM and decreased balance. Venkataraman et al. (2019) found similar statistically significance as seen in this research study with variables such as, balance, ROM and muscular strength of the ankle and knee. My study supports the study of Kruse, LeMaster and Madsen (2010) and Nadi, Bambaeichi and Marandi (2019) in developing and implementing balancing exercises, low intensity and resistance training into the exercise intervention programmes to include weight-bearing exercises to decrease fall risk, decrease pain and to improve balance and proprioception and to increase muscle mass and muscular strength. Overall, it appears to have been a clinically effective programme for people with DPN.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1. Conclusions

Diabetes mellitus is increasing rapidly worldwide each year and the prevalence of diabetic peripheral neuropathy is increasing along with the duration of DM (Ganu, Fletcher & Caleb, 2016). Thus, it is crucial that new treatment and rehabilitation protocols should be considered and that the exercise intervention programme should be evaluated and adjusted to individual needs. In this study, the researcher developed a training protocol and evaluated its effectiveness as a programme that could be used to treat diabetic peripheral neuropathy. It was hypothesised that this training protocol would have a positive effect on a number of clinical and fitness variables.

Although not many significant changes were observed as a result of the intervention, positive changes did occur in the majority of variables, which can be considered clinically significant. Therefore, individual, scientifically based rehabilitation protocols/interventions can be prescribed to DPN patients to improve muscular strength in the lower limbs and to improve overall muscular strength and endurance and improving functional capacity in the performance of daily living activities. The findings of this study indicate that an isometric evaluation is effective in the treatment of DPN to evaluate and determine an effective treatment plan/intervention for patients with DPN, and to determine muscular strength deficits in both lower limbs in patients with DPN.

6.2. Limitations

- Due to COVID-19 restrictions, some participants in the control and intervention group were unable to attend their final assessment, reducing the sample size.

- Small sample size/participant availability. Due to some participants not being cleared by their medical doctor to participate in any form of physical activity.
- Pre-COVID-19 restrictions, some participants in the control and intervention group missed their appointments/contact sessions, due to them not being compliant.
- Due to some of the participants having a chronic disease/condition, some participants were medically booked off work for certain periods during the intervention and could not attend their appointments.
- Due to time restriction/time management, some participants in the intervention group missed their Biokinetics appointments.
- Some of the participants in the intervention group experienced either hypo- or hyperglycaemia and/or hypo- or hypertension and were unable to attend Biokinetics appointments.

6.3. Recommendations

Practical recommendations include the following:

1. Conduct isometric clinical evaluations of the entire kinetic chain prior to the development of any rehabilitation protocol. To ensure that proper history taking is being done and that proper Biokinetics treatment can be implemented and individualised scientific rehabilitation can be done/implemented for each participant.

2. Take digital video photography of exercise prescriptions prior to distribution of individualised exercise training programmes. To ensure the patients perform the rehabilitation exercises correctly to minimize/limit any injuries.

3. Do a follow up clinical evaluation, followed by an individualised progression programme based on clinical evaluation outcomes. To ensure progression

rehabilitation/treatment are made by both clinician and patient and to ensure adequate progression and improvement.

4. Conduct a stress electrocardiography (ECG) test prior to any rehabilitation protocol. DPN patients may suffer from other co-morbidities such as hypertension. To evaluate and monitor heart function and aerobic capacity.

Recommendations for future research include the following:

1. Include evaluations of isotonic muscle contractions up the entire kinetic chain.
2. Develop and evaluate individualised isotonic-based exercise training programmes for people with DPN.
3. Develop and evaluate isometric rehabilitation protocols based on the PAB.
4. Include the use of electromyography (EMG) in the assessment of the distal musculature, to evaluate muscle function and to adapt specific rehabilitation exercises accordingly.

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APPENDIX A

SAMPLE LETTER TO HOSPITALS AND PRIVATE PRACTICES

Date:

To: (Hospitals/ Private practice)

Dear Sir/Madam

I am currently a Masters student at the University of the Western Cape, department of Sport, Recreation and Exercise Science. I wish to conduct a research study entitled: "Effects of an exercise training programme on muscular strength, ankle mobility, balance and gait patterns in patients with diabetic peripheral neuropathy in the lower legs", for which I request your permission and assistance to approach patients under your care who have been diagnosed with a diabetic neuropathy to participate in this study.

Participants will be divided into two groups: Intervention and comparison groups. The intervention group will receive a balance exercise training programme for 10 weeks (20 sessions) and the comparison group will do nothing. The comparison group will be allowed to undertake the exercise training programme only after all data have been collected, should it prove beneficial. Pre- and post-intervention assessments will include isometric testing of the hip, knee and ankle joints using a pressure air biofeedback system, range of motion of the ankle in plantar- and dorsiflexion, through goniometry, a balance test through a stork stand test, a gait pattern analysis and blood glucose levels (before, during and after exercise) to ensure patient safety.

I have submitted my proposal for ethics approval and received permission to proceed with my study from our Biomedical Research Ethics Committee (number: BM19/7/12). I confirm that participation of all the patients and the procedures conducted in this study will occur in an ethical manner. Information about the participants will be kept confidential and all participants will remain anonymous through the use of an alpha-numeric code system. I aim to conduct the data collection during November 2019 to March 2020.

I trust you will be able to assist me in this regard and look forward to further communication with you.

Yours sincerely,

Ronél du Plessis

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Tel: +2721-959 2409 **E-mail:** dbowers@uwc.ac.za

INFORMATION SHEET

Title: Effects of an exercise training programme on muscular strength, ankle mobility, balance and gait patterns in patients with diabetic peripheral neuropathy in the lower legs.

What is this study about?

This is a research project being conducted by Ronél du Plessis at the University of the Western Cape. I am inviting you to participate in this research project because you have been diagnosed by a physician with diabetic peripheral neuropathy. The purpose of this study is to determine if there is an effect of strength, balance and gait pattern training on diabetic neuropathy.

What will I be asked to do if I agree to participate?

You will be asked to go for an assessment at a private Podiatry practice, Dembskey Podiatry in Alberton, Johannesburg. You will also be asked to complete a consent form stating that you agree to voluntarily participate in the study and will be asked to undergo a variety of assessments conducted by the researcher. The assessments will include, range of motion assessment of the ankle, isometric strength assessment of the hip, knee and ankle and a balance test. The duration of the assessments will be one hour per session and will be conducted before, during and after a 10-week (20 sessions) exercise intervention period. Some participants will be randomly allocated to the intervention group, who will receive balance training for 10 weeks (20 sessions), whereas the rest of the participants will be a comparison group and receive no intervention initially. The control group would receive the exercise intervention once the study is completed, so they too can benefit from the study. During this time, all participants are asked to

continue with the treatment regime prescribed by your doctor.

Would my participation in this study be kept confidential?

I will ensure that your personal information is kept anonymous and confidential. A participant number will be assigned to each participant and only the researcher will have access to the key connecting the number to your name. All data will be stored on a password protected computer and in a locked filing cabinet. Data will be kept for 5 years after the study and will thereafter be destroyed. If I do write an article or report about this research, each participant's identity will be protected at all times.

What are the risks of this research?

Risks may include that someone may find the files that link the number to the participants information. Muscle stiffness/soreness may be present after assessments have been done. Participants may feel dizzy when participating in the intervention exercise programme. The researcher is a trained first aider and will provide necessary care if needed, or you will be referred to the appropriate medical professional.

What is the benefit of this research?

Each participant will receive a report about the assessments done. If you are in the intervention group, you will receive the intervention exercise programme for 10 weeks (20 sessions), as well as the rehabilitation equipment needed to be able to perform the exercises. If you are in the comparison group you will not undergo any exercise intervention for the 10-week period of the study, however you will be allowed to complete the intervention exercise programme after the study has been conducted. All participants will be asked to continue with the medical care being provided by their doctor during the study period. Furthermore, I hope that you will understand diabetic neuropathies better and benefit from the exercise activities. Each participant will receive free assessments and exercise treatment throughout the duration of the study.

Do I have to be in this research and may I stop participating at any time?

Your participation in this study is completely voluntary. You may choose not to participate at all. If you decide to participate in this study, you may feel free to stop at any time. If you decide to not participate or stop at any time during the study, you will not be penalised or lose any benefits to which you would otherwise qualify.

What if I have questions?

This research is being conducted by Ronél du Plessis at the University of the Western Cape. If you have any questions about the research, please feel free to contact Miss Ronél du Plessis at duplessisbio@gmail.com , my supervisor, Prof Susan Bassett at sbassett@uwc.ac.za or my co-supervisor, Nadia Dembskey at info@dembskey-podiatry.co.za

Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Dr Marie Young
Head of Department: SRES
University of the Western Cape
Private Bag X17, Bellville 7535
myoung@uwc.ac.za

Prof Anthea Rhoda
Dean of the Faculty of Community and Health Sciences
University of the Western Cape
Private Bag X17, Bellville 7535
chs-deansoffice@uwc.ac.za

This research has been approved by the University of the Western Cape's Biomedical Research Ethics Committee - (REFERENCE NUMBER: BM19/7/12)

Biomedical Research Ethics Committee
University of the Western Cape
Private Bag X17, Bellville 7535
Tel: 021 959 4111
e-mail: research-ethics@uwc.ac.za

APPENDIX C

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Tel: +2721-959 2409 **E-mail: dbowers@uwc.ac.za**

CONSENT FORM

Title: Effects of an exercise training programme on muscular strength, ankle mobility, balance and gait patterns in patients with diabetic peripheral neuropathy in the lower legs.

The study has been described to me that I understand and I freely and voluntarily agree to participate. All my questions about the study have been answered. I understand that my identity will not be disclosed to anyone. I understand that I may withdraw from the study at any time without giving a reason and without fear of negative consequences or loss of benefits.

Participant name: _____

Participant contact number: _____

Emergency contact number: _____

Participant signature: _____

Date: _____

APPENDIX D

UNIVERSITY of the WESTERN CAPE

OFFICE OF THE DIRECTOR: RESEARCH

RESEARCH AND INNOVATION DIVISION

Private Bag X17, Bellville 7535
South Africa
T: +27 21 959 4111/2948
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E: research-ethics@uwc.ac.za
www.uwc.ac.za

18 September 2019

Ms R Du Plessis
SRES
Faculty of Community and Health Sciences

Ethics Reference Number: BM19/7/12

Project Title: Effects of an exercise-training programme on muscular strength, ankle mobility, balance and gait in patients with diabetic peripheral neuropathy in the lower leg.

Approval Period: 17 September 2019 – 17 September 2020

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias

Research Ethics Committee Officer
University of the Western Cape

BMREC REGISTRATION NUMBER -130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

APPENDIX E

DATA COLLECTION SHEET

Participant ID	
Name	
Surname	
DOB	
Age	
Gender	

History:

Height:_____

Weight:_____

Activity Level:_____

_____

_____

	Initial			Avg		5 weeks			Avg		10 weeks			Avg
Plantarflexion	R L	R L	R L	R L		R L	R L	R L	R L		R L	R L	R L	R L
Dorsiflexion	R L	R L	R L	R L		R L	R L	R L	R L		R L	R L	R L	R L
Stork stand L (sec)														
Stork stand R (sec)														
Gait Pattern	1.N	2. H	3.S											
Treadmill Speed														
Time on Treadmill														

BLOOD PRESSURE (mmHg)			
Date	**Before**	**During**	**After**

BLOOD GLUCOSE (mmol/L)			
Date	**Before**	**During**	**After**

PRESSURE AIR BIOFEEDBACK SYSTEM – MAXIMUM STRENGTH (KG – 10sec)						
	Initial assessment		**10 sessions (5 weeks)**		**20 sessions (10 weeks)**	
	Left	**Right**	**Left**	**Right**	**Left**	**Right**
Knee Extension						
Hip Extension						
Ankle Plantarflexion						
Ankle Dorsiflexion						

APPENDIX F

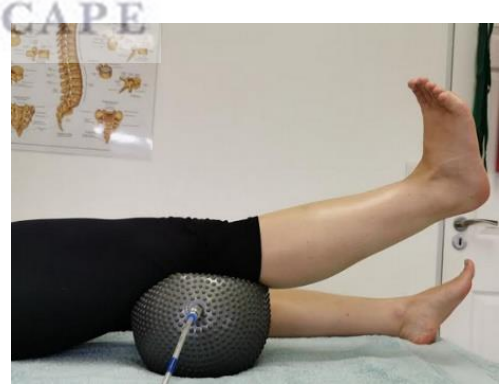
PRESSURE AIR BIOFEEDBACK SYSTEM® (PAB) ISOMETRIC STRENGTH ASSESSMENT

HIP EXTENSION

The participant was asked to stand and lean forward on a chair/desk with both hands, as demonstrated. One side of the strap was attached around the ankle of the non-supporting leg drawn back (no flexion of the knee was allowed) until a 45º angle is formed between the legs. The foot of the supporting leg was on strap number 1, 2 or 3 to fix it in place. The participant was then instructed to extend the hip as far as possible and hold the position for 10sec. The isometric strength of the hip extensors such as the gluteal muscle group, piriformis, adductor magnus and the long head of the biceps femoris was measured. The isometric strength (maximum strength) of the hip extensors was recorded in kilograms (kg).

KNEE EXTENSION

The participant was asked to be seated in an upright position on a plinth, with both legs extended in front of her. The touch ball was placed underneath the knee. The participant was instructed to extend the knee as hard as possible and hold the position for 10sec. The knee extension test assesses the isometric strength (maximum strength) of the quadriceps muscles of each knee and was measured and recorded in kilograms (kg). The knee extension test was be performed as a closed kinetic chain assessment.

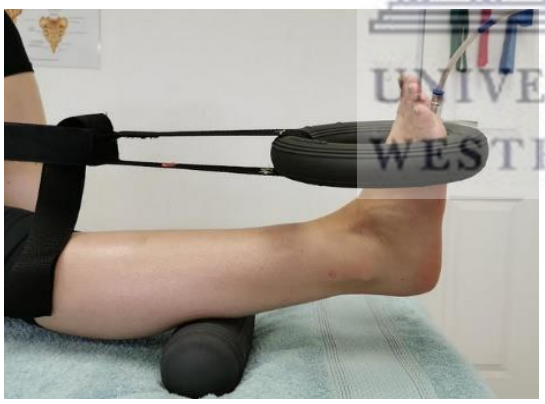


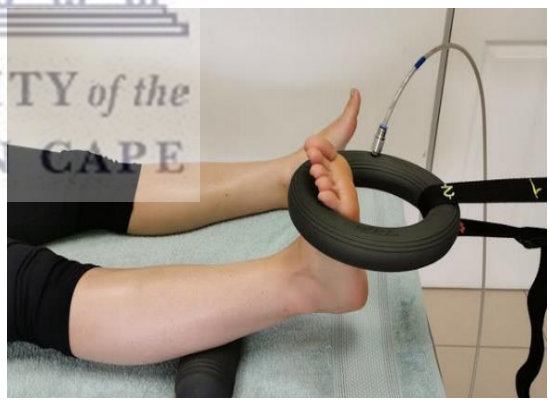
PLANTAR FLEXION

The participant was asked to sit on the plinth with legs extended out in front of her. The strap was attached on one side around a fixed position and the participants foot will be placed in the pull ring. The participant was instructed to push down on the ring as hard as possible with the knee extended and hold the position for 10sec. The plantarflexion test assesses the isometric strength (maximum strength) of the triceps surea muscle group of each ankle and was measured and recorded in kilograms (kg).

DORSIFLEXION

The participant was asked to sit in an upright position on a plinth with legs extended out in front of her. The researcher held one selected strap number (1, 2 or 3) and the participant was instructed to pull the toes up while keeping the knee extended and to hold the position for 10sec. The dorsiflexion test assesses the isometric strength (maximum strength) of the anterior tibialis muscle of each ankle and was measured and recorded in kilograms (kg).





APPENDIX G

MODIFIED TINETTI GAIT PATTERN ASSESSMENT/SCALE

Participant ID: _____

Gait Pattern: 1. Normal 2. High 3. Shuffle		**Pre-Assessment**	**Post-Assessment**
		Date:	**Date:**
Indication of gait	Any hesitancy or multiple attempts = 0 No hesitancy = 1		
Step length and height	Step to = 0 Step through R = 1 Step through L = 1		
Foot clearance	Foot drop = 0 L foot clears floor = 1 R foot clears floor = 1		
Step Symmetry	Right and left step length not equal = 0 Right and left step length appear equal = 1		
Step continuity	Stopping or discontinuity between steps = 0 Steps appear continuous = 1		
Path	Marked deviation = 0 Mild/moderate deviation or uses w. aid = 1 Straight without w. aid = 2		
Walking time	Heels apart = 0 Heels almost touching while walking = 1		
	Gait Pattern Score	**/10**	**/10**

APPENDIX H

UNIVERSAL HEALTH PRECAUTIONS

(Broussard & Kahwaji, 2019)

HAND HYGIENE

Hand hygiene is very important and a very effective way to reduce the risk(s) associated when working with blood.

Various steps will be followed to sure hand hygiene;

1. Hand wash facilities will be readily available.
2. Wash hands with water and soap for 40 – 60 seconds.
3. Clean soap will be available.
4. Clean hand towels will be available.
5. Alcohol-based hand rub will be available.
6. Hands will be wiped dry before working with patients.

PERSONAL PROTECTIVE EQUIPMENT

GLOVES

1. Clean gloves will be used between tasks and procedures.
2. Clean gloves will be changed between each procedure.
3. Gloves will be removed after use and hand hygiene will be followed once gloves has been removed.
4. Used gloves will be placed in a medical waste bin.

FASCIAL PROTECTION

1. Surgical masks and eye protection will be used during procedures.
2. Used surgical masks and eye protection will be placed in a medical waste bin.

PREVENTION OF NEEDLE STICK & INJURIES FROM OTHER SHARP INSTRUMENTS

1. Lancets will be handled with care and will be disposed of in a medical waste bin.

ENVIRONMENTAL CLEANING

1. Equipment will be disinfected frequently.
2. Frequently touched surfaces will be disinfected, before and after each consultation and session with patients.

EQUIPMENT CLEANING

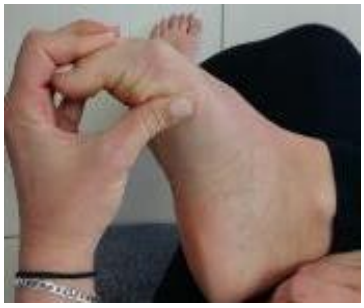
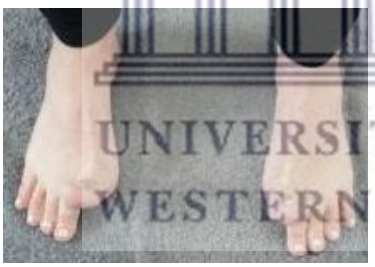
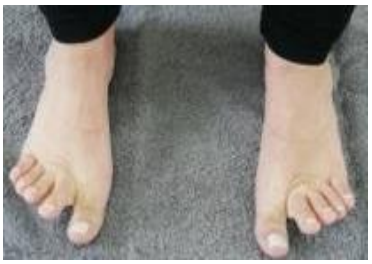
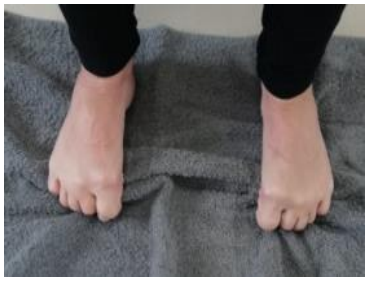
1. Equipment will be disinfected, before and after use.

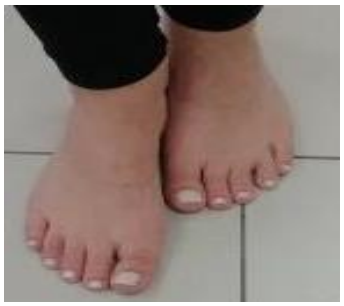
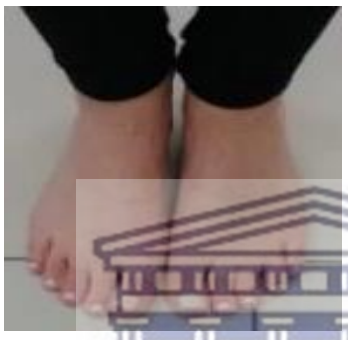
WASTE DISPOSAL

1. Safe waste management will be conducted.
2. Used lancets, alcohol swabs, tissues and plasters will be disposed of in a medical waste bin.

APPENDIX I

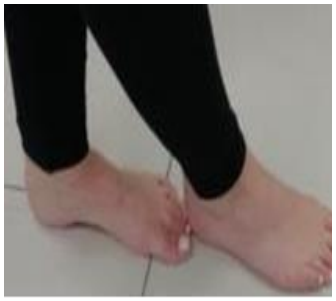
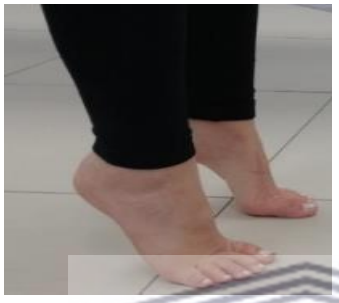
DAY 1 – EXERCISE INTERVENTION

Exercise	Demonstration	Time (secs)	Sets	Comments
Toe Flexors Stretch, with Gluteal Stretch (seated)		10	1	Sit with legs straight. Place one foot across the thigh and flex the toes with your hand. Hold for 10 seconds and repeat with the other leg.
Toe Extensors Stretch, with Gluteal Stretch (seated)		10	1	Sit with legs straight. Place one foot across the thigh and flex the toes with your hand. Hold for 10 seconds and repeat with the other leg.
Toe Flexors		15	2	Stand with feet comfortably apart. Keeping the heels on the ground, lift the big toe up whilst simultaneously pushing the other toes down.
Toe Extensors		15	2	Stand with feet comfortably apart. Keeping the heels on the ground, push the big toe into the ground whilst simultaneously lifting the other toes up.
Towel Crunches		15	2	Stand with feet comfortably apart. Crunch toes around the towel. Repeat for 15 seconds, keeping the heels on the ground.

Exercise	Demonstration	Time (secs)	Sets	Comments
Parallel Balance (eyes open) and Parallel Balance (eyes closed)		20	2	Place one foot half way along the other foot, feet together. Hold the position for 20 seconds (repeat with other foot in front). To increase the intensity – close eyes or stand on an uneven surface such as a foam pad.
Double Leg Stance (eyes open) and Double Leg Stance (eyes closed)		20	2	Stand with feet together and hold the position for 20 seconds. To increase the intensity – close eyes or stand on an uneven surface such as a foam pad.
Standing Rotation		20	2	The leg closer to the wall should be slightly more to the front to ensure thoracic rotation. Follow the hand as it rotates to the other side.

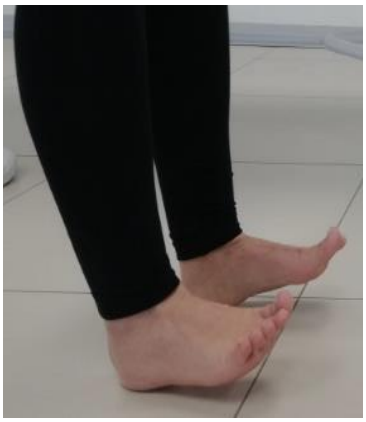
DAY 2 – EXERCISE INTERVENTION

Exercise	Demonstration	Time (secs)	Sets	Comments
Pectoralis Major Stretch		20	2	Place one arm on the wall, with the elbow in a 90° position. Place the leg closest to the wall a bit forward of the other leg. Rotate the torso away from the wall, maintaining elbow contact with the wall at all times.
Pectoralis Minor Stretch		20	2	Place one arm onto the wall, with the elbow in a 45° position. Place the leg closest to the wall a bit forward of the other leg. Rotate the torso away from the wall, maintaining elbow contact with the wall at all times.
Gastrocnemius Stretch		20	2	Place one leg in front, with the knee bent and the back leg straight. The heel of the back leg should be kept on the floor at all times. Push body weight slightly forward.
Plantarflexion		20	2	Plantarflex foot against resistance bend, keeping the leg straight. Place a rolled-up towel underneath the calf.
Dorsiflexion		20	2	Keep the leg straight. Place a rolled-up towel underneath the calf.

Exercise	Demonstration	Time (secs)	Sets	Comments
Tandem Balance (eyes open) and Tandem Balance (eyes closed)		20	2	Place right leg in front and hold the position for 20 seconds. Repeat with left leg in front. To increase the intensity – close eyes or stand on an uneven surface such as a foam pad.
Toes Standing (eyes open) and Toes Standing (eyes closed)		20	2	Stand up on the toes and hold the position for 20 seconds. To increase the intensity – close eyes or stand on an uneven surface such as a foam pad.
Single Leg Balance (eyes open)		20	2	Balance on one leg and hold the position for 20 seconds. Repeat with the other leg. To increase the intensity – stand on an uneven surface such as a foam pad.
Heel Walking		15	2	Walk for 15 seconds on the heels. To increase the intensity – close eyes or stand on an uneven surface such as a foam pad.

DAY 3 - EXERCISE INTERVENTION

Exercise	Demonstration	Time (sec)	Reps	Comments
T-Spine mobility		20	2	Stand with back against the wall, arms raised to 90^{o} at shoulders and elbows flexed, hands on the wall.. Step about ½ metre away from the wall, bending the knees to a 45° angle. Hold for 20 seconds.
90 Degree T-Spine Mobility, with Hamstring Stretch		20	2	Stand about a metre from a chair, holding onto the back of the chair. Bend the knees to a 45° angle. Bend forward from the hips and push the chest down to the ground. Hold for 20 seconds.
¼ Squat side stepping with a resistance band		15	2	Bend the knees to a 45° angle. Walk sideways in a ¼ squat position. Repeat for 15 seconds.
Standing calf raises with a myofascial ball		15	2	Stand on either a step or hold onto a chair for support. Squeeze the ball while lifting the body up on the toes and back down again. Repeat for 15 seconds.

Exercise	Demonstration	Time (sec)	Reps	Comments
Heels Standing (eyes open) and Heels standing (eyes closed)		20	2	Stand with feet comfortably apart. Hold onto something for support if required initially, and lift the toes off the ground. Hold for 20 seconds. To increase the intensity – stand on an uneven surface such as a foam pad.
Toe Walking		15	2	Walk on toes for 15 seconds. To increase the intensity – stand on an uneven surface such as a foam pad.
Single Leg Balance (eyes closed		20	2	Stand on one leg and hold the position for 20 seconds. Repeat with the other leg. To increase the intensity – stand on an uneven surface such as a foam pad.
Single Leg Balance with Weight Shifting		20	2	Stand on one leg with the knees bent at 45°. Shift body weight slightly forward and balance for 20 seconds. Repeat with the other leg. To increase the intensity – stand on an uneven surface such as a foam pad.