Effects of a long term exercise program on lower limb mobility in peripheral arterial disease patients

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Declaration of ethics

The research presented and reported in this thesis was conducted within the guidelines for research ethics outlined in the *National Statement on Ethics Conduct in Research Involving Human (1999)*, the *Joint NHMRC/AVCC Statement and Guidelines on Research Practice (1997)*, the *James Cook University Statement and Guidelines on Research Practice (2001)*. The proposed research methodology received clearance from the James Cook University Experimentation Ethics Review Committee (approval number H2395).

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Signature Date

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Abstract

Peripheral arterial disease (PAD) is a chronic arterial occlusive disease of the lower extremities caused by atherosclerosis. The most common presenting symptom of PAD is intermittent claudication (IC) with exercise induced pain experienced in the calves, thighs or buttocks that is relieved with rest. Research investigating the effects of PAD-IC on lower limb mobility is limited to five studies on the temporal-spatial gait parameters (e.g. stride length, cadence, support times, speed) in PAD-IC populations that produced conflicting results. Gardner et al. (2001) speculated that the temporal-spatial gait parameters of individuals with PAD-IC could be improved by participation in exercise programs. To date there has been no attempt to determine the validity of this proposition. There has also been no research on the underlying mechanism of these temporal-spatial gait parameters namely gait kinematics (angular joint displacement, velocity and acceleration). Observed limitations in temporal-spatial gait parameters may be explained by the effects of musculoskeletal abnormalities on lower limb joint kinematics during the gait cycle. Understanding of the relationships between temporal-spatial gait parameters and gait kinematics in PAD-IC allows more precise identification of gait abnormality and its effects on lower limb mobility in this population. Analysis of variability in gait kinematics is becoming more commonly used as a clinical tool for evaluation of lower limb mobility in the elderly, lower limb disease populations and individual responses to exercise programs. Increased movement variability in lower limb kinematics has been traditionally associated with decreased movement performance due to disease and aging. However, more recent research from a dynamical systems perspective has indicated that movement variability may be of functional importance in motor control and may provide flexibility when adjusting to movement constraints imposed by disease.

Therefore, for the purposes of this thesis, a series of studies were undertaken to investigate 1) the temporal-spatial gait parameters, gait kinematics, lower limb movement variability, walking performance, physiological responses to exercise and physical activity levels of individuals with and without PAD-IC and 2) the effects of a long term exercise program on these same variables in individuals with PAD-IC compared to individuals with and without PAD-IC.

Study 1 (Chapter 3) examined the lower limb mobility characteristics (temporal-spatial gait parameters and gait kinematics) of individuals with PAD-IC and the relationships between lower limb mobility, walking performance, physiological responses to exercise and physical activity levels in this population. Study 2 (Chapters 4 & 5) assessed intralimb joint coordination and single joint movement variability in patients with PAD-IC and without PAD-IC (CON). Lower limb mobility characteristics were determined via 2D motion analysis. A graded treadmill test was used to assess walking performance (pain free walking distance/time (PFWD/T) and maximal walking distance/time (MWD/T) and peak physiological responses to exercise (VO_{2peak}, HR_{peak}, RER_{peak} and VE_{peak}). Physical activity levels were measured via a 7 d pedometer recording following motion analysis. Intralimb coordination variability was measured using parameterization, vector coding and normalized root mean square techniques applied to relative motion plots of various joint couplings. Single joint movement variability was measured using spanning set and coefficient of variation. Study 3 (Chapter 6) examined the effects of a 12 mth exercise program on the lower limb mobility of individuals with PAD-IC. A further aim was to examine the extent to which lower limb mobility contributes to long term exercise induced changes in walking performance, peak physiological responses to exercise and physical activity levels in PAD-IC patients.

Finally study 4 (Chapter 7) investigated the effects of a 12 mth exercise program on walking performance and lower limb movement variability using intralimb joint coordination and single joint assessment techniques in individuals with and without PAD-IC.

Compared to CON, PAD-IC temporal-spatial gait parameters were significantly lower ($P < .05$), except for single support ipsilateral limb time. PAD-IC participants spent a greater percentage of time in gait support phases, took longer to complete a stride and had reduced stride length and walking speeds during the gait cycle. Participants with PAD-IC joint angular kinematics showed significantly reduced displacement of ankle plantar flexion ($P = .017$), knee ROM ($P = .021$) and hip extension ($P = .016$) compared to the CON participants during the gait cycle. All joint minimum and maximum angular velocities and accelerations, physiological responses to exercise (walking) and physical activity levels were significantly lower for PAD-IC compared to the CON participants. The PAD-IC participants displayed significantly higher levels of lower limb movement variability in all joints when assessed using the intralimb joint coordination and single joint movement variability techniques.

The 12 mth exercise program had no significant effect on lower limb mobility, peak physiological responses to exercise or physical activity levels in PAD-IC patients who received normal medical therapy treatment and a 12 mth exercise program (TPAD-IC) compared to PAD-IC patients who received normal medical therapy (CPAD-IC) . However, the TPAD-IC participants demonstrated significantly greater walking performance (171% improvement in PFWT and 120% improvement in MWT) compared with baseline. The 12 mth supervised exercise program made no significant

impact on the lower limb movement variability of the TPAD-IC group as determined by either intralimb joint coordination or single joint analysis techniques.

The results of these studies show that patients with PAD-IC have reduced lower limb mobility (temporal-spatial gait parameters and gait kinematics) and increased lower limb movement variability. The derived gait kinematics highlighted that the push-off (or toe-off) of the gait cycle in PAD-IC patients is significantly reduced compared to healthy age matched controls. The increased level of lower limb movement variability may be an adaptation to the gradual onset of claudication pain in this population. Patients with PAD-IC also demonstrated reduced walking performance, peak physiological responses to exercise and physical activity levels compared to healthy age matched controls. PAD-IC patients involved in a 12 mth supervised exercise program exhibited no change in lower limb mobility characteristics, physiological responses to exercise or physical activity levels. Gardner et al.'s (2001) speculation that the reduced temporal-spatial gait parameters of PAD-IC patients could be modified to resemble that of age matched controls through the use of an exercise program was not supported by the data. However, a 12 mth supervised exercise program did cause a significant improvement in walking performance in this population sample. It is suggested that the improvement in walking performance may be due at least in part, to adaptation of peripheral physiological mechanisms.

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Chapter 1

Introduction

Ageing population

Mean life expectancy in Australia increased dramatically during the 20th century, and is expected to continue to increase. The average life expectancy of a new-born male in Australia increased from 55.2 yr in 1901-10 to 76.2 yr in 1997-99, while the life expectancy of a new-born female increased from 58.8 to 81.8 yr during the same period representing an increase of 21 yr and 23 yr for males and females respectively. This increase in life expectancy is due to lower mortality rates at all ages which is caused by increased medical treatment and education. The proportion of the Australian population aged 65 yr – 84 yr is expected to increase substantially, from 12% in 1999 to between 24% and 27% in 2051 and to 25-28% in 2101. The proportion aged 85 yr and over is expected to almost quadruple, from 1.3% in 1999 to approximately 5% in 2051 and approximately 6% in 2101 (Australian Bureau of Statistics, 2002). With this increase in the elderly population of Australian the prevalence of cardiovascular disease will increase.

Cardiovascular disease in Australia

Cardiovascular disease (CVD) is a national health problem in Australia. More than three million adult Australians had a recent and/or long-term cardiovascular condition in 2001. Heart, stroke and vascular disease accounted for 50,290 deaths (37.6% of all

deaths) in 2002 in Australia. In 2002, coronary heart disease was the major cause of death, accounting for 51.8% of deaths followed by stroke (24.9%), heart failure (5.4%), peripheral vascular diseases (5.1%) and rheumatic fever and rheumatic heart disease (0.5%) (Australian Institute of Health and Welfare, 2004).

From 1991-2002 the CVD mortality rate declined at a rate of 4.3%·yr^{-1} for males and 4.0%·yr^{-1} for females. This decline is thought to be partly due to improved survival following cardiovascular events and partly due to a fall in the rate of morbidity of CVD, owing to improvement in and better management of the risk factors (Australian Institute of Health and Welfare, 2004). However, if the current trends in older population numbers continue there may be an increase in CVD mortality rates.

Peripheral arterial disease and mortality rates

Peripheral arterial disease (PAD) is a chronic arterial occlusive disease of the lower extremities caused by atherosclerosis (Aronow, 2004b; Curci & Sanchez, 2003; Gardner, 2001; Hirsch et al., 2001). Atherosclerosis is a condition whereby poor circulation in the blood vessels occurs due to blockages (Olin, 2002; Savage et al., 2001). More commonly known as “hardening of the arteries” it is a condition involving a gradual thickening, hardening, and loss of elasticity in the walls of the arteries, which can be caused by fatty deposits, platelets and calcium. For PAD affected individuals the most common affected arteries include those that supply blood from the heart, to the feet and legs via the aorta, iliac, femoral, popliteal, and tibial arteries (Gardner, 2001; Hiatt, Hirsch, Regensteiner, & Brass, 1995; Olin, 2002; Savage et al., 2001). PAD is estimated to have caused 2,581 (1.9%) of all deaths in Australia in 2002 and was

responsible for 24,288 hospitalisations (0.4% of all hospitalisations) in 2001-2002 with males being twice as likely to die from PAD as females. The mortality rate for PAD declined at a rate of 5.1%·yr^{-1} for males and 4.7%·yr^{-1} for females between 1991-2002. However, the condition is still a health concern particularly for older Australians (Australian Institute of Health and Welfare, 2004).

Cause and symptoms of PAD

In the early stages of PAD a common symptom is ischemic pain (cramping) or fatigue in one or both legs and buttocks during physical activity (Brook, Weder, Grossman, & Rajagopalan, 2002; Comerota, 2003; Gardner, 2001; Hiatt, Regensteiner, Hargarten, Wolfel, & Brass, 1990; Olin, 2002; Schmieder & Comerota, 2001). The symptoms usually subside within minutes of cessation of walking/exercise (Brook et al., 2002; Comerota, 2003). This condition is called "intermittent claudication" (IC) and it limits participation in daily physical activities which can impact on an individual quality of life (QOL) (Aronow, 2004b; Breek, Hamming, De Vries, Aquarius, & van Berge Henegouwen, 2001; Brook et al., 2002; Burns, Gough, & Bradbury, 2003; Johnstone, 2003; Schmieder & Comerota, 2001).

The main risk factors for PAD-IC are smoking, high blood pressure (hypertension), high cholesterol, diabetes, lack of physical exercise and obesity (Aronow, 2004b; Burns et al., 2003; Olin, 2002). Smoking is the most important risk factor for developing PAD-IC (Burns et al., 2003; Christman, Ahijevych, & Buckworth, 2001; Gardner, Killewich, Montgomery, & Katzel, 2004; Hiatt, 2001). Cessation of smoking has been shown to decrease PAD-IC symptoms improving health and consequently QOL

(Gardner, 2001; Hiatt et al., 1990; Olin, 2002; Savage et al., 2001; Schmieder & Comerota, 2001). Hypertension is another risk factor for PAD-IC (Burns et al., 2003; Olin, 2002) with individuals twice as likely to develop PAD-IC compared to those in comparable health who do not have high blood pressure (Armen & Smith, 2003; Burns et al., 2003; Olin, 2002). As well as high blood pressure, individuals who have diabetes have a greater risk of developing PAD-IC, but the condition also increases the possibility of several other risk factors occurring such as hypertension, poor cholesterol profile (low levels of high density lipoprotein (HDL) cholesterol and/or high levels of low density lipoprotein (LDL) cholesterol) and obesity (Aronow, 2004b; Burns et al., 2003; Olin, 2002). Research has shown that when cholesterol levels are improved, PAD-IC symptoms can remain stable or decrease (Feringa et al., 2007). In addition, controlling the risk factors for PAD-IC can prevent or ameliorate an existing condition (Burns et al., 2003; Olin, 2002). Other factors that may increase the risk of PAD-IC include family history and damaged arteries. Genetic factors are associated with specific lipid and cholesterol abnormalities, which in turn may increase the risk of PAD-IC (Valentine et al., 2004). Elevated levels of C-reactive protein are indicators of persistent inflammation in the arteries, which is known to cause significant damage in blood vessels and to be highly associated with PAD-IC (Narins et al., 2004).

As described earlier if an individual has PAD-IC, the arteries in the legs are obstructed with fatty deposits that can restrict blood flow (Feinglass, McCarthy, Slavensky, Manheim, & Martin, 1996). During any activity involving the lower limbs there is an increased demand for blood and oxygen in the legs that cannot be met when the arteries are blocked. This results in the lower limbs receiving an insufficient supply of blood and oxygen, resulting in pain/cramping in the lower limbs (Olin, 2002). Upon cessation

of activity the demand for oxygen and blood in the legs decreases and pain/cramps are eased. Symptoms of advanced PAD-IC involve obstruction of the arteries in the legs to the degree that even rest offers no relief and pain continues even when lying, sitting or standing. This condition is referred to as "ischemic rest pain" (Aronow, 2004b; Brook et al., 2002; Hiatt et al., 1990). In this severe situation, the arteries can become so obstructed that ulcers, withered calf muscles, hair loss over the toes and feet, thick toenails, shiny tight skin and gangrene can develop, which can lead to amputation of the limb(s) (Aronow, 2004b; Schmieder & Comerota, 2001).

Diagnosis of PAD-IC

Many individuals with PAD-IC either do not report symptoms and/or may not experience leg pain in the early stages (Aronow, 2004b; Olin, 2002). It is recommended that individuals should be evaluated for PAD-IC if they have risk factors such as heart disease, high cholesterol, obesity, smoking, leg pain during walking, or ulcers on their legs (Brook et al., 2002; Comerota, 2003). PAD-IC diagnosis is relatively simple, by comparing blood pressures taken in the arm and ankle arteries known as Ankle-Brachial Index (ABI) using Doppler ultrasonography, an assessment of PAD-IC is produced (Aronow, 2004b; Brook et al., 2002; Comerota, 2003). The ankle area will have a much lower or undetectable blood pressure reading compared to the arm. Also examination of the skin of the legs and feet for colour changes, ulcers, infection, or soft tissue injuries can be used to diagnose PAD-IC (Comerota, 2003; Olin, 2002). Angiography can also be used to diagnose and define this disease which involves taking x-ray pictures to visualise the inner internal diameter of arteries (Burns et al., 2003; Hirsch et al., 2001; Valentine et al., 2004). A treadmill test (either constant load or graded) can be used to

test an ABI if further assessment is needed (Gardner, 2001). Patients with PAD-IC demonstrate a 50-60% reduction in walking performance compared to healthy age matched controls, which is also comparable to the walking performance of patients with congestive heart failure. A treadmill test is also useful for determining the severity of the pain while walking and for assessing the effectiveness of treatment therapies (Gardner, 2001).

Questionnaires are also used in the assessment, diagnosis and analysis of treatment progression of PAD-IC as the patient is able to report functional impairments without having to undergo physical testing sessions (Breek et al., 2001; Carlon, Morlino, & Maiolino, 2003; Gardner, 2001; Menard et al., 2004; Stewart et al., 2003). One of the most important questionnaire measures of PAD-IC impact and treatment outcomes is perceived QOL (Breek et al., 2001; Carlon et al., 2003). Questionnaires have been used in PAD-IC studies to assess changes in QOL and include the Short Form-36 (SF-36®) (Ware, 1993), the Nottingham Health Profile, and the EuroQol (The EuroQoL Group, 1990) questionnaires (Chong, Garratt, Golledge, Greenhalgh, & Davies, 2002; Cook & Galland, 1997). However, these questionnaires are generic and are designed for application to other conditions and it has been suggested that they may fail to focus on PAD-IC and thus fail to assess changes in perceived QOL (Chong et al., 2002). The Walking Impairment Questionnaire (WIQ) (Regensteiner, Steiner, Panzer, & Hiatt, 1990) and the Intermittent Claudication Questionnaire (ICQ) (Chong et al., 2002) involve function-specific measures of outcome and have been shown to be practical, reliable, valid, and responsive measures of perceived QOL in PAD-IC affected individuals (Chong et al., 2002). It has become standard practice for researchers to use a combination of PAD-IC and non-PAD-IC questionnaires to quantify the impact of

PAD-IC on performing activities of daily living (ADL) and perceived QOL (Gardner, 2001).

Consequences of PAD-IC

The consequences of PAD-IC are a decrease in QOL, an increase in CVD risk and therefore an increase in CVD mortality rate. An individual diagnosed with PAD-IC, has the same risk of death from cardiac events or stroke as a person with evident heart disease (Burns et al., 2003). This risk increases with the degree of PAD-IC. In rare cases, blood clots can develop suddenly in the major arteries in the leg, a condition known as acute occlusion (Aronow, 2004b). Symptoms of acute occlusion include numbness, pain, coolness, pale skin colour, lack of pulse in the artery, and leg weakness (Aronow, 2004b). This is a very serious event, which can lead to amputation or even loss of life. Individuals that have severe PAD-IC demonstrate deterioration in several physiological aspects (e.g. peak oxygen uptake and heart rate) that may contribute to their inability to exercise and perform ADL which can then lead to diminished QOL.

Treatment of PAD-IC

PAD-IC treatment strategies aim to relieve the symptoms of IC, increase walking performance and physiological responses, modify the cardiovascular risk factors, and improve perceived QOL (Hiatt, 2001; Regensteiner & Hiatt, 1995). Treatment strategies used to manage leg pain and improve function can include vascular surgery, angioplasty, pharmacotherapy and exercise therapy (Figure 1)(Aronow, 2004b; Burns et al., 2003; Chong, Golledge, Greenhalgh, & Davies, 2000; Creasy, McMillan, Fletcher,

Collin, & Morris, 1990; Curci & Sanchez, 2003; de Vries et al., 2002; Gardner, 2001; Leng, Fowler, & Ernst, 2000; Olin, 2002; Ouriel, 2001; Wang, 2004).

Pharmacotherapy treatments such as anti-platelet agents are used to reduce blood clots and fatty deposits thus reducing the risk of heart disease and stroke. Aspirin acts as a non-specific anti-platelet agent to reduce cardiovascular risk in patients with PAD-IC (Olin, 2002). Clopidogrel (Plavix) is a more potent platelet inhibitor recommended for patients with PAD-IC (Aronow, 2004b; Federman, Bravata, & Kirsner, 2004; Olin, 2002). Cilostazol is an agent that improves blood flow and is proving to be useful for disabling PAD-IC (Aronow, 2004b; Dawson, 2001; Dawson et al., 2000; Dawson, Cutler, Meissner, & Strandness, 1998). Other drugs such as anti-hypertensive and cholesterol-lowering agents known as statins may also be beneficial for individuals with PAD-IC (Aronow, 2004b; Mohler, Hiatt, & Creager, 2003; Young-Xu, Chan, Liao, Ravid, & Blatt, 2003). Most patients take combinations of these medications to reduce further development of PAD-IC. Other treatments involve the use of anticoagulants such as aspirin, warfarin, or heparin, to thin the blood and prevent blood clots that occur during surgery (Burns et al., 2003; Curci & Sanchez, 2003). All of these agents however, increase the risk of bleeding. Alteplase also called “Activase” or “t-PA’ and reteplase also called “Retavase” are thrombolytic agents commonly known as a "clot-busters" which are used to diminish existing clots and may be used before, during, or after angioplasty if a blood clot is present (Burns et al., 2003; Curci & Sanchez, 2003).

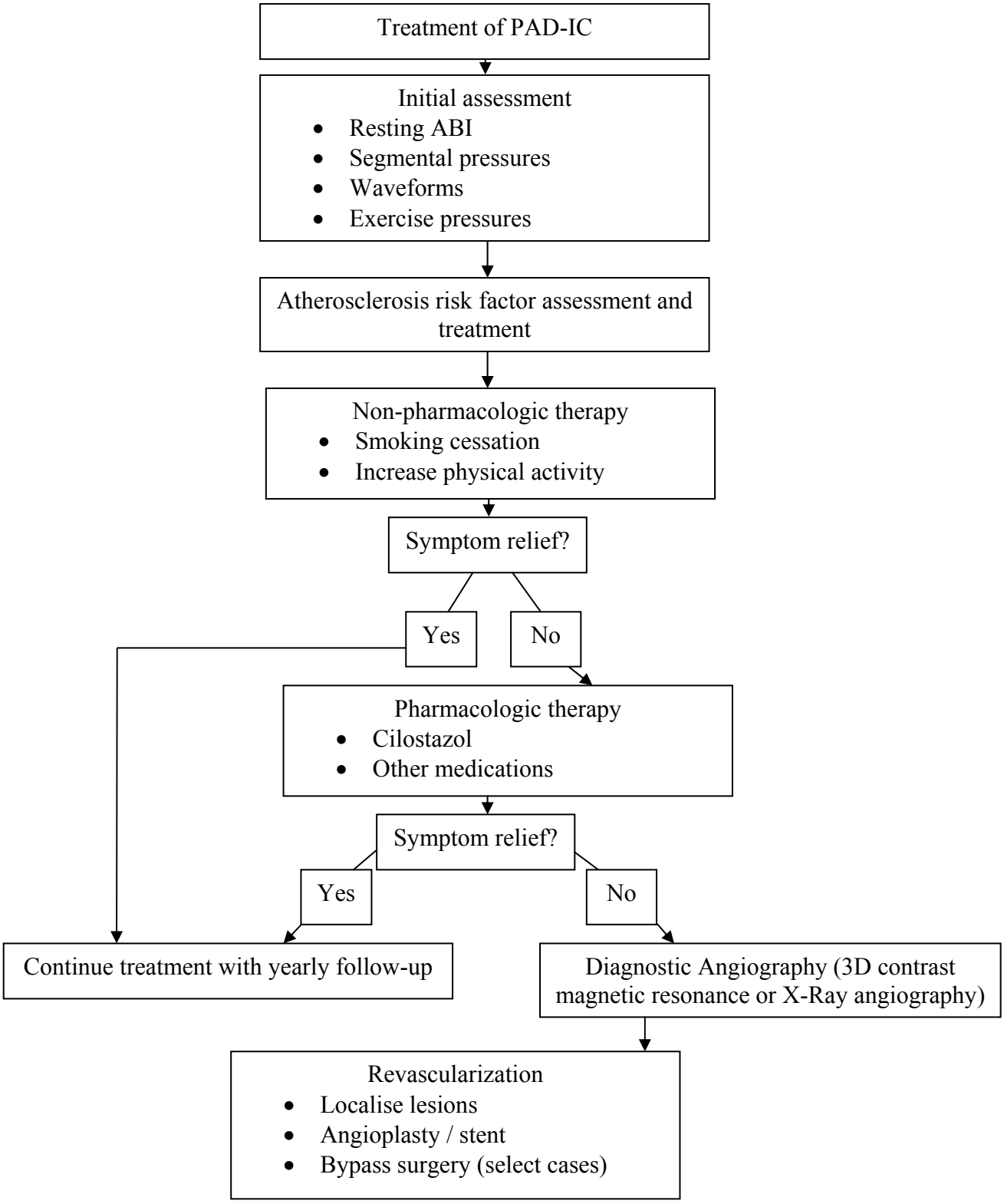

Figure 1 General approaches to the management of patients with PAD-IC (adapted from Brook et al., 2002).

In severe cases of PAD-IC where pharmacotherapy treatment is not beneficial other treatments such as opening the obstructed blood vessels (angioplasty) or bypass the obstructed blood vessels (graft surgery) may be undertaken (Chong et al., 2002; Chong et al., 2000; Creasy et al., 1990; de Vries et al., 2002; Gardner, 2001; Wang, 2004). Percutaneous transluminal angioplasty (PTA) is an a procedure used to widen the narrowed or totally-obstructed blood vessels causing IC (Creasy et al., 1990; de Vries et al., 2002; Gardner, 2001; Wang, 2004). This procedure is being increasingly used, especially in patients who have other medical conditions. Some authors believe that it is not only much less expensive, but is also more effective than surgical bypass (Chong et al., 2002; Chong et al., 2000; Creasy et al., 1990; de Vries et al., 2002; Gardner, 2001; Ouriel, 2001; Wang, 2004). The procedure is minor, requiring a local anaesthetic and the patient can return to normal activity in 24-48 h. The advantage of this procedure is that complication rates are low and the effects are permanent. However, if necessary the procedure can be repeated without any greater risk than with the original procedure (Burns et al., 2003).

Regardless of the initial treatment, PAD-IC patients are encouraged to increase their physical activity levels through the use of exercise/walking programs, thereby reducing the risk factors associated with PAD-IC (Hankey, Norman, & Eikelboom, 2006). These programs have been found to be very effective in reducing PAD-IC risk factors and improving QOL. The walking programs typically involve the patient walking until maximal leg pain occurs, followed by rest until the patient is able to walk again (Aronow, 2004b; Gardner, 2001; Regensteiner & Hiatt, 1995; Sorlie & Myhre, 1978; Tan, De Cossart, & Edwards, 2000b). The major benefit of exercise programs is their non-invasive nature and the ease with which patients can engage in the activity.

Over the past 40 yr there has been considerable research on the effects of exercise training on PAD-IC affected individuals. A meta-analysis of the effects of exercise rehabilitation studies (Gardner & Poehlman, 1995) reported that the average walking distance to the onset of claudication increased by 179% from 126 to 351 m and average walking distance to maximal claudication pain increased by 122% from 326 to 723 m following a 3 mth exercise rehabilitation program. Due to the dramatic improvement in walking performance of individuals with PAD-IC following an exercise program and the non-invasive nature of the program, exercise training is a good course of action for treatment of PAD-IC. However, it is recommended that a holistic treatment approach be adopted whereby an exercise program is undertaken in conjunction with pharmacology prescription. This holistic approach helps to reduce the risk of CVD and improves walking performance, ADL and perceived QOL in individuals with PAD-IC (Antignani, 2003; Bendermacher, Willigendael, Teijink, & Prins, 2005; Meru, Mittra, Thyagarajan, & Chugh, 2005).

PAD-IC and improved walking performance

It is not clear which mechanism(s) underlie improved walking performance in PAD-IC affected individuals following exercise program participation. Increased blood flow to the peripheral arteries, increased capillary growth in the muscles, increased oxygen perfusion and changes in lower limb mobility (Lumsden & Rice, 2006; Womack, Sieminski, Katzel, Yataco, & Gardner, 1997) have all been suggested as contributing to improved walking performance, yet there is no consensus as to the major contributing factor. Understanding the mechanisms of improved walking performance in this population may assist in the structure and management of PAD-IC treatment programs.

PAD-IC and lower limb mobility

In order to have freedom of movement and personal fulfillment, a level of functional independence is required (Daley & Spinks, 2000). However, as an individual becomes older, the risk of disease and possible injury increases with ongoing implications for health. The increased incidence of disease with age impacts on the physical activity level and general mobility of individuals and leads to further increases in disease states, risk of injury and reduced QOL (Gardner, Forrester, & Smith, 2001a; Maki, 1997). Research has shown that lower limb mobility characteristics (temporal-spatial gait parameters and gait kinematics) are predictors of functional decline (Brach, VanSwearingen, Newman, & Kriska, 2002; Gill, Williams, & Tinetti, 1995; Guralnik, Ferrucci, Simonsick, Salive, & Wallace, 1995; Spirduso & Cronin, 2001) and have been related to increased risk of falling (Daley & Spinks, 2000; Prince, Corriveau, Hebert, & Winter, 1997; Rubenstein, Powers, & MacLean, 2001; Sadeghi, Prince, Zabjek, Sadeghi, & Labelle, 2002). Therefore understanding how chronic disease influences lower limb mobility characteristics is very important.

PAD-IC is one such disease that can impact dramatically on the lower limb mobility of an individual. Research has indicated that PAD-IC significantly influences temporal-spatial gait parameters (Gardner et al., 2001a; Scherer, Bainbridge, Hiatt, & Regensteiner, 1998) however, other studies contradict these findings stating that PAD-IC has no effect on temporal-spatial gait parameters (McCully, Leiper, Sanders, & Griffin, 1999; Scherer, Hiatt, & Regensteiner, 2006). Gardner et al., (2001) speculated that exercise programs could be used to improve the temporal-spatial gait parameters of

PAD-IC affected individuals to the extent that they would more closely resemble the gait characteristics of healthy age matched controls.

The measurement of temporal-spatial gait parameters usually involves capturing video footage of a full gait cycle (ipsilateral heel contact to ipsilateral heel contact) and analysis of certain aspects (e.g. stride length, knee range of motion) of the gait cycle (Whittle, 2003). Typically, temporal-spatial gait parameters of interest in the gait cycle include stride length, cadence, stride time, contact time, swing time, support time and speed. Determination of temporal-spatial gait parameters and angular gait kinematics (joint angular displacement, velocity, acceleration) allows conclusions to be made about general mobility, health and therefore perceived QOL (Whittle, 2003).

PAD-IC and lower limb movement variability

Temporal-spatial gait parameters and joint angular kinematics may not always indicate alterations in the biomechanical patterns of the lower limbs. Variability of the lower limb angular kinematics (movement variability) was once thought to be "noise" and not beneficial to human walking. However, the lower limb joint movement variability has been shown to reveal more information about human locomotion. From a Dynamical Systems theory perspective variability is defined as the level of variation between multiple attractors (which represent states in which movement components are brought into relation with each other) that permits flexible and adaptive motor system behaviour, thereby encouraging free exploration of performance contexts by each individual (Newell & Corcos, 1993). Variability is said to share a relationship with stability, whereby an increase in movement variability will produce an increase in

instability. This relationship has been used to demonstrate the process of learning a motor skill. In the initial stages of learning a skill there is a high level of variability, as the person performing the skill has multiple attractors and so there is a high level of instability. As the skill is learnt, movement variability is reduced and therefore the performance becomes stable (Newell & Vaillancourt, 2001). This relationship exists in the processes of learning to walk. When an infant begins to walk there is a high level of movement variability and instability. However, as the child learns to move the legs, gain balance and control the number of possible independent dimensions of movement in a system (i.e. degrees of freedom), the movement variability is reduced and walking becomes more stable (Newell & Vaillancourt, 2001).

Lower limb movement variability research has determined that temporal-spatial gait parameter variability provides information about gait stability where measures of temporal-spatial gait parameters do not. High stride length and stride width variability has been shown to reveal underlining gait instability which may cause poor mobility leading to increased falls and poor obstacle avoidance (Hausdorff, 2005; Hausdorff, Edelberg, Mitchell, Goldberger, & Wei, 1997). However, due to temporal-spatial gait parameter variability being an outcome measure of locomotion and not the mechanism of walking, lower limb movement variability characteristics can be lost. Therefore, assessment of movement variability using joint angular kinematics (i.e. range of movement (ROM) of the knee) is required to provide an in-depth measurement of stability and/or gait changes.

Joint angular kinematics research has determined that both older and injured individuals exhibit reduced movement variability in the lower limbs (Heiderscheit, Hamill, & van

Emmerik, 2002; Van Emmerik, Hamill, & McDermott, 2005; Van Emmerik, Wagenaar, Winogrodzka, & Wolters, 1999). Therefore, it would appear that the assessment of movement variability using either temporal-spatial gait parameters or the joint angular kinematics would provide distinctly contrasting information about lower limb mobility and motor control characteristics during locomotion (Heiderscheit, 2000). However, given existing research findings it is not possible to conclude that higher movement variability in joint angular kinematics of the lower limbs is either beneficial or detrimental. Researchers continue to investigate this question in order to determine if movement variability can supply information regarding lower limb mobility in relation to disease, obstacle avoidance (risk of falls) and perceived QOL.

There has been only limited research into ways of quantifying variability of joint angular kinematics. Analysis techniques may include linear variable to variable relationships, which may be described as a variable-variable plot or intralimb coordination. The variable-variable plot can involve the angular kinematic ROM of a segment (thigh, shank and foot) and/or angular kinematic ROM of a joint (ankle, knee and hip) and/or angular kinematic velocity of a joint (e.g. hip angle vs. thigh angle, hip velocity vs. knee angle and knee velocity vs. knee angle). Variable-variable plots have been used to examine movement coordination in a variety of activities including slope walking and the effects of patellofemoral injury during walking (Goswami, 1998; Heiderscheit et al., 2002). The variable-variable plot was initially used as a qualitative tool and therefore did not provide any quantitative data concerning individual coordination patterns. However, in recent times these plots have been used to generate quantitative data for gait analysis. Parameterization, vector coding and normalized root mean square are three techniques that have been applied to variable-variable plots to

describe/quantify joint coordination variability (Goswami, 1998; Sidaway, Heise, & Schoenfelder-Zohdi, 1995; Tepavac & Field-Fote, 2001).

As well as intralimb joint coordination variability, single joint movement variability can be used to assess movement variability. Whereby single joint angular kinematics ROM is used (i.e. ankle, knee and hip) instead of data from two joints. This method of determining movement variability eliminates the effect of intra joint relationships of joint couplings. Spanning set and coefficient of variation are single joint techniques used to determine movement variability of the lower limbs (Kurz, Stergiou, & Blanke, 2003; Winter, 1991). The use of movement variability analysis as a clinical tool is becoming more common as a means of evaluating the lower limb mobility, disease and responses of individuals to intervention programs (Hausdorff, 2005).

In summary, PAD-IC is a health concern for the elderly Australian population as this condition has been shown to reduce walking performance, physiological responses to exercise, physical activity level and QOL. There have been contradictory research findings concerning the effects of PAD-IC on lower limb mobility (temporal-spatial gait parameters and gait kinematics) and it has been suggested that the lower limb mobility of PAD-IC affected individuals could be improved via participation in exercise programs. It has also been suggested that improved lower limb mobility may be a factor in the improved walking performance seen in patients with PAD-IC engaged in an exercise program. Assessment of lower limb movement variability may also provide additional information regarding changes in lower limb mobility as a result of participation in exercise programs. However, the extent to which lower or higher movement variability is beneficial or detrimental to human gait is not clear.

Furthermore, different techniques have been used to calculate lower limb variability and to date none of these have been considered superior.

Statement of the problem

PAD-IC is a health concern which may well become more common with the increasing number of elderly adults in the population. PAD-IC has been shown to affect walking performance, physiological responses to exercise, physical activity levels and QOL. Research has shown that management of PAD-IC using non-surgical methods such as pharmacotherapy and exercise programs can improve walking performance and perceived QOL. However, the mechanism(s) underlying improved walking performance post exercise training in PAD-IC patients is unclear. Potential mechanisms include increased peripheral blood flow, increased muscle capillary growth and alteration of lower limb mobility characteristics. To date there has been no research that has examined the effects of exercise interventions on the lower limb mobility characteristics of PAD-IC affected individuals. Gardner et al. (2001) proposed that an exercise program could improve the lower limb mobility characteristics of individuals with PAD-IC to resemble more closely those of healthy age matched controls. Thus this study aimed to determine if a long term (12 mth) exercise program influenced the lower limb mobility, physiological responses to exercise, walking performance and physical activity levels of PAD-IC patients compared to healthy age and mass matched controls.

Hypotheses

The following thesis consists of: Studies 1 and 2) examination of the temporal-spatial gait parameters, gait kinematics, lower limb movement variability, walking performance, physiological responses to exercise and physical activity levels of individuals with and without PAD-IC; studies 3 and 4) an investigation of the effects of a long term exercise program on the temporal-spatial gait parameters, gait kinematics, lower limb movement variability, walking performance, physiological responses to exercise and physical activity levels of individuals with PAD-IC compared to individuals with PAD-IC who did not undertake the exercise program and individuals without PAD-IC.

For studies 1 and 2 it was hypothesised that individuals with PAD-IC (compared to individuals without PAD-IC) would demonstrate:

1. Reduced lower limb mobility as demonstrated by reduced temporal-spatial gait parameters and gait kinematics.
2. Reduced walking performance, physiological responses and physical activity levels.
3. Reduced movement variability of the lower limbs.

For studies 3 and 4 it was hypothesised that individuals with PAD-IC following a 12 mth exercise program compared to individuals with or without PAD-IC (without a 12 month exercise program) would demonstrate:

1. Improved temporal-spatial gait parameters and gait kinematics.
2. Improved walking performance, physiological responses to exercise and physical activity levels.

3. Changes in lower limb movement variability.

Format for investigation

Firstly, an in-depth review of the current literature pertaining to PAD-IC involving disease rate, assessment and treatment as well as lower limb mobility including gait analysis, motor control and movement variability is presented in the review of the related literature (Chapter 2). The first experimental study (Chapter 3) examined the relationship between temporal-spatial gait parameters, gait kinematics, walking performance, physiological responses to exercise and physical activity levels in individuals with and without PAD-IC. The second experimental study (Chapters 4 & 5) examined lower limb movement variability in individuals with and without PAD-IC, by assessing movement variability via intralimb joint coordination techniques (Chapter 4) and single joint techniques (Chapter 5). The third experimental study (Chapter 6) examined the effects of a long term exercise program on temporal-spatial gait parameters, gait kinematics, walking performance, physiological responses to exercise and physical activity level in PAD-IC individuals. The fourth experimental study examined the effects of a long term exercise program on walking performance and lower limb movement variability (Chapter 7) in individuals with PAD-IC. Finally a summary of the findings of the study, the conclusions arising from the results of the research and recommendations for future research are discussed (Chapter 8).

Limitations and delimitations – Studies 1 & 2

Limitations

The findings of this study were limited to:

1. The sample sizes.
2. Non-random selection of participants.
3. Variation in the health and fitness levels of the participants.
4. Validity and reliability of the instrumentation.
5. Control of testing procedures.

Delimitations

The findings of this study were delimited to:

1. Male and female individuals resident in the Townsville region who had been diagnosed with PAD-IC.
2. Investigation of selected biomechanical, physiological, physical activity levels and walking performance variables in individuals with and without PAD-IC.

Limitations and delimitations – Studies 3 & 4

Limitations

The findings of this study were limited to:

1. The sample sizes.
2. Non-random selection of participants.
3. Variation in the health & fitness levels of the participants.
4. Validity & reliability of instrumentation.

5. Control of testing procedures

Delimitations

The findings of this study were delimited to:

1. Male and female individuals resident in the Townsville region diagnosed with and without PAD-IC.
2. Investigation of selected biomechanical, physiological, physical activity levels and walking performance variables in individuals with and without PAD-IC before and after a 12 mth exercise program.

Definition of terms

- Angle-angle plots – Graph of angular kinematic ROM of a joint/segment plotted against angular kinematic ROM of another joint /segment.
- Cadence – the number of steps taken per minute.
- Contact time – Time taken from the initial ipsilateral foot heel strike to the toe-off of the ipsilateral foot.
- Double support time – Time spent with both the ipsilateral and contralateral feet in contact with the ground.
- Swing time – The period in the gait cycle when the ipsilateral limb is not in contact with the ground.
- Gait – term giving to walking pattern, manner, style or rate of moving.
- Intralimb joint coordination variability – Variation in angular kinematic ROM of a joint-joint coupling.

- Joint-joint coupling – Two joints that are connected by a segment (e.g. knee-ankle).
- Lower limb movement variability – Variability of lower limb joint angular kinematics during movement.
- Single leg support time – Time spent with either the ipsilateral or contralateral foot in contact with the ground by itself.
- Single joint techniques – Assessment techniques used in lower limb movement variability that only involve a single joint.
- Stride length – The horizontal distance covered by the heel of the ipsilateral limb. The measurement is taken from heel strike of the ipsilateral foot to the next heel strike of the ipsilateral foot.
- Stride time – Time taken to complete one stride.
- Swing time – Time spent with either the ipsilateral or contralateral foot no in contact with the ground.
- Temporal-spatial gait parameters – Characteristics of human gait including stride length, swing time, support time, contact time, cadence and speed.
- Walking speed / speed – Distance covered divided by the total time to complete one stride.

List of abbreviations and nomenclature

- ABI – Ankle Brachial Index
- ADL – Activities of daily living
- AUSVIQUOL – Australian Vascular Quality of Life Index
- BMI – Body mass index

- CHF – Congestive heart failure
- CLAU-S – Claudication scale questionnaire
- CON – Age and mass matched control participants
- CPS – Claudication Pain Scale
- CV – Coefficient of variation
- CVD – Cardiovascular disease
- ECT – Encoded Chain Technique
- EUROQOL – standardised instrument for use as a measure of health outcome
- HDL – High density lipoprotein
- HR_{peak} – Peak heart rate
- IC – Intermittent claudication
- ICC – Intraclass correlation coefficient
- ICQ – Intermittent Claudication Questionnaire
- LDL – Low density lipoprotein
- MHC – Myosin heavy chain
- MWD – Maximal walking distance
- NoRMS – Normalized root mean square
- PAD – Peripheral arterial disease
- PAD-IC – Peripheral arterial disease with intermittent claudication
- PFP – Patellofemoral pain
- PFWD – Pain free walking distance
- PTA – Percutaneous transluminal (balloon/stent) angioplasty
- QOL – Quality of life
- RER_{peak} – Peak respiratory exchange ratio
- RPE – Rating of Perceived Exertion

- ROM – Range of motion/movement
- SF-36® – Medical outcome short form (36) health survey®
- VC – Vector coding
- VEGF – Vascular endothelial growth factor
- VE_{peak} – Peak ventilation
- VO_{2peak} – Peak oxygen uptake
- WIQ – Walking Impairment Questionnaire

Significance of the study

PAD-IC is a chronic arterial occlusive disease of the lower extremities caused by compromised circulation in the toes, feet and legs leading to pain, cramping and/or fatigue in the legs and buttocks during physical activity. This intense pain usually subsides when the individual reduces activity however, the pain impacts on ADL and QOL. In 1998, PAD-IC was estimated to have caused 1.6% of all deaths in Australia and accounted for $149 million in total health care costs. With the percentage of the elderly population increasing in Australia, the incidence of PAD-IC may increase substantially placing greater demands on the health care system in the future. Studies have shown that exercise training programs can improve walking performance in PAD-IC affected individuals and may lead to increased functional capacity and QOL. However, to date there is no agreement on the mechanism(s) responsible for the improved walking performance of PAD-IC patients following an exercise program. It has been suggested that the mechanism(s) that changes in lower limb mobility characteristics may contribute to increased walking performance however, this has not been investigated. Therefore, the purpose of this thesis was to examine the lower limb mobility

characteristics (temporal-spatial gait parameters, gait kinematics and movement variability), walking performance, physiological responses to exercise and physical activity levels of individuals with and without PAD-IC and to examine the effects of a long term exercise program on these variables.

Chapter 2

Literature review

Characteristics of the Australian population

The Australian population is continuing to increase from the current level of 21,020,238 people. Figure 1 represents the age structure in 2005 with an Australian population of 20,300,00 people. Current predicted increases of one birth every 2 mins, one death every 3 mins and 55 s, a net gain of one international migrant every 4 mins and 47 s will lead to an overall total population rate of increase of one person every 2 mins and 12 s (Australian Bureau of Statistics, 2006).

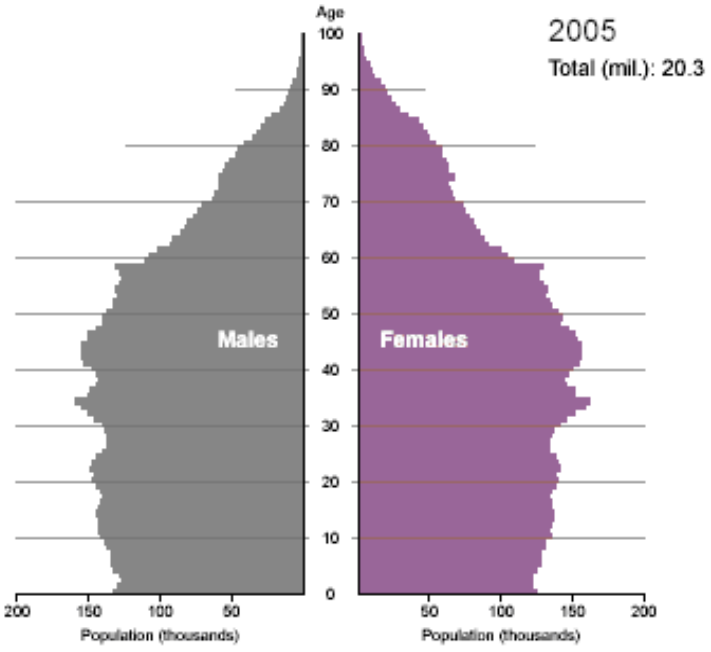

Figure 1 Age structure of Australia (Australian Bureau of Statistics, 2006)

Aging is one of the major transformations being experienced in the Australian population. The current focus of the Australian government is on issues associated with the increasing number of older adults in the population, for example, expenditure associated with income support, the provision of health and disability services and family and community care. The population aged 65 yr and over is projected to increase from 2.5 million in 2002, to between 6.1 and 11.7 million in 2101. As a proportion of the current population, this is an increase from 13% to between 29% and 32% (Australian Bureau of Statistics, 2006).

With the projected increase in older members of the Australian population, more people may develop some form of cardiovascular disease (CVD) such as coronary heart disease, stroke, heart failure and peripheral arterial disease (PAD). In Australia CVD accounts for more deaths and more health expenditure than any other disease or injury (Australian Institute of Health and Welfare, 2005). Although mortality rates have fallen significantly in the past 5 yr, due to decreases in some risk factors (smoking and high blood pressure) and major advances in treatment and care, CVD remains Australia's largest health problem (Australian Bureau of Statistics, 2002). Expenditure on CVD in the period 1993-94 to 2000-01 increased by 28%. In 1993-94 PAD accounted for $149 million per annum in total health care costs and although the cost of PAD was not reported in 2000-01, expenditure on PAD is likely to have increased (AIHW, 2001). PAD mortality in the age group 55-85+ yr has decreased from the 1980s to the start of 21st century (AIHW, 2005) (Figure 2). However, it should be noted that not all PAD patients will die from the disease but may die from other cardiovascular complications such as myocardial infarction (Criqui et al., 1992).

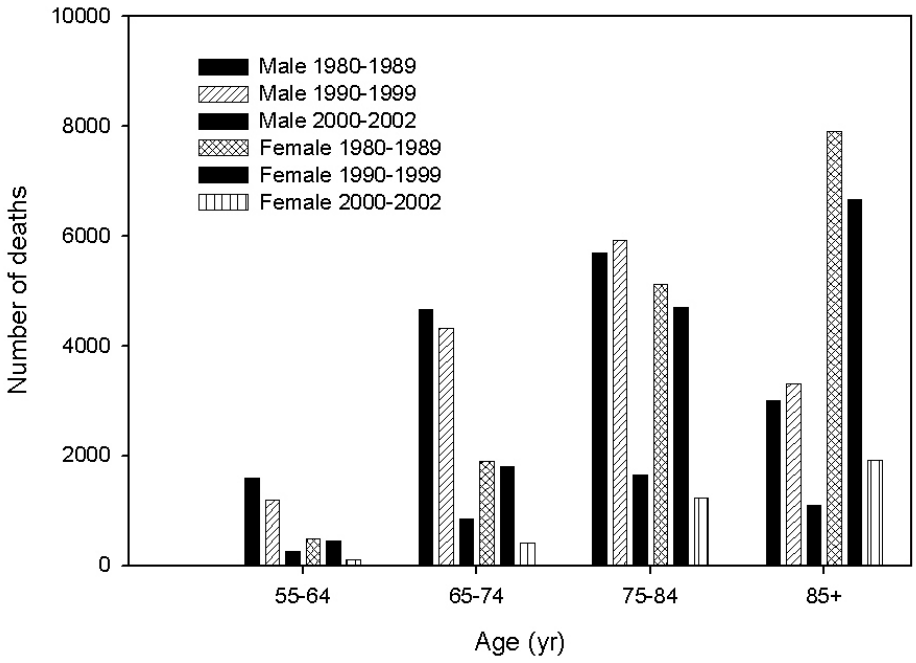

Figure 2 Australian PAD death rates (adapted from National Cardiovascular Diseases and Diabetes Database, AIHW, 2006)

To reduce the mortality rates caused by CVD further research is required. Prevention and understanding of risk factors is the key to reducing the effect of CVD on the aging Australian population. Keeping the older Australian adult population active and mobile is one of the best methods of reducing the burden placed on the medical system. PAD is one area of CVD that affects the mobility of the older population.

Peripheral arterial disease

PAD is a medical condition that results from occlusion (blockage) or stenosis (narrowing) of peripheral arteries (such as Iliac, Femoral, Popliteal and Tibial arteries) that supply blood to the extremities (Figure 3) (Beard, 2000; Bulmer & Coombes, 2004; Dormandy & Rutherford, 2000). Usually, occlusion and stenosis of the arteries occur as a result of atherosclerosis, a process in which deposits of fatty substances, cholesterol,

cellular waste products, calcium and other substances build up on the inner lining (endothelium) of an artery (Figures 4) (Bick, 2003; Ouriel, 2001).

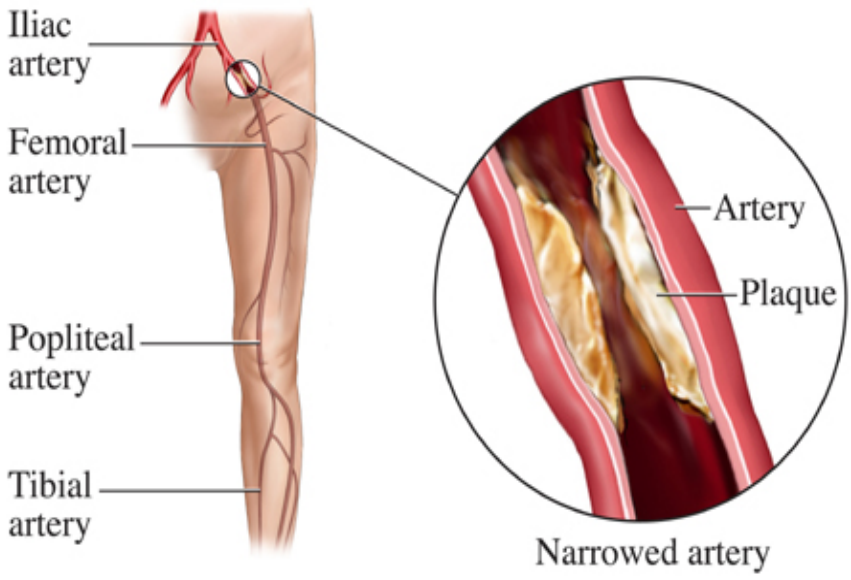

Figure 3 Site of peripheral arterial disease (Nucleus Communications, 2003)

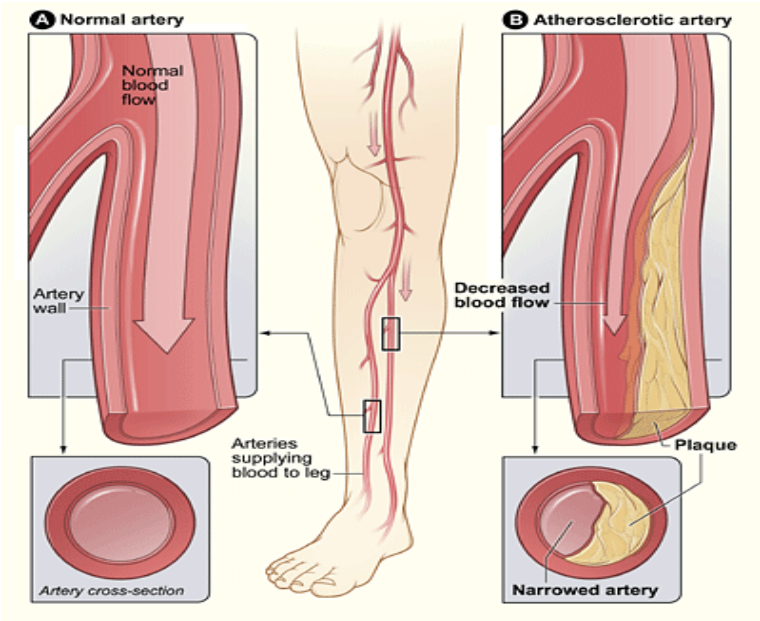

Figure 4 Atherosclerotic blockage with diseased artery (National Heart Lung and Blood Institute, 2006)

Atherosclerotic blockages in the lower limbs leads to inadequate blood flow that can cause various levels of ischemic pain particularly when walking (Aronow, 2004b; Bick, 2003). This activity induced ischemic pain results in a symptom called "Intermittent Claudication" (IC) (derived from "claudication," meaning "to limp"). The ischemic pain is relieved when the individual ceases the activity and rests (Beard, 2000; Bick, 2003; Bulmer & Coombes, 2004; Dormandy & Rutherford, 2000; Olin, 2002). The degree of ischemic pain experienced during IC is difficult to quantify. Egun et al. (2002) reported that the severity of muscle ischemia during walking was related to the ischemic pain level in patients with PAD-IC and that muscles used during walking compensate for insufficient oxygen delivery. It has been suggested (Boccalon, 1999) that many people who suffer the disease do not report symptoms to their medical practitioner, presuming that the symptoms of PAD such as IC are a natural consequence of aging. Without treatment, PAD-IC develops significantly, reducing the mobility of affected individuals, increasing the risk of contracting other CVD conditions and reducing quality of life (QOL) (Bick, 2003; Dawson, 2001; Gardner et al., 2001a). Although ischemic pain is a central mobility symptom for PAD-IC individuals, PAD-IC causes reduced QOL and therefore increases risk factors which leads to increase in other CVD (such as myocardial infarction) and/or cerebrovascular disease, leading to potentially death (Aronow, 2004b; Criqui et al., 1992; Curci & Sanchez, 2003).

Diagnosis of PAD-IC

Diagnosis is very important to identify the presence and severity of PAD-IC and to evaluate the effects of treatment. There are a variety of methods used to assess the presence and level of severity of PAD-IC. The most common methods include physical

findings, artery palpation, systolic blood pressure measurements (hemodynamic assessment), vascular imaging, health related questionnaires and treadmill walking tests.

Physical findings

Signs of chronic limb ischemia caused by PAD-IC include subcutaneous atrophy, brittle toenails, hair loss, pallor and coolness of skin. Serve ischemia produces tenderness, ulceration or gangrene (Figure 5). Palpation of the femoral, popliteal, posterior tibial and dorsalis pedis pulses may allow the level of arterial obstruction to be ascertained (Figure 6A) (Dormandy & Rutherford, 2000; Halperin, 2002).

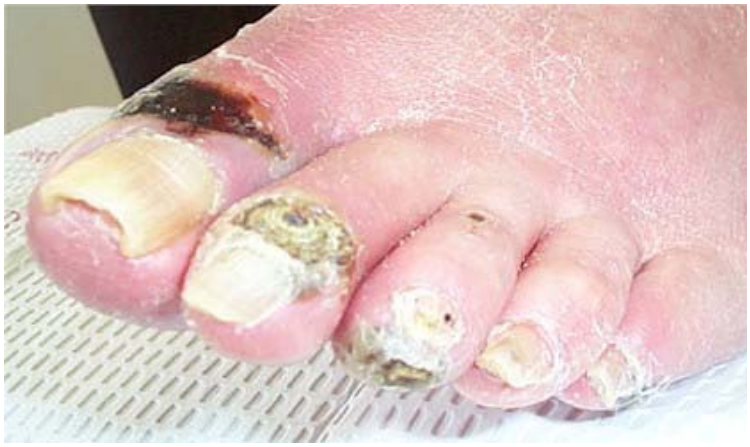

Figure 5 Trophic skin in severe PAD-IC (adapted from MyFoot Shop, 2007)

Ankle-brachial pressure index

Initial screening for PAD-IC can involve the palpation of the lower limb peripheral pulses of a patient however, the most effective assessment of PAD-IC irrespective of whether the patient is in the early or late stages of the disease is the assessment of ankle–brachial pressure index (ABI) (Figure 6B). The ABI is the standard preliminary evaluation for PAD-IC and involves measuring the ratio of the ankle to brachial systolic

blood pressures (Aronow, 2004b; Bick, 2003; Comerota, 2003; Donnelly, Hinwood, & London, 2000; Dormandy & Rutherford, 2000). This assessment procedure utilizes a sphygmomanometer cuff and a Doppler probe. The cuff is placed immediately above the ankle and the Doppler probe is positioned over either the posterior tibial or the dorsalis pedis arteries. The cuff is then inflated until no sound is heard and then deflated. Measurement is taken once the flow of blood is heard (systolic pressure) (Dormandy & Rutherford, 2000; Khan, Rahim, Anand, Simel, & Panju, 2006). Under normal healthy conditions, the systolic pressure at the ankle level should be at least equal to or higher than the upper arm (Donnelly et al., 2000; Weitz et al., 1996). Therefore, a normal ABI should be ≥ 0.1. A patient who suffers from PAD-IC will have an ABI of 0.5-0.9 whereas a patient with severe resting ischemia would typically have an ABI < 0.5 (Aronow, 2004b; Donnelly et al., 2000; Khan et al., 2006).

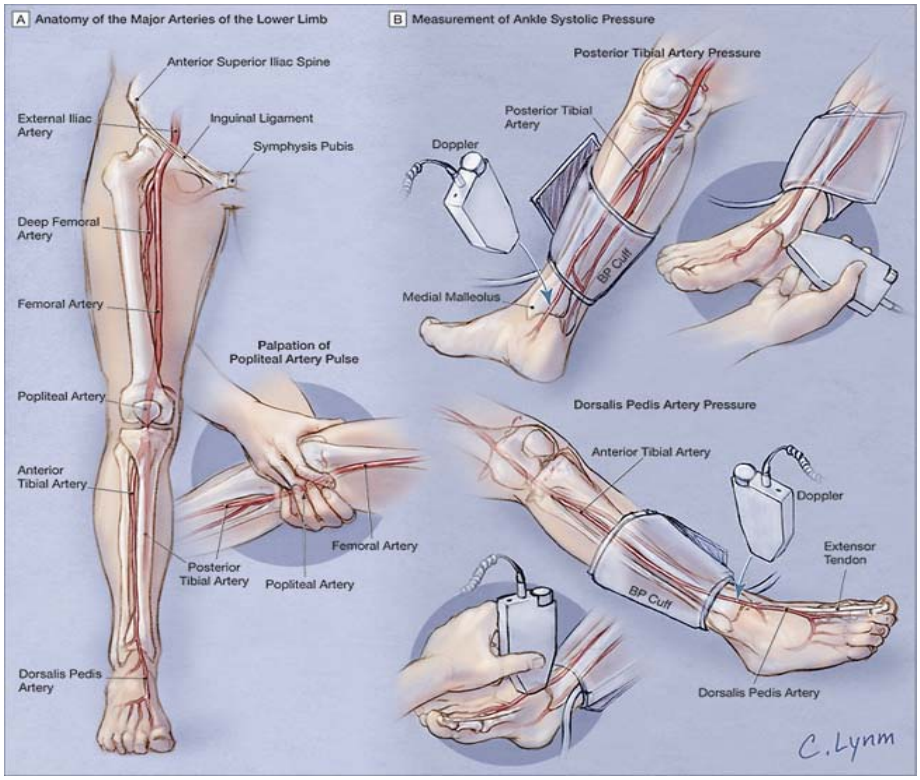

Figure 6 A) Palpation of lower limb arteries B) Ankle Brachial Index (ABI) test (Khan et al., 2006)

Research on the variability of ABI measurements has found a high level of reproducibility (95% prediction interval ± 2.33%) when performed by experienced testers and with little variation in ABI between testing days for the same patients (Caruana, Bradbury, & Adam, 2005; Fowkes, Housley, Macintyre, Prescott, & Ruckley, 1988). While inexperienced testers may make some small errors in ABI assessment, this measure assists in the diagnosis of PAD-IC and is very useful as a baseline measure for follow-up purposes (Hiatt et al., 1995; Weitz et al., 1996). The assessment of ABI has also been used to evaluate the effects of exercise training on PAD-IC patients by examining the post-exercise ankle systolic pressure (post-exercise ABI), and the time for the ABI to return to resting level (post-recovery ABI) to examine blood flow post exercise (Feinberg et al., 1992; Jonason & Ringqvist, 1987; Weitz et al., 1996).

Vascular imaging

In addition to ABI measures vascular imaging of the arteries can be undertaken to provide detail on blockage location. Nuclear magnetic resonance, contrast angiography, intravascular angioscopy and ultrasound are a few examples of vascular imaging that are predominantly used in clinical settings. Due to the prohibitive cost of these tests, they are rarely used in intervention studies (Donnelly et al., 2000; Halperin, 2002; Isbell et al., 2006).

Questionnaire assessment

Assessment questionnaires can be utilized when it is not possible to perform physical tests on a PAD-IC patient (e.g. due to location). Questionnaires provide researchers and clinical physicians with additional information such as ability to undertake activities of daily living and perceived QOL. A number of general questionnaires have been used,

including the SF-36 health survey (SF-36) (Ware, 1993), ED-5Q (The EuroQoL Group, 1990), the Nottingham Health Profile (Hunt, McEwen, & McKenna, 1985) and the Profile of Mood States (McNair, 1981). These questionnaires are used to assess the physical and social functioning and therefore act as QOL measures for individuals with PAD-IC (Breek et al., 2001; Chong et al., 2002; Hunt et al., 1985; Regensteiner, 2004; Regensteiner et al., 1990). Several questionnaires have been developed to provide an overall view of the physical capacity, mobility and QOL of PAD-IC individuals (Breek, de Vries, van Heck, van Berge Henegouwen, & Hamming, 2005). Examples of disease specific questionnaires include the VascuQol (Morgan, Crayford, Murrin, & Fraser, 2001), the Intermittent Claudication Questionnaire (ICQ) (Chong et al., 2002), the Claudication Scale (CLAU-S) (Spengel, Brown, Dietze, Kirchberger, & Comte, 1997), the Australian Vascular Quality of Life Index (AUSVIQUOL) (Smith, Borchard, Hinton, & Scott, 2007) and the Walking Impaired Questionnaire (which is also used for other walking impairments) (Regensteiner et al., 1990). All of these disease specific questionnaires are beneficial for use in PAD-IC diagnosis and treatment programs. Researchers and clinicians use a combination of general health and disease specific questionnaires to obtain a complete assessment of disease status, walking ability, and QOL.

Walking assessment

Walking tests have been used in both clinical and research contexts to independently diagnose the severity of PAD-IC and to measure the walking capacity of PAD-IC patients. These tests are used to assess the pain free walking distance/time (PFWD/PFWT) and maximal walking distance/time (MWD/MWT) before cessation of exercise due to the occurrence of severe cramping/pain in the legs (Gardner, Skinner,

Cantwell, & Smith, 1991a). An increase in PFWD may be of greater practical significance because most individuals do not typically exert themselves to the extent that they reach maximal pain levels (Jones, Skinner, Smith, John, & Bryant, 1996). To obtain PFWD and MWD, researchers and clinicians may use either the 6-minute walking test, the constant-load treadmill test and/or the graded treadmill test.

The most commonly used walking test for disease populations is the 6-minute test. The patient is required to walk repeatedly around two markers, spaced 30.5 m apart, at their own pace, attempting to cover as much distance as possible in 6 mins (Bittner et al., 1993; Carter et al., 2003). The 6-minute test has not only been used for individuals with PAD-IC, it is also commonly used to assess exercise capacity in congestive heart failure and chronic obstructive pulmonary disease (Bittner et al., 1993; Carter et al., 2003; Montgomery & Gardner, 1998; Peeters & Mets, 1996). The advantages of this test are that it is self paced, requires less time than constant load and graded treadmill tests and has been shown to be a reliable (ICC = 0.94) measure of walking ability (Montgomery & Gardner, 1998). However, as the individual does not walk on a treadmill it is problematic to determine physiological measures such as peak oxygen uptake (VO_{2peak}) without a portable gas analyzer.

A variation of the 6-minute walking test is the shuttle walking test which involves the patient walking back and forth between two cones placed 10 m apart on level ground (Zwierska et al., 2004). This test controls the walking speed like the Multistage Shuttle run test (Leger & Lambert, 1982), where an audible beep is used to increase the pace of walking. The benefit of using an audible beep is that the initial walking speed can be set at 3 $km \cdot h^{-1}$ and at the end of each minute, the time between audible beeps decreases,

causing an increase in walking speed by 0.5 $km \cdot h^{-1}$ thereby providing performance evaluation levels (Zwierska et al., 2004). Zwierska et al. (2004) compared the shuttle walking test to the constant load treadmill test and found that the shuttle test, like the 6-minute walking test exhibited similar test-retest reliability (ICC = 0.87) to the constant load treadmill test and induced lower cardiovascular stress levels.

The constant load test is the traditional disease specific treadmill test and requires patients to maintain a walking speed within the range 2.4-3.2 $km \cdot h^{-1}$ at a grade of 8-12% (Degischer, Labs, Aschwanden, Tschoepl, & Jaeger, 2002a; Labs, Nehler, Roessner, Jaeger, & Hiatt, 1999). The advantage of this test is that it is performed on a treadmill and does not require much space. However, due to variability in the treadmill speed and grades selected, the distances that PAD-IC patients can walk are not comparable. This prohibits exact comparison of some results from research and clinical trials. Secondly, patients with a greater level of disease may find it difficult to walk at such a high workload (Degischer et al., 2002a; Labs et al., 1999). Patients with a more severe case of PAD-IC cannot walk more than 100 m and a workload of 3.2 $km \cdot h^{-1}$ at a grade of 12% is too stressful. This causes a substantial drop in between-subject variance for the constant load treadmill test (Labs et al., 1999). A progressive grade treadmill test should be used to assess walking capacity in PAD-IC patients (Labs et al., 1999).

The graded treadmill test starts with a low workload which then increases until PAD-IC pain forces cessation of exercise. The test speed is set at 3.2 $km \cdot h^{-1}$ and the grade is increased from 0% by 2% increments every 2 mins until MWD is reached (Gardner et al., 1991a). Research has demonstrated that PFWD and MWD occur later in the graded test compared to the constant treadmill test due to the initial starting workload (Gardner

et al., 1991a). The reliability measures for walking performance such as PFWD and MWD are greater for graded treadmill tests (ICC = 0.93) compared to the constant load treadmill test (ICC = 0.55) and only one graded test is needed to obtain reliable PFWD and MWD measures of PAD-IC patients (Gardner et al., 1991a; Gardner, Skinner, Vaughan, Bryant, & Smith, 1992).

However, a concern with any treadmill test is the effect of handrail support on hemodynamic responses in individuals. Handrail support produces lower VO_{2peak} and HR_{peak} in healthy young men compared to treadmill tests without handrail support (Manfre et al., 1994; Zeimetz, McNeill, Hall, & Moss, 1985). Research involving PAD-IC patients found that MWD is greater when handrail support is allowed with repeated testing leading to increased MWD, thereby reducing the reliability of the test (Gardner, Skinner, & Smith, 1991b). However, it was found that the reliability of each hemodynamic variable (foot transcutaneous oxygen tension, ankle systolic pressure, brachial systolic press, ankle/brachial index and heart rate) was not affected by hand rail support. However, as long as handrail support is used during subsequent tests the results can be compared. Despite stability and supervision concerns related to the use of the graded and constant treadmill tests, there are so many advantages (progression, space, metabolic response assessment) in using this apparatus that it should be used whenever possible.

Prediction of PFWD and MWD

Questionnaires or walking analysis procedures can be used to assess walking ability of PAD-IC patients however, where walking assessment is impossible (e.g. due to location), performance can be predicted using multiple regression calculations. Gardner,

Ricci, Case & Pilcher, (1996) developed an equation to predict PFWD and MWD using resting ABI, body mass index, gender, and current smoking status. The regression equations were found to be more accurate than questionnaires in assessing walking ability (Gardner et al., 1996).

All of the above diagnosis tools (ABI, questionnaires and walking tests) are valuable to assess severity of PAD-IC and its influence on walking performance, daily activity levels and perceived QOL in PAD-IC patients at initial diagnosis and during treatment programs. These assessment tools also allow medical practitioners to place PAD-IC patients into clinical categories or classification stages according to the severity of the disease. These clinical categories or classification stages include the Rutherford categories (Table 1-2) and the Fontaine stages (Table 3).

Table 1. Rutherford clinical categories of acute limb ischemia (Rutherford, 1991)

					Doppler signals	
Category	**Description**	**Capillary return**	**Muscle weakness**	**Sensory loss**	**Arterial**	**Venous**
Viable	Not immediately threatened	Intact	None	None	Audible, ankle pressure > 30 mmHg	Audible
Threatened	Salvageable if promptly treated	Intact, slow	Mild, partial	Mild, incomplete	Inaudible	Audible
Irreversible	Major tissue loss, amputation regardless of treatment	Absent (marbling)	Profound, paralysis (rigor)	Profound, anesthetic	Inaudible	Inaudible

Table 2. Rutherford clinical categories of chronic limb ischemia resulting from PAD-IC (Rutherford, 1991)

Grade	Category	Clinical description	Objective criteria
0	0	Asymptomatic – no hemodynamically significant occlusive disease	Normal treadmill or stress test

I	1	Mild claudication	Completes treadmill exercise*, postexercise AP > 50 mmHg but > 25 mmHg less than normal
	2	Moderate claudication	Between categories 1 and 3
	3	Severe claudication	Cannot complete treadmill exercise; postexercise AP <50 mmHg
II	4	Ischemic rest pain	Resting AP ≤ 40 mmHg; flat or barely pulsatile ankle or metatarsal plethysmographic tracing (PVR); TP < 30 mmHg
	5	Minor tissue loss – non-healing ulcer, focal gangrene with diffuse pedal ischemia	Resting AP ≤ 60 mmHg; ankle or metatarsal PVR flat or barely pulsatile; TP < 40 mmHg
III	6	Major tissue loss	Same as category 5

AP, ankle pressure; TP, toe pressure
* 5 mins at 2 mph (3.22 $km \cdot hr^{-1}$) at a 12^{o} incline

Table 3. Fontaine stages of classification of PAD-IC (Lampman & Wolk, 2003)

Stage	Description
I	Asymptomatic
IIa	Mild claudication
IIb	Moderate-severe claudication
III	Ischemic rest pain
IV	Ulceration or gangrene

Treatment of PAD-IC

The two major goals of PAD-IC treatment are to reduce the progression of the disease and to improve QOL (Lumsden & Rice, 2006). In the early and middle stages of PAD-IC the disease is not life threatening and treatment may require simple treatment programs consisting of risk factor reduction via the use of pharmacological agents and increased physical activity levels. When PAD-IC is severe, it can have a dramatic negative influence on QOL and can impinge on other areas of health. When PAD-IC has reached this point, extreme treatment measures such as intense pharmacological treatment and surgery may be the only options. However, regardless of the initial treatment, PAD-IC patients are encouraged to increase their physical activity levels, as

it has been shown to be beneficial at any stage of PAD-IC treatment progress (Hankey et al., 2006; Meru et al., 2005; Regensteiner, 2004).

Risk factors

Risk factor management can influence the degree of severity and improvement in clinical outcomes in PAD-IC patients (Aronow, 2006; Gardner, 2001; Lumsden & Rice, 2006). Risk factors for PAD-IC include smoking, diabetes mellitus, obesity, hyperlipidemia, hypertension, and homocysteine elevation (Aronow, 2006; Dormandy & Rutherford, 2000; Regensteiner & Hiatt, 2002). Cigarette smoking has been found to be the most important factor in the development and continuing effect of PAD-IC (Christman et al., 2001; Girolami et al., 1999; Regensteiner & Hiatt, 2002), however, there is no consensus on the effectiveness of smoking cessation in the acute treatment of PAD-IC (Girolami et al., 1999; Waller, Solomon, & Ramsay, 1989).

Gardner (1996) investigated the effect of smoking on the exercise capacity of PAD-IC patients and determined that patients who smoked had more severe claudication pain, reduced circulation, and reduced cardiopulmonary measurements at peak exercise intensity compared to non-smokers. However, it was found that smokers can still improve walking performance over a 6 mth training program (Gardner et al., 2004). Other research has indicated that individuals with PAD-IC who exercise regularly can negate the deleterious effect of smoking on the peripheral arteries (Anton et al., 2006). Aside from smoking, positive changes to other risk factors such as obesity, blood pressure, glucose metabolism, body fat percentage, aerobic capacity and daily physical activity levels have been shown to reduce the development of the disease (Dormandy &

Rutherford, 2000; Mohler, 2004; Rehring, Sandhoff, Stolcpart, Merenich, & Hollis, 2005).

Pharmacological treatment of PAD-IC

There are currently two specific drugs, Pentoxifylline and Cilostazol, which are approved for pharmaceutical therapy of PAD-IC. Pentoxifylline a methylxanthine derivative is a haemorheologic agent and has been shown to decrease plasma viscosity and improve red and white blood cell flexibility. Cilostazol is a phosphodiesterase III inhibitor and causes vascular smooth muscle cell proliferation, vasodilatation and antiplatelet activity (Aronow, 2006; Collinson & Donnelly, 2004; Hiatt, 2001, 2004; Regensteiner et al., 2002; Samlaska & Winfield, 1994).

Two meta-analysis studies conducted on the randomized controlled trials of the effect of Pentoxifylline on PAD-IC found that in six studies (randomized and double or assessor-blind) Pentoxifylline increased both PFWD and MWD by an average of 21 m and 43.8 m respectively. These studies only investigated the effects of Pentoxifylline on walking performance on a treadmill (Girolami et al., 1999; Hood, Moher, & Barber, 1996). There is no evidence of the benefits of this drug on patient functional capacity and QOL (Hiatt, 2004).

The other specific drug 'Cilostazol' has been shown to significantly increase PFWD in patients with PAD-IC (Beebe et al., 1999; Dawson et al., 2000; Dawson et al., 1998; Regensteiner et al., 2002). Regensteiner et al., (2002) and Beebe et al., (1999) investigated the effect of Cilostazol on walking ability and health related QOL and

found that taking 50–100 mg bid of Cilostazol improved MWD, PFWD and baseline values for WIQ and SP-36 questionnaire responses over 12, 16 and 24 wk programs.

When the effectiveness of Cilostazol and Pentoxifylline were compared it was found that Cilostazol was significantly more effective than Pentoxifylline in increasing PFWD and MWD (Hiatt, 2006). However, the side effects of Cilostazol included palpitations, diarrhea, and headaches (Dawson et al., 2000). These side effects can limit the usefulness of this drug due to other medical health conditions that PAD-IC patients may have such as CHF (Hiatt, 2004).

Non PAD-IC specific drugs used for treatment of risk factors (such as high cholesterol) include drugs such as 3-Hydroxy-3-methylglutaryl coenzyme A (HMG-Co-A) reductase inhibitor (a statin) commonly used for treatment of atherosclerosis by lowering cholesterol levels. However, some studies have indicated a beneficial effect of statins on PAD-IC patients (Aronow, 2006; Aronow, Nayak, Woodworth, & Ahn, 2003; McDermott et al., 2003; Mondillo et al., 2003; Young-Xu et al., 2003) and these are now recommended for all PAD-IC patients. McDermott et al., (2003) found that PAD-IC patients taking statins had better 6-minute walk performance (388.92 m versus 371.24 m) and faster walking velocity than patients who did not. Young-Xu et al., (2003) also investigated the effects of long term statin use on psychological well-being in PAD-IC patients and found that over 4–7 yr, patients taking statins had lower risk of abnormal depression, anxiety, hostility and increased QOL.

As well as the previously mentioned pharmacological treatments, antioxidants, oral anticoagulants, antiplatelet, angiotensin-converting enzyme inhibitors and thrombolytic

drugs are being investigated to determine if they play a role in the treatment of PAD-IC (Aronow, 2004a, 2006; Cosmi & Palareti, 2004; Giannini & Balbarini, 2004; Leng et al., 2000; Violi, Loffredo, & Marcoccia, 2004).

Surgical treatment of PAD-IC

If claudication symptoms continue during rest, severe obstruction has occurred and limb threatening ischemia can be a serious consequence of chronic PAD-IC. If untreated this condition leads to gangrene and eventual limb amputation (Aronow, 2004b; Palmer-Kazen & Wahlberg, 2003; Schmieder & Comerota, 2001). If individuals with PAD-IC continue to suffer after noninvasive treatment programs such as risk factor reduction, and pharmacological and exercise rehabilitation interventions, they may then require surgical intervention and endovascular treatment which can include operative by-pass surgery, percutaneous transluminal (balloon/stent) angioplasty (PTA) or atherectomy (Bachoo & Thorpe, 2003; Comerota, 2001; Dormandy & Rutherford, 2000). Some patients with severe PAD-IC cannot be treated with noninvasive therapy and may need surgery before other treatment programs can be utilized or patients may simply decide to undergo surgery instead of engaging in non-invasive rehabilitation treatment programs in the first instance.

The most common treatment for mild and moderate-severity PAD-IC is PTA. This treatment is normally used for more focal PAD-IC such as the distal abdominal aorta, common iliac arteries, and external iliac arteries where a balloon is inserted into the blocked artery and then inflated at the site of the blockage (Figure 7) (Dormandy & Rutherford, 2000). The balloon is then deflated and removed from the artery. Vascular stenting, which is often performed at the same time as an angioplasty, involves the

placement of a small wire mesh tube called a stent in the newly opened artery. This may be necessary after some angioplasty procedures if the artery is very narrow or completely blocked. The stent is a permanent device that once implanted during angioplasty is left in the artery and holds the artery in an open position during the healing process (Figure 8) (Aronow, 2004b; Bachoo & Thorpe, 2003). Although it has been shown that the functional capacity and QOL of PAD-IC patients improved after PTA treatment (Spronk, Bosch, Veen, den Hoed, & Hunink, 2005) there exists limited research on the long term benefits of this treatment regime to patients (Whyman et al., 1997). Whyman et al. (1997) examined the outcomes resulting from PTA compared to conventional medical treatment involving low daily doses of aspirin, cessation of smoking and exercise after 2 yr. It was found that PTA had no significant effect on patient reported MWD, treadmill PFWD and MWD, ABI or QOL (Nottingham Health Profile) compared to conventional medical treatment (Whyman et al., 1997).

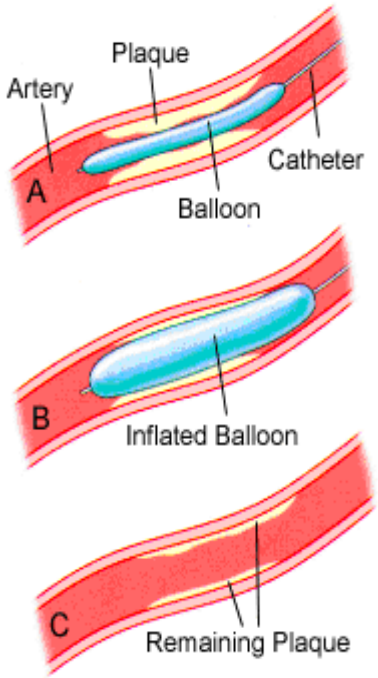

Figure 7 Balloon angioplasty (Texas Heart Institute, 2006)

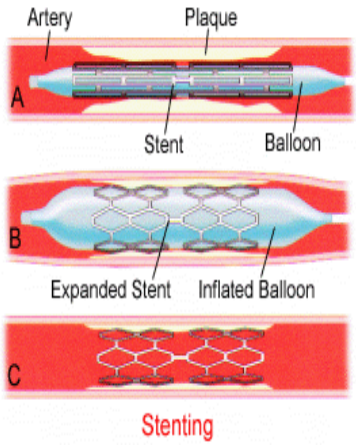

Figure 8 A peripheral artery being treated with stenting. A) Balloon angioplasty of the blockage. B) Positioning of a balloon-expandable stent & deployment of the stent. C) Final result with the stent in place (Texas Heart Institute, 2006).

Furthermore, an open surgical revascularization procedure is commonly used when the lower limb is at critical limb ischemia which can involve tissue loss (Dormandy & Rutherford, 2000; Weitz et al., 1996). Even then some authors have suggested that surgery should not be used until all other treatment options have been addressed (Dormandy & Rutherford, 2000; Weitz et al., 1996). However, research has indicated that surgery can result in significantly improved ABI readings and walking performance (Chong et al., 2000; Regensteiner, Hargarten, Rutherford, & Hiatt, 1993a).

Another surgical treatment option is atherectomy, which involves a plaque excision system called SilverHawk (Newman et al., 1988; Zeller et al., 2004). A guide wire and catheter are inserted into the skin and through the femoral artery in the groin and eased towards the blockage site (Figure 9A). Once the guide wire is maneuvered through the narrowing or blockage in the artery a small cutting tool is activated and shaves off the plaque (Figure 9B) which is then collected in the catheter and flushed from the body (Figure 9C) (Zeller et al., 2004).

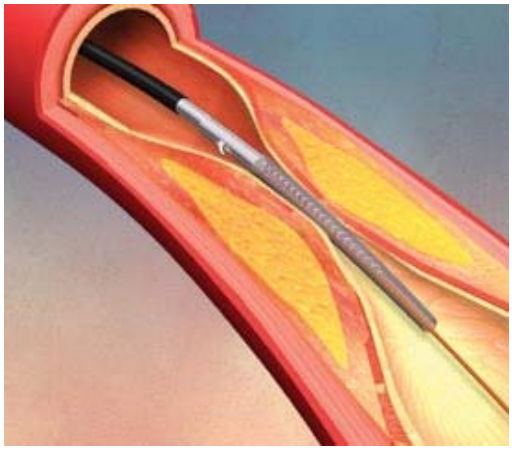

Figure 9A SilverHawk - guide wire (Mayo Clinic, 2006)

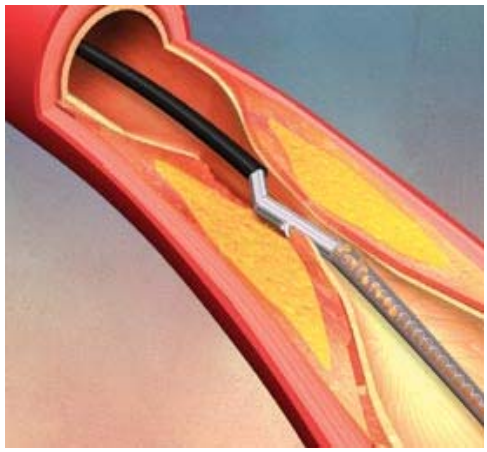

Figure 9B SilverHawk – shaves off the plaque (Mayo Clinic, 2006)

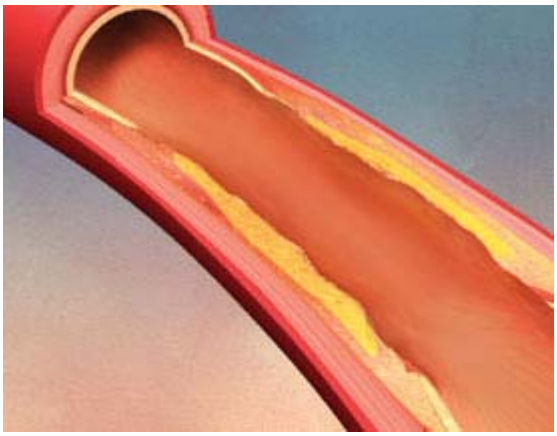

Figure 9C SilverHawk – clean artery (Mayo Clinic, 2006)

Exercise programs

Apart from pharmacotherapy and surgery, exercise programs are very important in the treatment of PAD-IC. This form of therapy not only improves walking performance via improved lower limb mobility, but it also improves QOL and physical activity levels that lead to the reduction of risk factors such as obesity (Antignani, 2003; McDermott et al., 2006; Menard et al., 2004; Serracino-Inglott et al., 2007). Although exercise programs are known to be beneficial to PAD-IC patients they are not commonly

utilized due to the cost of involving exercise professionals in the design, delivery and evaluation of these programs (Regensteiner, 2004). However, home-based exercise training programs have been shown to produce improved walking performance in PAD-IC patients even though there is little or no supervision of training activities by an exercise professional (Savage et al., 2001).

Exercise program modes

Walking and cycling have been the preferred modes of exercise used in PAD-IC research. These activities have resulted in improved PFWD, MWD, calf blood flow, VO_{2peak} and walking economy. Relatively few research studies have investigated the effects of other modes of exercise including resistance training, stair-climbing and pole-stride walking on individuals with PAD-IC. The research that has been conducted on different exercise modes indicates that walking is the more effective mode because it involves an important activity of daily living (Gardner & Poehlman, 1995). Tables 4 and 5 provides a summary of all exercise programs conducted with patients with PAD-IC

Supervised exercise programs

The effects of supervised walking programs on PAD-IC have received a significant research attention over the past 45 yr. Programs which involve physical activities such as walking, cycling, stair climbing, and gymnastics offer an advantage over other methods of treatment by being relatively cost free and noninvasive (Dormandy & Rutherford, 2000; Gey, Lesho, & Manngold, 2004; Regensteiner, 2004; Schmieder & Comerota, 2001). However, these studies varied in such fundamental characteristics as intensity, duration, frequency and mode of exercise sessions and testing protocols.

These variations account for differences in research outcomes for PFWD, MWD, physiological responses to exercise and perceived QOL. Table 4 outlines the research methods utilized and Table 5 reviews the results (PFWD and MWD) of these studies.

Gardner et al. (1995) conducted a meta-analysis of studies that examined the effects of exercise programs on PAD-IC and determined that exercise programs improved PFWD and MWD by an average of 179% and 122% respectively. All previous studies have demonstrated some form of improved PFWD following an exercise program (Regensteiner, 2004). The meta-analysis concluded that for optimal improvement, patients should walk 3 day·wk^{-1}, 30 mins·d^{-1} at an intensity approaching maximal pain for a program extending over 6 mth. When this protocol was tested participant PFWD increased by 115%, MWD increased by 65%, calf blood flow increased by 27% and VO_{2peak} improved by 10% (Gardner et al., 2000). It has also been found that a 10 wk supervised exercise program will have long term benefits in terms of improved walking performance in individuals with PAD-IC (Ratliff et al., 2007).

Table 4. PAD-IC exercise programs research protocol review

Study	Exercise mode	Claudication pain end point during training	Length of program	Frequency ($d \cdot wk^{-1}$)	Duration (mins)	Treadmill test protocol
Larsen & Lassen, 1966	Walking	Near max	6 mth	7	60	Constant load
Ericsson et al., 1970	Comb	Onset	11 mth	2	45	…
Dahllof et al., 1974	Comb	Onset	6 mth	3	30	Constant load
Dahllof et al., 1976	Comb	Onset	6 mth	3	30	Constant load
Ekroth et al., 1978	Comb	Onset	4-6 mth	3	30	Constant load
Jonason et al., 1979	Comb	Near max	3 mth	2	30	Graded
Clifford et al., 1980	Comb	Onset	4 wk	…	…	Constant load
Jonason et al., 1981	Comb	Near max	3 mth	2	45	Constant load
Lepantalo et al., 1984	Comb	Onset	6 mth	7	…	Constant load
Ruell et al., 1984	Comb	Onset	8 wks	3	30	Constant load
Rosetzsky et al., 1985	Comb	Onset	3 mth	3	45	…
Ernst et al., 1987	Treadmill	Near max	2 mth	5 (2 session$\cdot day^{-1}$)	Until max distance	Constant load
Jonason et al., 1987	Comb	Near max	3 mth	2	45	Constant load
Johnson et al., 1989	Comb	Near max	5 mth	3	60 intermittent	Graded
Lundgren et al., 1989	Comb	Onset	6 mth	3	30	Constant load
Mannarino et al., 1989	Comb	Onset	6 mth	2 + 7 walking	30 + 20-60 walking	Constant load
Rosfors et al., 1989	Comb	Onset	6 mth	2	30	Graded
Mannarino et al., 1991	Comb	Onset	6 mth	2 + 7 walking	30 + 20-60 walking	Constant load
Hiatt et al., 1990	Treadmill	Near max	12 wk	3	50 intermittent	Graded

Hiatt et al., 1994	Treadmill & strength	Near max	24 wk	3	50 intermittent	Graded
Pancera et al., 1995	Treadmill & cycle	Near max	1 mth	14	30	Constant load
Jones et al., 1996	Treadmill & stairmaster	Near max	12 wk	2	60 intermittent	Graded
Regensteiner et al., 1996	Treadmill & walking	Near max	12 wk	3	50 intermittent	Graded
Patterson et al.,1997	Treadmill & walking	Near max	12 wk	3	60 intermittent	Graded
Sly, 1998	Strength	…	12 wk	2	60	Graded
Gardner et al., 2000	Treadmill	Near max	24 wk	3	Intermittent	Graded
Tan et al., 2000	Treadmill	Near max	12 wk	5	60 intermittent	Constant load
Gardner et al., 2001b	Treadmill	Near max	24 wk	3	intermittent	Graded
Savage et al., 2001	Treadmill	Near max	12 wk	3	40 intermittent	
Gardner et al., 2002	Treadmill	Near max	1 yr	3-2	15+ Intermittent	Graded
Degischer., 2002a	Walking	Near max	12 wk	3-7	60	Graded
Mika et al., 2005	Treadmill	Onset	12 wk	3	Walk to 85% PFWD x 3	Constant load

Ellipses (…) indicate data were not given in the source study; Comb = combination of two or more of the following: walking, running, cycling, stair climbing dancing, rope skipping, jumping, playing ball, heel raises, straight–leg raise, limbering up, sitting and standing, knee bends, dynamic leg exercises, and static leg exercises.

Table 5. PAD-IC exercise program research results review

Study	Subjects (N)	Group	PFWD/ PFWT			MWD/MWT		
			Pretest	Posttest	IMP	Pretest	Posttest	IMP
Larsen & Lassen, 1966	14	Exercise Control	105.2±33.4m	268.3±104.5m	155%	226.9±112.8m	626.5±423.1m	176%
Ericsson et al., 1970	13	Exercise	186±163m	380±366m	104%	273±196m	537±370m	97%
Dahllof et al., 1974	18	Exercise Control	91.0±11m 55±42m	265±103m No change	191% 0%	296±53m 340±80m	650±104.3 No change	120% 0%
Dahllof et al., 1976	34	Exercise Control	127±21m 173±32m	345.4m	172% 120%	318±37m 301±68m	725m	128% 75%
Ekroth et al., 1978	129	Exercise	108±33m	392±75m	263%	283±42m	720±67m	154%
Jonason et al., 1979	60	Exercise	…	…	…	261m	583m	123%
Clifford et al., 1980	21	Exercise	299.4±30m	535.1±46.4m	79%	…	…	…
Jonason et al., 1981	15	Exercise	101m	169m	67%	423m	679m	61%
Lepantalo et al., 1984	12	Exercise	75±34.6m	173±152.4m	131%	…	…	…
Ruell et al., 1984	21	Exercise	67.0±59.5m	402.5±267.2m	501%	283.0±193.2m	795.5±149.5m	181%
Rosetzsky et al., 1985	79	Exercise	…	…	…	133.0±190.5m	401.0±112.1m	202%
Ernst et al., 1987	42	Exercise	59±37m	120±52m	103%	127±59m	281±91m	121%
Jonason et al., 1987	63	Exercise	114±74m	197±125m	73%	430±213m	717±304m	67%
Johnson et al., 1989	10	Exercise	256±294y	476.4±387.7y	86%	742±481.6y	1052.1±503.3y	42%
Lundgren et al., 1989	21	Exercise	67±7m	187m	179%	183±110m	459m	151%
Mannarino et al., 1989	8	Exercise	40±17m	75±27.6m	88%	76.4±18.7m	127.4±26.3m	67%
Rosfors et al., 1989	25	Exercise	111±105m	270±340m	143%	575±345m	924±460m	61%
Mannarino et al., 1991	30	Exercise & antipletelet	50.4±22.5m	95.3±30.9m	89% 120%	80.8±33.6m	150.3±35.3m	86%
Hiatt et al., 1990	19	Exercise	…	…	…	604±1.7mins	13.9±3.5mins	117%
Hiatt et al., 1994	29	Exercise	3.3±2.0mins	10.2±7.2mins	209%	9.6±5.7mins	17.2±7.3mins	79%
Pancera et al., 1995	15	Exercise	195m	300m	54%	830m	900m	8%

Jones et al., 1996	12	Treadmill	…	+117.7secs	…	…	+171.7secs	…
		Stairmaster		+35.5secs			+15.0 secs	
Regensteiner et al., 1996	20	Supervised	2.0±1.3mins	5.0±3.4 mins	150%	4.6±2.4mins	10.9±4.5 mins	137%
		Home	2.3±2.0mins	2.9±1.4 mins	26%	6.2±3.6mins	6.5±4.2 mins	5%
Patterson et al., 1997	55	Supervised	…	…	337%	…	…	207%
		Home			207%			70%
Sly, 1998	10	Exercise	2.0±1.6mins	6.6±5.2mins	228%	12.1±4.5mins	15.8±3.1 mins	30%
Gardner et al., 2000	63	Supervised	178±22m	383±34m	115%	389±29m	641±34m	65%
Tan et al., 2000	23	Unsupervised	…	…	…	133±60.7m	242.5±137.1m	82%
Gardner et al., 2001	28	Supervised	172±26m	402±6m	134%	396±43m	702±57m	77%
	24	Control	163±23m	203±43m	25%	379±48m	425±56m	12%
Savage et al., 2001	11	Supervised	241±188m	457±317m	90%	522±263m	833±376	60%
	10	Home	183±151m	225±151m	23%	532±264m	737±290	39%
Gardner et al., 2002	17	Supervised	…	…	189%	…	…	80%
Degischer., 2002	18	Supervised	187.5±250.1m	495.9±361.6m	164%	496.4±250.1m	905.6±439.8m	82%
	20	Home	177.7±92.4m	255.6±134.3	44%	559.4±92.4m	588.5±212.9m	5%
Mika et al., 2005	41	Exercise	87.4±38m	191.6±94.8	119%	…	…	…
	39	Control	86.9± 0m	101.6±50.1	16.9%			

Pretest and posttest values are shown as mean ±SD, except in cases where no SD is available; Ellipses (…) indicate data were not listed in the source study; Improvement percentage (IMP%) = (Posttest – pretest distance)/pretest. PFWD = pain free walking distance; PFWT = pain free walking time; MWD = maximal walking distance; MWT = maximal walking time; Supervised = all training was supervised by researcher; Home = patients were not supervised during training; Control = control PAD-IC patients

Home exercise programs

Researchers have examined the effects of home based exercise programs on PAD-IC patients to determine if the results obtained from supervised exercise programs can be achieved when the patient undertakes unsupervised exercise programs at home. Both supervised and non-supervised PAD-IC patients have shown improved PFWD and MWD after a 12 wk exercise program (Degischer et al., 2002b; Patterson et al., 1997; Savage et al., 2001). Degischer et al. (2002) found that MWD improved following a supervised program of walking $3d \cdot wk^{-1}$ for 1 hr at 60% maximal claudication pain (MCP) however, a home-based program of walking for 1 $hr \cdot day^{-1}$ until 60% MCP did not lead to a significant improvement in MWD. PFWD was significantly greater for both groups at 3 mth compared to baseline data. However, the level of improved PFWD has been found to be significantly higher for supervised exercise training compared to home-based training (Bendermacher, Willigendael, Teijink, & Prins, 2006; Degischer et al., 2002b; Patterson et al., 1997; Regensteiner, Meyer, Krupski, Cranford, & Hiatt, 1997; Savage et al., 2001). Both home-based and supervised exercise programs resulted in increased perceived QOL with no significant difference between the experimental groups (Imfeld et al., 2006).

While supervised exercise programs may produce greater MWD and PFWD in PAD-IC patients, if supervised programs cannot be undertaken, a well structured home-based program will still result in improved walking ability and perceived QOL (Degischer et al., 2002b; Imfeld et al., 2006; Savage et al., 2001). Factors which can affect the outcome of a home-based exercise program include the exercise mode (e.g. walking, cycling, resistance training), the level of patient motivation, and the level of supervision (Savage et al., 2001).

As both home and supervision based programs have been shown to improve walking performance the intensity and mode of exercise have been examined as factors likely to produce greater increases in PFWD and MWD for PAD-IC patients.

Intensity

The level of exercise intensity that should be prescribed for PAD-IC patients during a exercise program has received little attention (Bulmer & Coombes, 2004). Gardner, Montgomery, Flinn & Katzel (2005) investigated the effects of a low-intensity exercise program (40% of the graded treadmill maximal workload achieved at baseline) versus high-intensity exercise (80% of the graded treadmill maximal workload achieved at baseline) over a 6 mth period. The volume of exercise for the high-intensity training group was reduced to enable comparison between the groups. The improvement in walking performance was almost identical for both groups. PFWD increased by 109% for both groups while MWD increased by 61% for the low-intensity group and 63% for the high-intensity group. VO_{2peak} and perceived QOL also improved for both groups. These findings indicate that high-intensity exercise can be just as beneficial as low-intensity exercise for PAD-IC affected individuals when undertaking the same volume of exercise (Gardner et al., 2005). The effects of varying volume and duration of exercise at set intensities on walking performance, physiological responses and perceived QOL requires further investigation.

Mechanisms for improved walking performance in PAD-IC

As previously described, IC is the most common symptomatic manifestation of mild to moderate atherosclerotic PAD, whereby blood flow to the exercising musculature in the legs is restricted. This restriction causes cramps and/or aching in the leg brought on by walking and is relieved by rest (Regensteiner, 2004; Weitz et al., 1996). Numerous studies have investigated the effects of pharmacology, surgery and exercise programs on PAD-IC walking capacity. However, the mechanism(s) underlying improved walking capacity is not clear and may included oxygen uptake, leg musculature changes, peripheral blood flow, angiogenesis and changes in lower limb mobility characteristics.

Oxygen uptake

One mechanism which may improve walking capacity is an exercise-related improvement in sub-maximal cardiovascular fitness. Research conducted on PAD-IC patients found lower VO_{2peak} of 13–20 $ml \cdot kg^{-1} \cdot min^{-1}$ compared to values of 27–30 $ml \cdot kg^{-1} \cdot min^{-1}$ for healthy age matched controls (Askew, Green, Hou, & Walker, 2002; Bauer, Brass, Nehler, Barstow, & Hiatt, 2004; Bauer, Regensteiner, Brass, & Hiatt, 1999; Hiatt, Nawaz, & Brass, 1987; Hiatt, Regensteiner, Wolfel, Carry, & Brass, 1996; Hiatt, Wolfel, Regensteiner, & Brass, 1992; Ng, Hollingsworth, Luery, Kumana, & Chaloner, 2005; Regensteiner et al., 1993b; Slordahl et al., 2005; Womack et al., 1997). Implementation of an exercise rehabilitation program of 3 or more mth duration can improve the VO_{2peak} of PAD-IC affected individuals by 1-3 $ml \cdot kg^{-1} \cdot min^{-1}$ depending on the intensity and duration of the exercise (Gardner et al., 2000; Slordahl et al., 2005; Womack et al., 1997). However, it has

been found that VO_{2peak} did not increase following a 6 mth exercise program (Gardner et al., 2001b). A recent study (Ng et al., 2005) found no improvement in VO_{2peak} over an 8 wk exercise program. This result is most likely due to the short duration of each exercise bout. The exercise regime consisted of 10 treadmill walks of 90 s each, with a 90 s period of rest 3 days·wk^{-1} (total of 15 mins duration). The treadmill speed and gradient was set to produce a moderate degree of claudication pain. However, the PAD-IC patients improved their PFWD (65.5 m) and MWD (339.5 m) walking performance. Therefore, VO_{2peak} may not be a mechanism for improved walking performance in PAD-IC in this population. Improved walking performance may be due to peripheral mechanisms such as changes in the lower limb musculature, peripheral blood flow, lower limb mobility characteristics or a combination of these mechanisms.

Leg musculature

Analysis of the effectiveness of exercise programs via examination of skeletal muscle histology and function has determined that PAD-IC patients with a unilateral diseased leg and the most severely diseased leg in bilateral patients, had reduced calf muscle strength (Regensteiner et al., 1993b). Knee and hip strength are significantly poorer in PAD-IC patients (McDermott et al., 2004) and the muscle fibre characteristics of PAD-IC patients have been found to be different to healthy controls. McGuigan et al. (2001) examined the myosin heavy chain (MHC) and histochemical changes in the gastrocnemius muscle in PAD-IC patients and found that MHC I muscle fibres were significantly smaller and the proportion of MHC IIx fibers was larger in PAD-IC patients. The cross-sectional area of

type I and type IIa muscle fibres is significantly reduced in PAD-IC patients. Whether this is due directly to PAD-IC or reduced activity levels is unclear.

Enhanced capillary density in leg skeletal muscles is also commonly seen in the PAD-IC patients (Askew et al., 2005; McGuigan et al., 2001). Hiatt et al. (1996) examined the effects of a 12 wk exercise program on skeletal muscle histology and metabolism in PAD-IC patients and found that type I and type II muscle fibre area and citrate synthase activity did not change but that there was an increase in the percentage of de-enervated muscle fibres. Improved walking capacity was believed to be associated with a decrease in the plasma and muscle short-chain acylcarnitine (intermediates of oxidative metabolism) concentrations (Hiatt et al., 1996). These findings suggest that muscle intermediary metabolism and not fibre and muscle strength may improve the walking performance of PAD-IC patients.

Peripheral blood flow

Exercise has a limited effect on peripheral blood flow in PAD-IC patients. Bauer et al. (2004) found that limb reactive hyperemic blood flow was reduced for PAD-IC patients compared to subjects without PAD-IC (20.7 ± 8.3 versus 46.1 ± 17.1 $ml \cdot 100ml^{-1} \cdot min^{-1}$) during exercise training. A 6 mth exercise program determined that reactive hyperemic and maximal calf blood flow increased from 9.84 ± 0.68 to 12.50 ± 0.85 $ml \cdot 100\ ml^{-1} \cdot min^{-1}$ and 13.50 ± 0.69 to 17.60 ± 1.24 $ml \cdot 100\ ml^{-1} \cdot min^{-1}$ respectively in PAD-IC patients (Gardner et al., 2001b; Gardner et al., 2005). However, the evidence for exercise induced increases in

peripheral blood flow in PAD-IC patients remains limited and inconsistent (Lumsden & Rice, 2006).

Angiogenesis

Healthy individuals engaged in exercise programs involving walking have demonstrated changes in the capillary blood vessels in the legs due to angiogenesis. This adaptation is to serve to optimize oxygen transport to active skeletal muscle fibres (Hudlicka, Brown, & Egginton, 1992; Prior, Yang, & Terjung, 2004). Angiogenesis is a process whereby capillaries are constructed from the pre-existing capillary network. Vascular endothelial growth factor (VEGF) appears to be necessary for angiogenesis to occur (Prior et al., 2004). Examination of plasma VEGF responses in PAD-IC patients following a 6 wk exercise program showed no significant effect on plasma VEGF despite significantly improved MWT (15.15 ± 8.53 - 20.06 ± 8.20 mins) (Wood et al., 2006). These results demonstrated that there may not be angiogenesis adaptation in patients with PAD-IC. Wood et al. (2006) suggested that a longer sampling time and a detailed review of VEGF responses to the endothelial receptors should be undertaken in future research.

Improved walking performance in PAD-IC patients and associated changes in VO_{2peak}, muscle histology and peripheral blood flow parameters may be related to other factors such as dietary changes, medication, psychological state and lower limb mobility characteristics. Although exercise programs have been shown to improve PFWD and MWD the mechanism for this improvement is unclear (Lumsden & Rice, 2006). Lumsden & Rice (2006) concluded that lower limb mobility characteristics may cause a secondary

disadvantage in terms of increasing the oxygen cost of walking. Womack et al. (1997) suggested that lower levels of claudication pain following exercise programs may be due to altered lower limb mobility characteristics resulting in improved walking performance and physiological responses.

Lower limb mobility characteristics

Human bipedal locomotion involves a very complex sequence of events and each individual will perform the actions slightly differently from others. The mechanism of walking takes time to learn but once it has been perfected it becomes largely subconscious. However, the ability to walk can be affected by a number of neuromuscular and muscular injuries, diseases or general aging degeneration. Research on understanding and treating walking disorders still continues to increase knowledge of how the human locomotion system works (del Olmo & Cudeiro, 2005; Kirtley, 2006; Perrault, 2006; Sparrow & Tirosh, 2005; Springer et al., 2006). To understand how an individual walks researchers can utilize task outcomes called temporal-spatial gait parameters including speed, stride length, cadence, ipsilateral and contralateral support, swing time and double support time.

Gait cycle

To undertake the basic function of walking, each stride involves an ever-changing support and advancement of the lower limb. These basic functions result in a series of motion patterns performed by the hip, knee and ankle which can be broken down into a specific phase of the gait cycle, allowing a greater understanding of gait function. The gait cycle is

defined as the time taken to complete two repetitive contacts (the point at which initial contact is made between the heel and the ground) with the ipsilateral (same) lower limb. The cycle time is the duration of a complete gait cycle, subdivided into stance time and swing time which is then broken down into events, periods and tasks (Figure 10) (Kirtley, 2006; Perry, 1992; Whittle, 2003). The analysis of the characteristics of the gait cycle enables temporal-spatial gait parameters to be examined.

Temporal-spatial gait parameters

Cadence

Cadence is defined as the number of steps·min^{-1} and is fundamentally reliant on height and leg length. As there are two steps in every stride, and 60 s in one min, steps·min^{-1} can be converted to strides·s^{-1} by dividing by 120, hence cadence can be calculated by the following formulae (Kirtley, 2006; Whittle, 2003):

$$\text{Cadence (steps·min}^{-1}\text{)} = 120 / \text{stride time (s)} \quad (1)$$

Speed/velocity

The speed of walking is the distance that the whole body covers in a given time, usually measured in m·s^{-1}. Alternately ‘velocity’ can be used in place of ‘speed’ however, velocity should only be used when the direction of walking is also included. Individuals have a free (or self-selected) walking speed which is continuously changed to deal with different environmental conditions. Walking speed can be changed to avoid collisions with obstacles

and is consciously and subconsciously varied according to mood and time schedule. In activities of daily living individuals normally change their walking speed by modifying both cadence and stride length. For example, if two people walk together they will adopt a mutual speed in order to stay close to each other together (Kirtley, 2006; Whittle, 2003). Speed can thus be calculated from cadence and stride length using the following formula:

$$\text{Speed } (m \cdot s^{-1}) = \text{stride length (m) x cadence } (steps \cdot min^{-1})/120 \quad (2)$$

Stride time can be used instead of cadence:

$$\text{Speed } (m \cdot s^{-1}) = \text{stride length (m)/stride time (s)} \quad (3)$$

Stride length

Stride length is defined as the linear distance between two successive points of foot to ground contact of the ipsilateral foot. Stride length can be determined from cadence and/or time and speed and is usually measured in meters (m).

$$\text{Stride length} = (120 \text{ x speed})/\text{cadence} \quad (4)$$

$$\text{Stride length} = \text{speed } (m \cdot sec^{-1}) \text{ x stride time (s)} \quad (5)$$

Double support

Double support (or double limb stance) occurs when initial ground contact of the ipsilateral limb occurs while the contralateral foot is still in contact with the ground and lasts until the

contralateral foot reaches the toe-off stage. During the swing phase of the contralateral lower limb, only the ipsilateral limb is in contact with the ground, giving a period of ipsilateral single support (or single limb stance). Double support occurs again once the contralateral side has made contact with the ground following the swing phase and will continue, until toe-off of the ipsilateral lower limb. The contralateral side is then in a period of contralateral single support and the cycle ends with the next initial contact of the ipsilateral foot (Kirtley, 2006; Perry, 1992; Whittle, 2003). Therefore, in each gait cycle there are two double and two single support phases. The stance phase usually lasts about 60% and the swing phase about 40% and each period of double support accounts for 10% of the gait cycle. These percentages can vary with the speed of walking as the swing phase becomes longer and the stance and double support phases become shorter as speed increases (Kirtley, 2006; Murray, 1967; Perry, 1992). The double support phase is eliminated once running begins. During running there is a period of time when neither foot is in contact with the ground (non-support phase) (Kirtley, 2006; Whittle, 2003).

These temporal-spatial gait parameters aid researchers and clinicians to diagnosis and assess exercise programs affects on lower limb mobility problems. However, temporal-spatial gait parameters are only task outcome and the underline mechanism i.e. joint angular kinematics should also be investigated.

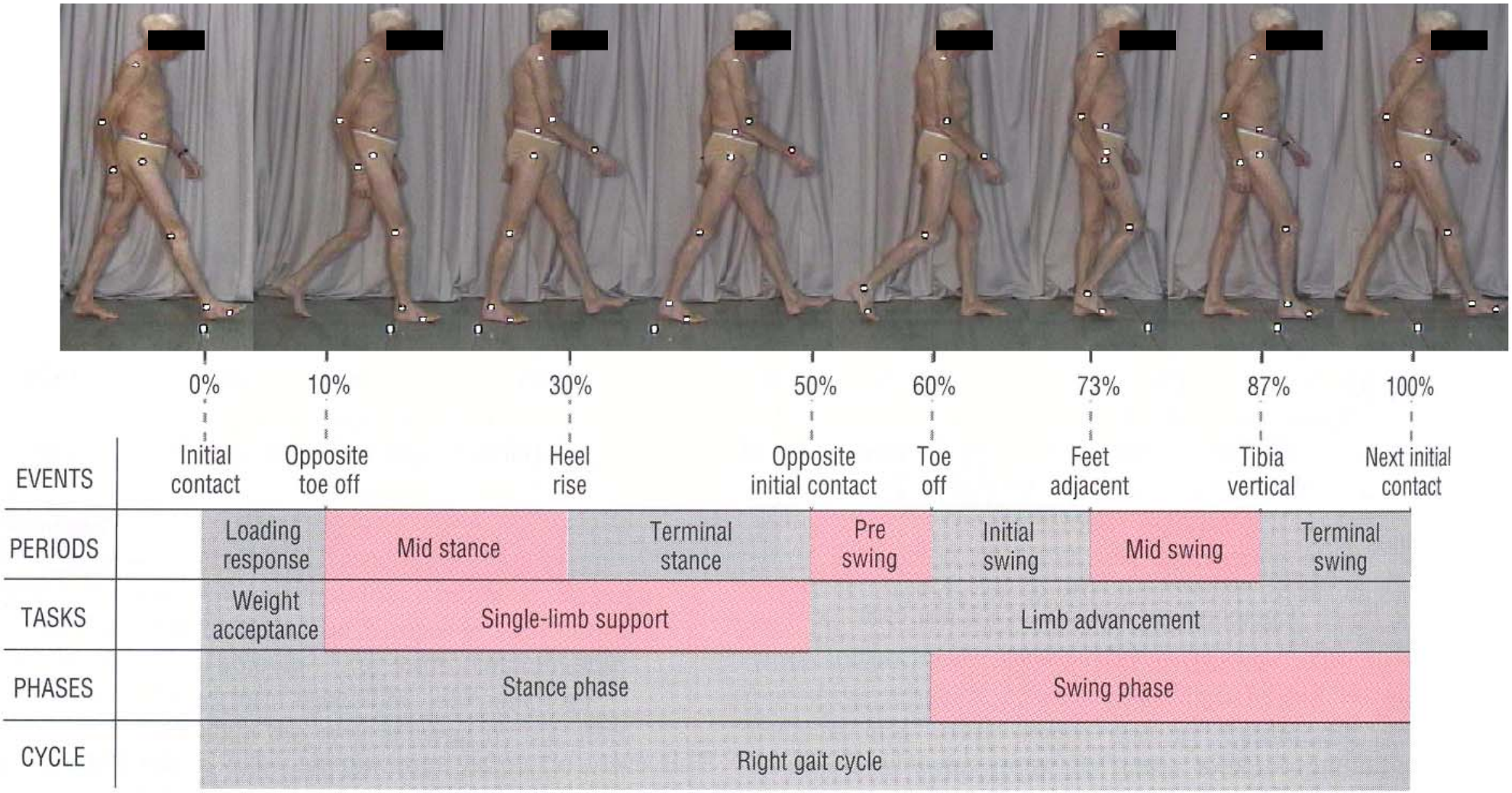

Figure 10 Events of the gait cycle (adapted from Neumann, 2002)

Kinematics of the gait cycle

This section of the literature review will identify common joint angular kinematic characteristics of walking that will serve as a model for comparison between patients with and without PAD-IC and the effects of supervised exercise training. The angular conventions used to describe the movement of the trunk, hip, knee and ankle during the gait cycle are depicted in Figure 11.

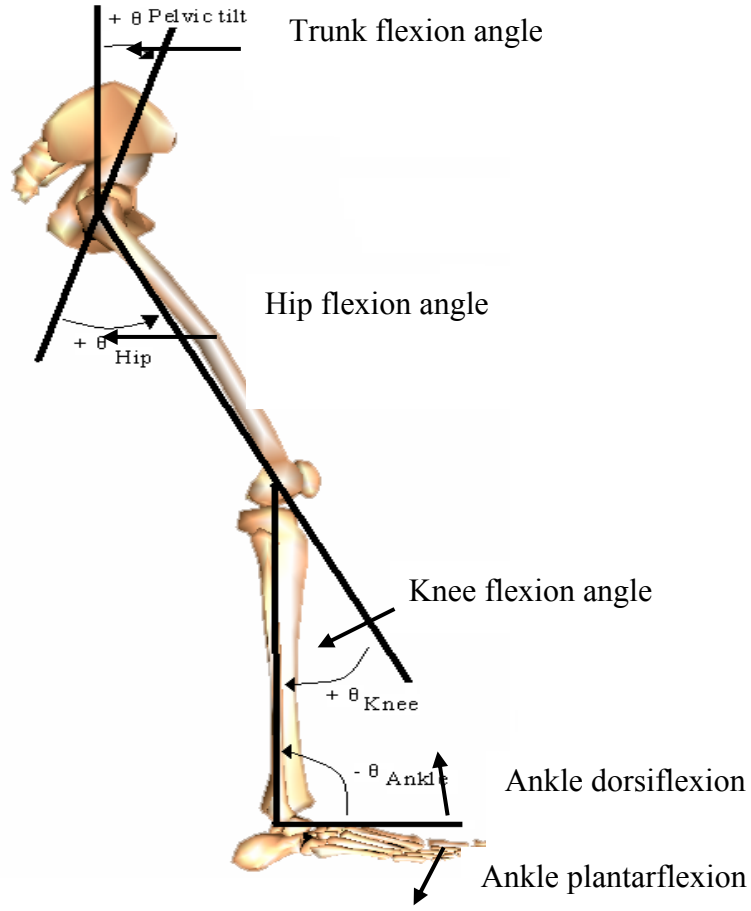

Figure 11 Angle conventions used to describe the angular displacements of the trunk, hip, knee and ankle in the sagittal plane during the walking cycle.

Kinematics of the hip

During walking the hip moves through two movements, extension during stance and flexion during the swing phase (Figure 12). The normal ROM of the hip will average approximately 40º through a gait cycle (Ounpuu, 1994; Perry, 1992). This movement is provided through rotation of the femur, with small pelvic tilting movement (Murray, 1967).

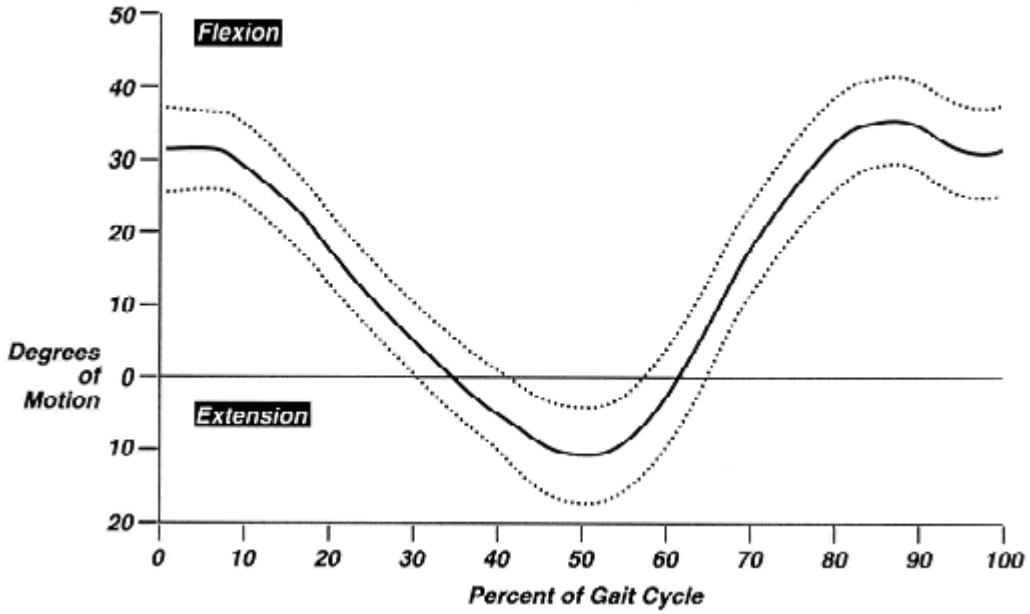

Figure 12 Mean (—) ± SD (·····) of hip ROM during normal walking (adapted from Perry, 1992)

Kinematics of the knee

The knee angular motion is more complex than the hip pattern with two flexions and two extensions within each gait cycle (Figure 13). Normal knee ROM during walking represents greater and lesser degrees of flexion within the full ROM of 0º-70º (Ounpuu, 1994; Perry, 1992). Research has indicated varying flexion and extension ROM values due

to differences in walking speed and anthropometric landmarks selected to determine ROM (Handling, n.d.; Murray, Kory, Clarkson, & Sepic, 1966; Schuyler et al., n.d.)

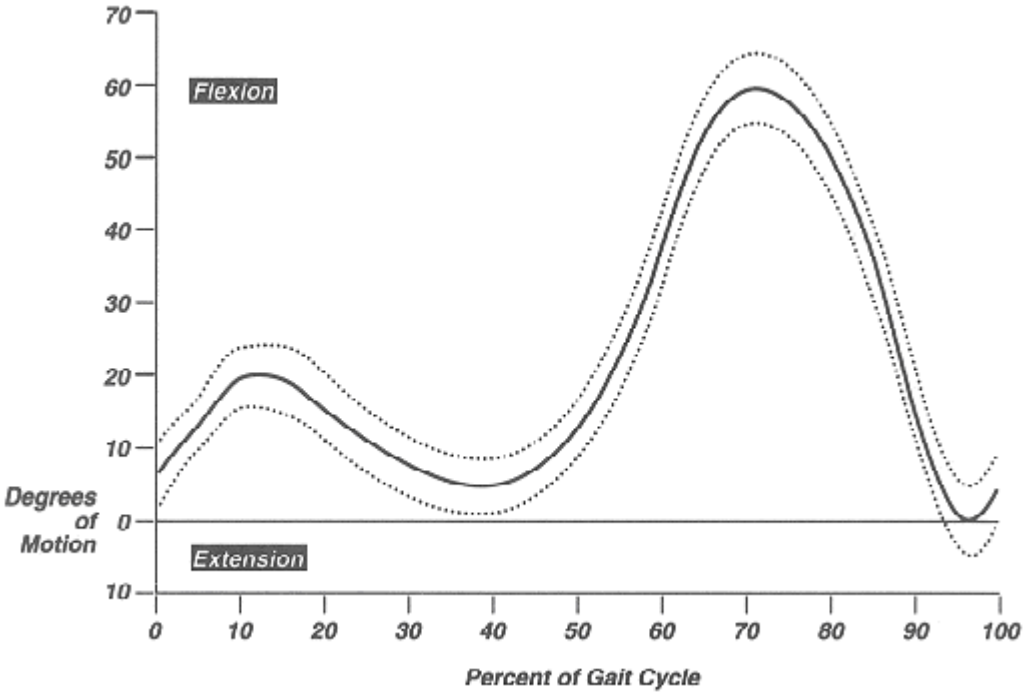

Figure 13 Mean (—) ± SD (·····) of knee ROM during normal walking (adapted from Perry, 1992)

Kinematics of the ankle

There are also two flexion and extension movements for ankle ROM (~30º) during a gait cycle (Ounpuu, 1994) (Figure 14). Murray (1964) found that for normal healthy adults the excursions of the ankle movement were strikingly similar in the various age and height groups, except for subjects ages 50 – 60 yr.

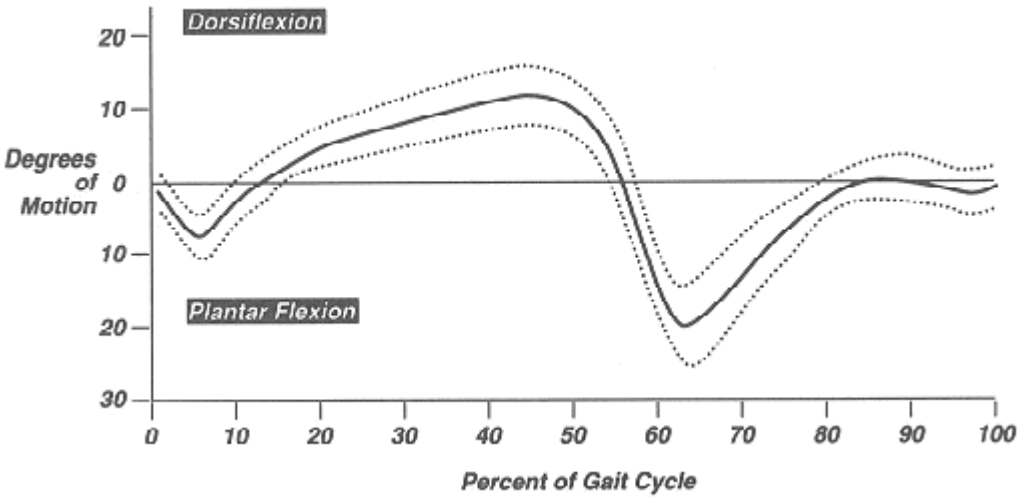

Figure 14 Mean (—) ± SD (·····) of ankle ROM during normal walking (adapted from Perry, 1992)

Gait across the lifespan

Lower limb mobility of the elderly population is very important for individual QOL (Spirduso & Cronin, 2001). The changes in gait characteristics of the elderly population are well known. A number of investigations have reported a gradual slowing of gait movement with aging (Maki, 1997; Murray, Kory, & Clarkson, 1969; Murray, Kory, & Sepic, 1970; Nigg, Fisher, & Ronsky, 1994; Prince et al., 1997; Sparrow & Tirosh, 2005; Whittle, 2003; Winter, 1991; Winter, Patla, Frank, & Walt, 1990). The slowing of the gait movement is mainly due to prolongation of the single and double stance support phases of the gait cycle. Stride and step length decrease, speed decreases, stride width increases and contact time increases to provide a more stable base of support (Tables 6 & 7)(Whittle, 2003). Murray et al. (1969) suggested that the movement patterns of older men did not resemble a pathological gait and concluded that the purpose of gait changes in the elderly is to

improve safety of walking by decreasing the stride length and increasing the walking base. This requires less effort to maintain balance while walking (Murray et al., 1969).

Table 6. Female gait range characteristics (Whittle, 2003)

Age (yr)	Cadence (steps·min^{-1})	Stride time (s)	Stride length (m)	Speed (m·s^{-1})
13-14	103-150	0.80-1.17	0.99-1.55	0.90-1.62
15-17	100-144	0.83-1.20	1.03-1.57	0.92-1.64
18-49	98-138	0.87-1.22	1.06-1.58	0.94-1.66
50-64	97-137	0.88-1.24	1.04-1.56	0.91-1.63
65-80	96-136	0.88-1.25	0.94-1.46	0.80-1.52

Table 7. Male gait range characteristics (Whittle, 2003)

Age (yr)	Cadence (steps·min^{-1})	Stride time (s)	Stride length (m)	Speed (m·s^{-1})
13-14	100-149	0.81-1.20	1.06-1.64	0.95-1.67
15-17	96-142	0.85-1.25	1.15-1.75	1.03-1.75
18-49	91-135	0.89-1.32	1.25-1.85	1.10-1.82
50-64	82-126	0.95-1.46	1.22-1.82	0.96-1.68
65-80	81-125	0.96-1.48	1.11-1.71	0.81-1.61

Decreased mobility has been shown to lead to decreased independence and reduced physical activity which then leads to increase CVD risk factors and poor stability (falls) (Brach et al., 2002; Daley & Spinks, 2000; Gill et al., 1995; Guralnik et al., 1995; Prince et al., 1997; Rubenstein et al., 2001; Sadeghi et al., 2002; Spirduso & Cronin, 2001). Research on aging and falling has found that an increase in the incidence of falls is related to variability within the temporal-spatial gait parameters such as stride length, stride width and cadence (Hausdorff et al., 1997; Maki, 1997). Aging is not the only cause of changes in temporal-spatial gait parameters and joint angular kinematics during walking. Pathologies that affect the lower limbs can also have a dramatic impact on lower limb mobility.

Pathologies affecting gait

A large number of pathologies can cause abnormal lower limb gait patterns including neurological conditions such as cerebral palsy, spastic hemiplegia, spastic diplegia, myelomeningocele and parkinsonism. Diseases that occur in the lower limb such as joint diseases (e.g. rheumatoid arthritis), diabetic neuropathy and PAD-IC can also impact on gait patterns (Whittle, 2003).

Gait and PAD-IC

The mechanism for improved walking performance in patients with PAD-IC following an exercise rehabilitation program has lead researchers to question what impact these interventions have on lower limb mobility characteristics of this population (Lumsden & Rice, 2006; Schoop, 1973).

Rochester & Clarke (1994) investigated the gait of rats as a model for studying the effects of PAD-IC on lower limb gait. The results indicated no significant differences for walking speed and stride lengths during walking with unilateral ligation of the common iliac artery. However, internal balance was disturbed with reduced stance and extended swing phases for the ligated limb relative to the nonligated limb. The nonligated limb exhibited gait changes with the initial limb contact occurring earlier during the ligated limb stance. It was concluded that gait and footfall analysis should be undertaken when examining gait in PAD-IC human patients during natural exercise conditions to determine what affect PAD-IC has on lower limb mobility (Rochester & Clarke, 1994).

Research involving kinetic gait analysis of PAD-IC patients found that there was no systematic difference between the peak values of force moments except for the transverse horizontal force component which was found to be stronger in healthy controls during foot contact (Carlsoo, Dahlof, & Holm, 1974). It was concluded that the kinetic gait patterns of PAD-IC patients did not change following exercise training.

Furthermore, two studies have shown differences in the lower limb mobility characteristics of patients with PAD-IC and control subjects during normal walking (Gardner et al., 2001a; Scherer et al., 1998) while another three have shown no significant effect of PAD-IC on lower limb mobility (McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006).

McCully et al., (1999) investigated the effects of PAD-IC on temporal-spatial gait parameters including speed, step length, step time, swing time, stance time and double support time and found no significant effect of treadmill walking on the gait patterns of patients with PAD-IC when free of claudication pain. However, after exercise PAD-IC patients were found to walk more slowly, had shorter step lengths, slower step time and longer stance time (McCully et al., 1999). These findings were in contrast to those of Scherer, Bainbridge, Hiatt & Regensteiner (1998) who found that PAD-IC patients regardless of disease severity, walked more slowly and had decreased step length and decreased cadence. McDermott et al. (2001a) showed similar results to McCully et al. (1999) finding that over 6 mins of walking, the first and last 30.48 m of walking resulted in non-significant differences in gait compared to control patients, however, there was a trend

towards reduced walking speed in the PAD-IC patients over the last 30.48 m compared to the controls. There were no between group differences in stride length and cadence. Later research (Gardner et al., 2001a) showed that walking speed, stride length, swing phase and single-stance phase are significantly smaller and single and double-stance phases are significantly longer in PAD-IC patients. Recently Scherer, Hiatt and Regensteiner (2006) found that there were no significant differences between PAD-IC and control subjects for stride length, cadence, stride width or toe-out angle during self paced and maximal walking speed.

As well as temporal-spatial gait parameters, the balance characteristics of patients with PAD-IC have been investigated. Gardner & Montgomery (2001) investigated the effect of PAD-IC on balance and whether there is an increase in the prevalence of falling in patients with PAD-IC. Unipedal stance time was 28% shorter in PAD-IC patients compared to controls (15.9 s ± 0.9 versus 22.1 ± 1.0 s). Unsteadiness/stumbling and history of falling were found to be more prevalent in PAD-IC patients (86%) compared to controls (73%). The 6-minute walk test, self-reported ambulatory function and daily physical activity were all found to be significantly related to balance and history of falling measures. The results demonstrated that the impaired gait-related neuromuscular function of PAD-IC patients can impact on QOL in this population.

The contradictory results of the above lower limb mobility research indicates the need for more research on the effects of this condition on the lower limb mobility characteristics of PAD-IC patients. Gardner et al. (2001) speculated that exercise programs could improve

lower limb mobility characteristics in PAD-IC patients to the extent that they resemble healthy age matched individuals. While the research focus has been on temporal-spatial gait parameters no studies to date have examined the underlying mechanism of these parameters namely gait kinematics (lower limb joint angular velocities, accelerations and displacements). Research should also consider the joint angular kinematic characteristics of PAD-IC patients. Observed limitations in temporal-spatial gait parameters may be explained by the effects of musculoskeletal abnormalities (e.g. compromised blood and nerve supply, injury) on lower limb joint kinematics during the gait cycle. Understanding of the kinematics of affected temporal-spatial gait parameters in individuals allows more precise identification of the aetiology of the idiosyncrasy and its effects at the joint-muscle interface which in turn allows for more specific formulation of exercise treatment plans (Davis, 1997).

Furthermore analysis of movement variability using biomechanical degrees of freedom (joint angular kinematics) may provide more information about the level of variability during locomotion. This information will represent how individuals interact with the unique range of task, organismic and environmental constraints impinging upon them, and has implications for the choice of movement variability assessment techniques. Examination of lower limb mobility characteristics such as temporal-spatial gait parameters, joint angular kinematics and movement variability may provide valuable information about lower limb mobility and motor control patterns of PAD-IC patients.

Theories of motor control

The information processing theory of human motor control assumes the existence of a command centre in the brain that makes executive decisions regarding movement. Once an action decision has been made, a plan (motor program) is accessed from memory and commands are sent to the motor system to implement the action (Keele, 1968; Schmidt, 2003). The dynamical systems theory of motor control argues that the brain cannot store in memory the number of movement plans created by a central command centre or inform novel tasks including variations and adjustments associated with skilled movement. Instead, dynamical systems theory proposes that movements 'emerge' or self-organise from a dynamical interaction of numerous variables in the body, the environment and the task (Davids, Glazier, Araujo, & Bartlett, 2003; Williams, Davids, & Williams, 1999). These variables impose constantly changing constraints upon movement and the movement pattern that emerges is a function of these constraints (Newell, 1986). Bodily constraints include anthropometric, (height, weight, body shape), biomechanical, cognitive and emotional characteristics. Environmental constraints include gravity, light, temperature and objects and surfaces that are interacted with. Task constraints include intentions and goals, and machines, tools or implements that must be used and rules (as in sporting activities) (Clark, 1995; Davids et al., 2003; Kugler, Kelso, & Turvey, 1980).

How are combinations of joint movements chosen for a particular goal-directed act if, as dynamical systems theory suggests, the brain does not send commands down to individual joints in order to produce goal-directed movement? The dynamical systems view is that the

elements of a system are constrained to act together in a specific relationship thus reducing the degrees of freedom (number of possible independent dimensions of movement in a system) which need to be controlled (known as the degrees of freedom problem). The notion of coordinative structures or (emergent self-organized) synergies is proposed to describe this constraint. Constraints alone are not sufficient to produce movement. As indicated above a process is required to produce organised action and in a dynamical system that process is self organisation wherein highly complex systems with multiple simpler elements will spontaneously develop organisation (Clark, 1995).

Patterns & pattern formation are fundamental to dynamical systems and all the possible states of a dynamical system (known as 'state space') may be represented geometrically in a phase portrait (Handford, Davids, Bennett, & Button, 1997; Williams et al., 1999). Attractors (states in which movement components are brought into relation with each other) are formed when a system is drawn to specific regions of state space. For example, a phase portrait for motion of the lower leg represents stable collective states of a dynamical system with the system returning quickly to state space following small perturbations. Therefore, a stable pattern is a behavioural state that is reproducible & independent of others and equates to low variability. When variability increases the system becomes unstable. Loss of stability represents a system in transition (e.g. when progressing from crawling to walking or from normal walking to affected walking due to injury or disease). This transition point enables determination of the extent to which a constraint acts as a control variable (i.e. influencing direction, force, speed, accuracy, or perceptual information). Patterns of change in movement can be attributed to changes in one or more

constraints which can lead to an increase in variability (Clark, 1995; Handford et al., 1997; Williams et al., 1999).

Variability

Variation between multiple attractors (patterns) permits flexible and adaptive motor system behavior, thereby encouraging free individual exploration of performance contexts (Newell & Corcos, 1993). The relationship between stability and movement variability is used to explain why a skilled performer can persevere and change motor output during movement. Movement variability allows performers to explore task and environmental constraints in order to develop a stable motor solution over time and to facilitate motor learning (Glazier, Davids, & Bartlett, 2003). Skilled performers can freeze or unfreeze the degrees of freedom in the chain of movement as the demand of the task constraints occurs (Davids et al., 2003; Newell & Vaillancourt, 2001). Less skillful (or affected) performers fix the degrees of freedom and may demonstrate as much or more movement variability that is not functional (Newell & Vaillancourt, 2001).

Traditionally movement variability has been viewed as "noise" representing random fluctuations in all levels of biological systems (Newell & Corcos, 1993) which should be controlled or reduced. However, noise can be a contributor to the qualitative properties of the dynamical output as part of a nonlinear dynamical system (van Emmerik, Rosenstein, McDermott, & Hamill, 2004). Noise can be beneficial by facilitating adaptation to task demands as noise variation could provide information about the state of the biological system (Davids et al., 2003; Newell & Corcos, 1993; Van Emmerik et al., 2005). These

variations may be assessed by moving away from dynamical systems theory and examining the peripheral degrees of freedom that are at the level of biomechanical task outcomes. However, both peripheral and dynamical assessment of degrees of freedom provide information about the source of variability in human movement and movement variability is one of the most powerful indicators of performance (Van Emmerik et al., 2005).

Human locomotion research has traditionally assumed that increased variability in temporal-spatial gait parameters (stride length, stride width and stride frequency) is associated with instability (Hausdorff, Cudkowicz, Firtion, Wei, & Goldberger, 1998). However, research on thorax and pelvis movement identified variability as a determinant for postural stability during walking (Murray, Sepic, Gardner, & Downs, 1978) and over a period of time, gait measures will change from one stride to the next, even when there is an external stimulus (Hausdorff, 2005). Relatively small stride to stride fluctuations have been found in healthy adults (Gabell & Nayak, 1984; Hausdorff et al., 1997) and are thought to be due to the accuracy and reliability of the fine tuned motor systems that regulate gait. Variations in the noise of gait characteristics such as stride length, stride time, walking speed and angular kinematics displacement have been shown to display hidden information about the peripheral degrees of freedom of the human locomotion system (Hausdorff, 2005).

Movement variability with aging, injury and disease

Increased movement variability (in terms of magnitude and dynamics) is a quantifiable feature of walking that can be altered by clinical relevant syndromes such as aging, injury,

falling, frailty and neuron-degenerative diseases such as Parkinson's and Alzheimer's (Buzzi, Stergiou, Kurz, Hageman, & Heidel, 2003; Hausdorff, 2005; Hausdorff et al., 1998; Hausdorff, Rios, & Edelberg, 2001). Stride-to-stride magnitude fluctuations in stride length, stride width and stride time have been found to be unaltered in healthy older adults however the variability of these temporal-spatial gait parameters has been found to be significantly higher, demonstrating a greater level of instability in the lower limbs. Variability measures can predict poor stability, falls in elderly fallers and other populations that may be at risk of falls and/or have poor obstacle avoidance ability. (Grabiner, Biswas, & Grabiner, 2001; Hausdorff et al., 1997; Maki, 1997; Mbourou, Lajoie, & Teasdale, 2003). Intralimb joint coordination research has also demonstrated that movement variability is increased when in transition from walking to running (Diedrich & Warren, 1995). However, reduced movement variability in Parkinson's disease represents the ability of affected individuals to transfer from one movement pattern to another (Van Emmerik et al., 1999). Movement variability may be of functional importance in motor control (Van Emmerick et al., 2005) and it may provide flexibility when adjusting to perturbations in the environment. It is fundamental to change coordination patterns during locomotion, thus higher movement variability may be beneficial (Heiderscheit et al., 2002; Van Emmerik et al., 2005; Van Emmerik et al., 1999). On the other hand, pain or injury may result in reduced movement variability (Hamill, van Emmerik, Heiderscheit, & Li, 1999; Heiderscheit et al., 2002; Pollard, Heiderscheit, van Emmerik, & Hamill, 2005).

Therefore, it would appear that the assessment of movement variability in human walking using either temporal-spatial gait parameters or the joint patterns would provide distinctly

opposing information about individual motor control during locomotion (Heiderscheit, 2000). Traditional movement variability was thought to be a characteristic of pathological state, however, the dynamic system perspective has provided researchers with a new way of viewing movement variability. Movement variability is now thought to be an essential part of the solution to the problem of performing tasks. Therefore, movement variability should not be viewed as something that should be abolished in the clinical practice. Rather movement variability may be beneficial or an adaptive mechanism (Hamill, Haddad, Heiderscheit, Van Emmerik, & Li, 2006). However, it should be noted that higher or lower movement variability is relative and research is yet to determine the levels of movement variability that might reflect injury and disease states or be beneficial in terms of locomotion (Van Emmerik et al., 2005).

The use of movement variability (joint kinematics or temporal-spatial gait parameters) can be used as a clinical tool to evaluate the mobility of elderly and pathological populations to examine stability, mobility, fall risk, obstacle avoidance ability and responses to intervention programs providing more information about the underlying control mechanism than temporal-spatial gait parameters and joint angular kinematics ever can (Hausdorff, 2005). However, the utility of the techniques used to determine movement variability have not been agreed upon.

Methods of determining movement variability

Intralimb joint coordination

Different methods are used to interpret movement variability in human walking. Linear methods involve using temporal-spatial gait parameters such as stride length, stride width and stride time from a number of trials and then the coefficient of variation and the mean deviation for each characteristic is calculated. Other methods involve time normalization of the gait kinematics from each gait cycle to a standard length (100%) and then the average of each trial is used to calculate a mean gait cycle. Although this approach has been used to address clinical questions related to walking disorders, it ignores the intrinsic dynamical nature of locomotion. Any information about the control of locomotion from one cycle to the next is lost (Dingwell & Cusumano, 2000; Glazier et al., 2003). To gain a better understanding of how the body segments coordinate during walking, segmental interactions illustrated by variable-variable plots or angle-angle plots can be investigated by analyzing sets of time series data (linear analysis) obtained from adjacent body segments or joints (Grieve, 1968; Grieve, 1969). This provides a combined qualitative and quantitative analysis that is commonly used by motor control researchers (Glazier et al., 2003; Grieve, 1968; Grieve, 1969; Hershler & Milner, 1980; Sparrow, 1992). Lower limb movement variability assessment can also involve analysis of linear single joint movement variability (ankle, knee and hip kinematic displacement) and nonlinear (Lyapunov exponent) single joint techniques.

Angle-angle diagrams

Angle-angle diagrams have been used to analyze one joint/segment motion relative to another joint/segment motion (Figure 15). Angle-angle diagrams can also utilize the joint/segment motion and angular kinematic velocity of that joint/segment (called a phase-plot diagram) in order to examine the effect of joint velocity (Figure 16). Angle-angle diagrams are an effective qualitative means of monitoring human gait pathologies such as cerebral palsy in children (de Bruin, Russell, Latter, & Sadler, 1982; Hershler & Milner, 1980). There are a number ways of quantifying the angle-angle diagram namely, parameterization, normalized root mean square (NoRMS) and vector coding (Goswami, 1998; Sidaway et al., 1995; Tepavac & Field-Fote, 2001).

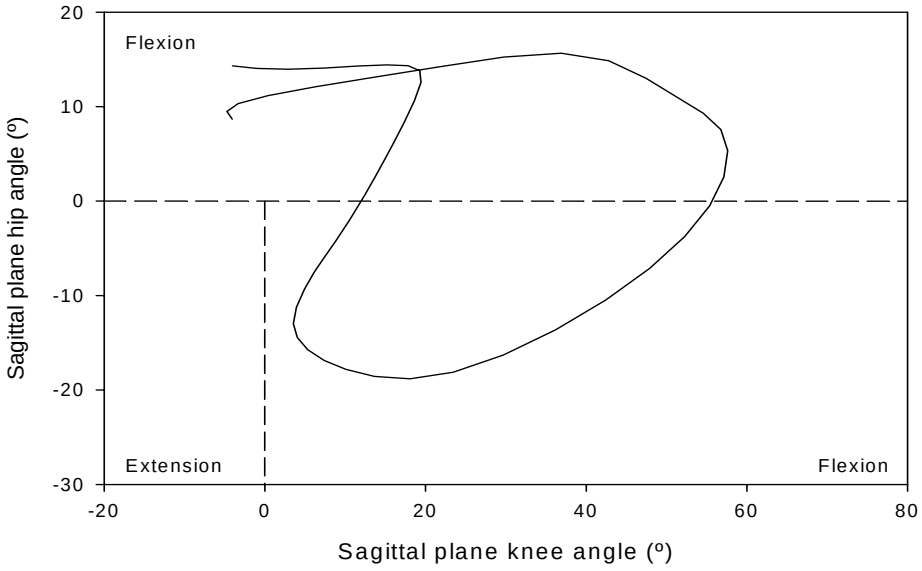

Figure 15 Angle-angle plot of the sagittal plane hip and knee during a gait cycle

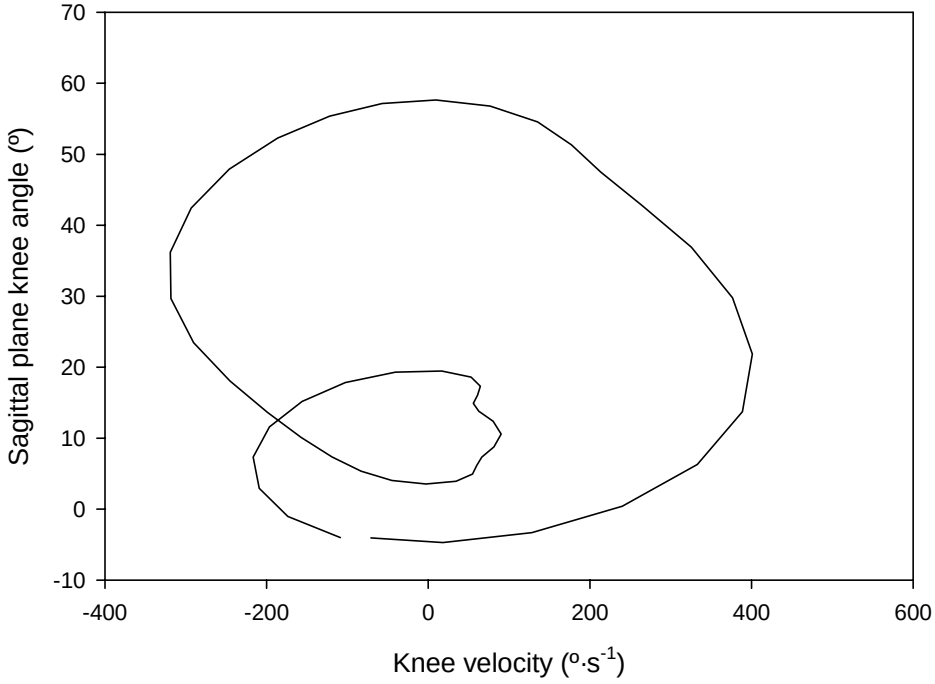

Figure 16 Phase-plane plot of the knee angle and knee velocity during a gait cycle

Parameterization

Parameterization is a technique used to examine the area, perimeter and location of the center of mass in the shape of an angle-angle diagram (Goswami, 1998). Although this method does not involve a calculation of movement variability it does however, present a quantitative characterization of normal gait and allows for clinical identification of pathological conditions. This technique was initially used by Goswami (1998) to quantify changes in gait patterns during human slope walking. Goswami (1998) concluded that gait parameterization can be used to quantify normal gait, compare gaits, identify pathological conditions and to track patient progress during a rehabilitation program.

NoRMS

The NoRMS technique was designed to quantify the consistency and stability of changes in angle-angle diagrams and involves measuring the resultant distance between the angle-angle coordinate of a curve and the angle-angle coordinate of the mean curve at each instant. The root mean square difference is then calculated at each point and then normalized with respect to the number of cycles and the excursion of the mean plot (Equation 7) (Mullineaux, Bartlett, & Bennett, 2001; Sidaway et al., 1995; Wheat & Glazier, 2006).

$$NoRMS = 100 * \left(\frac{\sum_{j=1}^{k} \sqrt{\sum_{j=1}^{n} (\bar{x}_A - x_{Ai})^2 + (\bar{x}_B - x_{Bi})^2 / n_j}}{R} \right) \quad (7)$$

A & B denote the two variable, *k* is the number of cycles, *n* is the number of data points, R is the resultant excursion of the mean angle-angle curve over the entire cycle (estimated using the hip and knee corresponding to the maximum and minimum values at either the two joints), $\bar{x}$ is the mean position of a given variable at the *i*th data point and x is the position of a given variable at the *i*th data point on the *j*th cycle (Wheat & Glazier, 2006).

High NoRMS values for an angle-angle plot demonstrate greater movement variability in the coordination patterns. Sidaway et al. (1995) used NoRMS to examine the differences in coordination between the angles of the left and right knee on a ski-simulator task for expert and novice skiers. The authors determined that NoRMS was a successful technique for distinguishing the movement variability in expert and novice skiers' coordination.

Vector coding

Vector coding (VC - also referred to as Encoded Chain Technique - ECT) was first employed by Freeman (1974) and involves placing an image of an angle-angle plot on a grid and the perimeter of the image encoded using an eight point scale (Figure 17) based on the direction of the line between two consecutive data points (frame-frame interval).

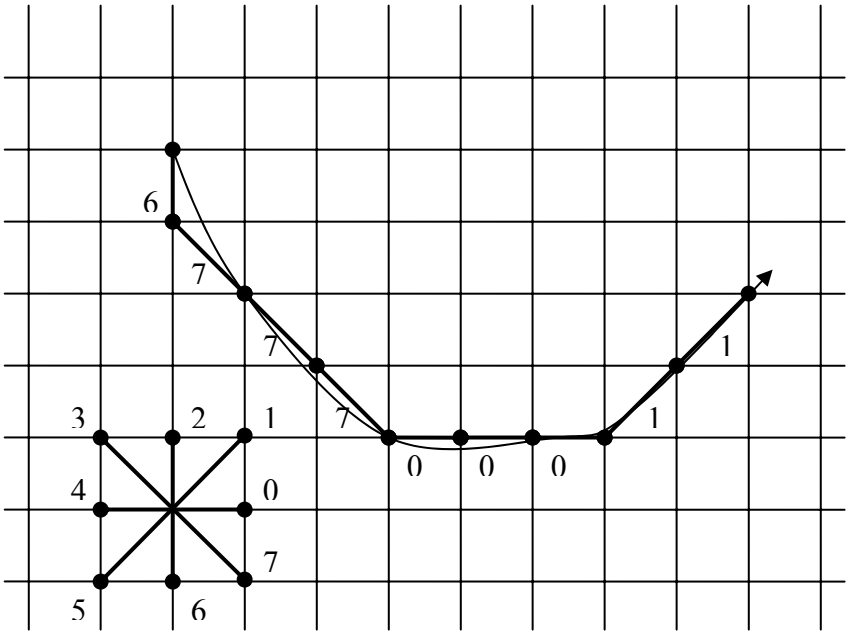

Figure 17 Vector coding technique

This VC technique has been used in the study of gait (Hershler & Milner, 1980; Whiting & Zernicke, 1982). However, a limitation of Freeman's (1974) method is that it requires the data to be equally spaced and additionally this technique converts ratio scale data to the normal scale, causing the loss of important information and limiting statistical analysis (Sparrow, Donavan, van Emmerik, & Barry, 1987; Tepavac & Field-Fote, 2001). Therefore a revised ratio-scale vector-based coding method used to quantify relative motion data that

takes into account the length of each frame to frame interval has become the standard technique for VC (Tepavac & Field-Fote, 2001).

The VC technique initially involves placing the image of an angle-angle plot on a grid and the direction of the line located as a number. The magnitude and direction of the vector connecting the two points of the angle-angle plot is then calculated. The VC data is then used to identify high or low movement variability of the angle (a), magnitude (m) and vector (v) over multiple cycles. Higher mean v values demonstrate a more consistent intersegmental relationship (less variable) (Tepavac & Field-Fote, 2001). Field-Fote & Tepavac. (2002) used the VC technique to assess joint coordination movement variability between the hip and knee in patients with incomplete spinal cord injury. The authors found that participants who engaged in a 12 wk walking program had increased walking consistency represented by reduced movement variability.

Heiderscheit, Hamill & van Emmerik (2002) modified the technique developed by Tepavac & Field-Frote (2001). This modification was similar to the method of Sparrow et al. (1987). The coupling angle was defined as the orientation of the vector (relative to right horizontal) between two adjacent points on the angle-angle plot. Movement variability was calculated at each frame-to-frame interval however, the magnitude of the frame-to-frame vector was not performed**.** This has been shown to be a limitation of this technique (Wheat & Glazier, 2006). Heiderscheit, Hamill & van Emmerik, (2002) used this technique to examine subjects with unilateral patellofemoral pain (PFP). It was found that the affected limb had lower movement variability than did the contralateral limb. The advantage of VC

technique is that there is no requirement to normalize the data, thereby maintaining true spatial information. However, the disadvantage of this technique is that it provides spatial information only, with no regard to temporal data (Hamill, Haddad, & Mcdermott, 2000).

Single joint movement variability

Coefficient of variation (CV)

Winter (1984) calculated the CV in single joint mean ensemble curve to determine movement variability over the gait cycle. This CV calculation is an adaptation of the CV equation that is used in many fields of research (CV = (SD/M)*100%). The CV is calculated as follows:

$$CV = \frac{\sqrt{\frac{1}{N}\sum_{i=1}^{N} S_i^2}}{\frac{1}{N}\sum_{i=1}^{N}\left|X_i\right|} \tag{8}$$

Where S is the standard deviation of the mean gait cycle, x is the ith point on the mean gait cycle, and N is the number of points in the mean gait cycle. The higher the CV value the more variable the mean gait cycle (Winter, 1984).

The use of the CV equation is used in the area of human walking movement variability (Brach, Berlin, VanSwearingen, Newman, & Studenski, 2005; Brach, Berthold, Craik, VanSwearingen, & Newman, 2001; Dubost et al., 2006; Hausdorff et al., 1997; Webster,

Merory, & Wittwer, 2006). However, Kurz & Stergiou (2004) believe that there may be a problem with using CV to compare movement variability across subjects as the results can be influenced by different mean joint pattern values. For example, if subject A has a larger mean value compared to subject B the amount of true variability can be lost due to the mean value being located in the denominator of the CV equation. Different mean joint magnitudes will affect the reliability of the CV measure between subjects. A way of overcoming this problem is to utilize the spanning set technique (Kurz et al., 2003) which can be used to measure movement variability without being susceptible to changes in the joint mean curve.

Spanning set

The spanning set was developed by Lay (2000) (cited in Kurz & Stergiou, 2004) and is composed of vectors that describe the possible linear combinations for a system of equations for a single joint mean curve. The larger the number of possible linear combinations of the vectors, the greater the variations in the possible solutions (Kurz & Stergiou, 2004). The spanning set is described as a plane in R^n (Figure 18).

R^n is the dimension of the given set of variables meaning the vectors that compose the spanning set can be viewed as the edges of the plane, and the surface as variations in the solutions of the system of equations. The span of the plane is dependant on the distance between the vectors (edges of the plane) that define the spanning set. Greater variability in the possible solutions of the two vectors will be represented as a larger distance between the vectors and a greater span (Kurz & Stergiou, 2004).

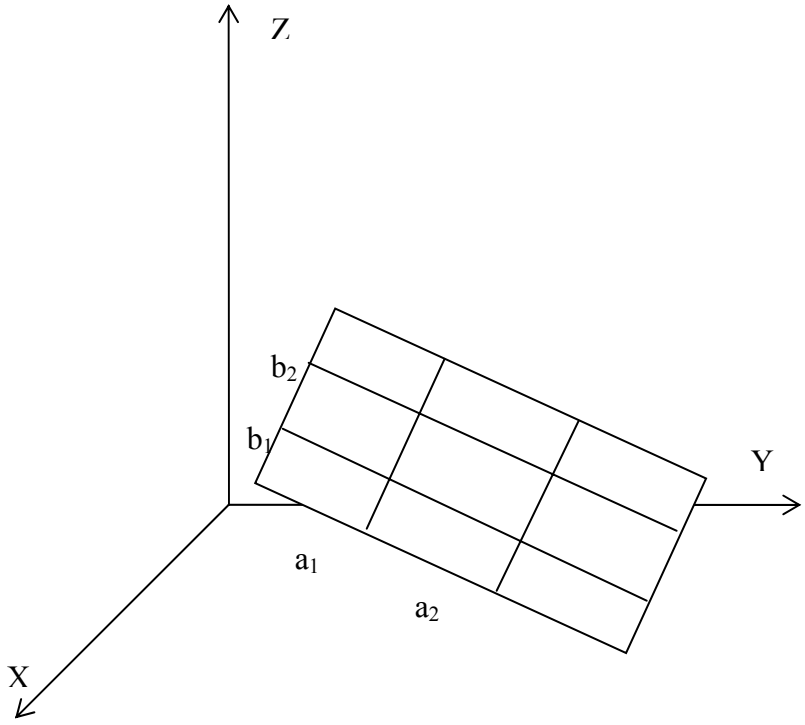

Figure 18 R^n represents the span of the two vectors, where a_1, a_2, b_1 and b_2 represent the components of the respective vectors (Kurz & Stergiou, 2004)

The standard deviations about the joint mean curve can be used as two vectors for spanning set analysis (Kurz & Stergiou, 2004; Lay, 2000). The greater the distance between the mean & standard deviation curves the greater the span of the two vectors and therefore the larger the joint variability. A spanning set is created by a least-square method utilized to fit a seventh-order polynomial to the standard deviation curves of the mean joint curve. Coordinate mapping introduces a familiar coordinate system that is used to describe the properties of the polynomials in R^n (Kurz & Stergiou, 2004). Coefficients from the respective polynomials are used to map a vector space which in turn is used to define vectors in the spanning set. The magnitude of each spanning set that describes movement variability is determined by the norm of the difference between the two vectors of the

spanning set (Buzzi et al., 2003; Dingwell & Cusumano, 2000; Hausdorff et al., 1997). Spanning set has been used to examine the effects of footwear and to quantify variability in locomotive pattern and may provide an alternative technique for evaluation of variability from the mean ensemble curve of human walking (Kurz & Stergiou, 2003; Kurz et al., 2003).

Summary of the literature review

As the Australian population continues to increase the risk of CVD will also rise. PAD-IC is one of many health concerns for the Australian elderly population and this condition has been shown to influence walking performance, physiological responses to exercise, physical activity levels and QOL. Although patients with PAD-IC are normally treated conservatively with medications to reduce CVD risk factors such as high blood pressure and cholesterol, research has shown that patients with PAD-IC engaged in exercise programs will improve their walking performance, reduce risk factors and improve their QOL. However, the mechanism that causes improvement in walking performance is unclear. Increased cardiac output, development of collateral lower limb arteries, improved efficiency of oxygen delivery, adaptation of muscle metabolism and changes in lower limb mobility (Lumsden & Rice, 2006; Womack et al., 1997) have been suggested as contributors to improved walking performance but, there is no agreement as to the major contributing factors. Previously, only five studies have investigated the effects of PAD-IC on lower limb mobility characteristics. These studies have conflicting results, with some research determining that individuals with PAD-IC demonstrate reduced lower limb

mobility characteristics (Gardner et al., 2001a; Scherer et al., 1998) while other studies have indicated no effect on temporal-spatial gait parameters (McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006).

Gardner et al. (2001) speculated that the reduced temporal-spatial gait parameters could be modified to resemble that of age match controls through the use of an exercise program. It has also been suggested that this improved lower limb mobility may be a factor in the improved walking performance seen in patients with PAD-IC engaged in an exercise program. While the research has focused on temporal-spatial gait parameters of PAD-IC patients no studies to date have examined the underlying mechanism of these parameters namely gait kinematics (lower limb joint angular velocities, accelerations and displacements). Furthermore, no studies to date have examined the lower limb movement variability of gait kinematics and this may also provide additional information regarding changes in lower limb mobility during exercise programs. However, there exist different methods to calculate lower limb movement variability and no one method has been label superior.

Chapter 3

Relationship between temporal-spatial gait parameters, gait kinematics, walking performance, exercise capacity and physical activity level in peripheral arterial disease

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Abstract

Objective: Impaired physical function is a feature of patients with peripheral arterial disease (PAD) who present with symptoms of intermittent claudication (PAD-IC). Previous research found that temporal-spatial gait parameters do not discriminate between PAD-IC patients and control subjects during normal and maximal walking despite the PAD-IC patients having decreased physical function characteristic of the disease. This study examined the hypothesis that patients with PAD-IC would demonstrate decreased temporal-spatial gait parameters, gait kinematics, walking performance, physiological responses to exercise and physical activity level compared to control subjects. The aim was to examine the temporal-spatial gait parameters and gait kinematics of individuals with PAD-IC and to determine the relationship between these variables and walking performance, exercise capacity and physical activity level in these individuals.

Method: A cross sectional study of PAD-IC subjects (PAD-IC, n=28) and age and mass matched controls (CON, n=25) was conducted in a medical faculty human performance laboratory. PAD-IC subjects had a history of PAD, ankle brachial pressure index (ABI) <0.9 in at least 1 leg and a positive Edinburgh claudication questionnaire response. Gait characteristics were determined via 2D motion analysis. A graded treadmill test was used to assess walking performance and peak physiological responses to exercise. Physical activity levels were measured via a 7 d pedometer recording following motion analysis. Differences between groups were examined by one-way ANOVA.

Results: Compared to CON, PAD-IC temporal-spatial gait parameters were significantly lower ($P < .05$), except for single support ipsilateral limb time. PAD-IC subjects spent a greater percentage of time in gait support phases, took longer to complete a stride and had

reduced stride length and walking speeds during the gait cycle. PAD-IC joint angular kinematics showed significantly reduced displacement of ankle plantar flexion (P = .017), knee ROM (P = .021) and hip extension (P = .016) compared to the CON subjects during the gait cycle. All joint minimum and maximum angular velocities and accelerations, walking physiological responses and physical activity levels were significantly lower for PAD-IC compared to the CON subjects.

Conclusion: PAD-IC subjects walk with a shuffling gait pattern indicated by reduced joint angular displacement, velocities and accelerations which results in reduced walking performance, physiological responses and physical activity compared to age, mass and physical activity matched controls.

Clinical Relevance

Research on temporal-spatial gait parameters (e.g. stride length, cadence, support times) in PAD-IC patients while free of claudication pain is conflicting. However, there has been no research on the underlying mechanism of these parameters namely gait kinematics (angular displacement, velocity and acceleration). Observed limitations in temporal-spatial gait parameters may be explained by the effects of musculoskeletal abnormalities on lower limb joint kinematics during the gait cycle. Understanding gait kinematics in PAD-IC allows more precise identification of gait abnormality and its effects on lower limb mobility which in turn permits more precise formulation of exercise rehabilitation treatment plans.

Introduction

Peripheral arterial disease (PAD) is a chronic arterial occlusive disease of the lower extremities caused by atherosclerosis (Meru et al., 2005). The most common presenting symptom of PAD is intermittent claudication (PAD-IC) with exercise induced pain experienced in the calves, thighs or buttocks that is relieved with rest (Beebe, 2001; Dormandy & Rutherford, 2000; Regensteiner, 2004). However, many patients with significant PAD do not report or complain of IC pain (Doyle & Creager, 2003).

Compared to healthy age matched controls, patients with PAD-IC demonstrate reduced physiological capacity, lower limb mobility, walking performance, physical activity levels and decreased health-related quality of life (Bauer et al., 2004; Gardner et al., 2002). Decreased lower limb mobility results in reduced temporal-spatial gait parameters such as stride length and speed (Daley & Spinks, 2000).

The research on temporal-spatial gait parameters in PAD-IC patients while free of claudication pain is inconsistent. Some research has determined that PAD-IC individuals walk slower, have slower cadence rates and smaller stride lengths due to an increase in double limb support and stride time (Gardner et al., 2001a; Scherer et al., 1998) while other studies have indicated no effect on temporal-spatial gait parameters (McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006). While the research focus has been on temporal-spatial gait parameters no studies to date have examined the underlying mechanism of these parameters namely gait kinematics (lower limb joint angular velocities, accelerations and displacements). Observed limitations in temporal-spatial gait parameters

may be explained by the effects of musculoskeletal abnormalities (e.g. compromised blood and nerve supply, injury) on lower limb joint kinematics during the gait cycle. Understanding of the kinematics of affected gait parameters allows more precise identification of the aetiology of the abnormality and its effects at the joint-muscle interface which in turn allows for more precise formulation of exercise rehabilitation treatment plans (Davis, 1997).

The aim of this study was to examine the temporal-spatial gait parameters and gait kinematics of individuals with PAD-IC and the relationship between gait kinematics, walking performance, exercise capacity and physical activity level in this population. It was hypothesized that individuals with PAD-IC would demonstrate decreased temporal-spatial gait parameters, gait kinematics, walking performance, physiological responses to exercise and physical activity level compared to healthy age and mass matched controls.

Methods

Subjects

Subjects (n=28) presenting with PAD-IC (IC) were selected based on an appropriate history, demonstrating occlusive peripheral artery disease with absence of significant peripheral neuropathy and physical examination by a consultant vascular physician. PAD-IC was confirmed by absence of peripheral pulses, imaging confirmed lower limb artery stenosis or occlusion, ankle-brachial pressure index <0.9 and +ve Edinburgh Claudication Questionnaire response (Leng & Fowkes, 1992). Details of the subject's medical history and medications were recorded as previously described (Golledge et al., 2006). A further

group of subjects (n=25) free of PAD (ABI >0.9) and who were non regular exercisers were recruited from the community via email bulletin boards and local newspaper and television coverage to act as age and mass matched controls (CON). Subjects were excluded from the study if they required mobility aids, had observable gait abnormalities (e.g. Steppage, vaulting, circumduction and hip hiking) or medical conditions which influenced gait (e.g. orthopedic conditions and neurological impairment). Co-morbidity and smoking history was determined via questionnaire. All subjects volunteered and gave written informed consent to participate in this study as approved by the James Cook University Human Research Ethics Committee.

Procedure

All testing was conducted in the Human Performance Laboratory, Institute of Sport and Exercise Science, James Cook University, Townsville campus. Subjects were assessed early in the morning arriving at the laboratory in a fasting state (12 h). After completing informed consent and study information procedures, underwent ABI, body composition, gait and exercise performance testing.

Ankle/brachial index (ABI)

ABI measurements were taken by a qualified sonographer using a handheld bidirectional Doppler instrument (MD6, Hokanson, Bellevue, Washington, USA) with a 5-MHz transducer and standard blood pressure cuffs after the subject had rested supine for 10 min. Systolic blood pressure was measured at the ankle (taking the highest of either the dorsalis pedis or posterior tibial arteries) and then dividing that value by the systolic blood pressure

in the brachial artery (taking the highest of either the left or right arm arteries)(Caruana et al., 2005).

Anthropometry

Subject height was determined by a wall mounted telescopic metal stadiometer (Seca, model 220, Seca Scales, Hamburg, Germany). Body mass and composition (% body fat) were determined via bioelectrical impedance scales (TANITA TBF 521, TANITA Corporation, Arlington heights, Ill, USA). Body mass index (BMI) was calculated by using subjects' body mass (kg) divided by the square of the subjects' height (m).

Gait

Major joint segments were identified using reflective markers placed on five landmarks on the ipsilateral (right side) of the subject's body. The landmarks were determined via palpation and the reflective markers were positioned at the shoulder (acromion), hip (greater trochanter of femur), knee (lateral epicondyle of femur), ankle (lateral malleolus of fibula) and head of the 5^{th} metatarsal.

Subjects were instructed to walk normally without shoes along a 10 m walkway which was marked at 1 cm intervals whilst the subject was in a pain free state. Digital imagery was obtained via a high-speed digital video camera (Canon MV550i, Canon Australia, North Ryde, Australia) set at a frame rate of 50 Hz and placed 3 m perpendicular to the line of motion providing an uninterrupted video field. Five complete trials were achieved. A walking trial was deemed to be complete and suitable for analysis if all anatomical markers

were visible at the first and last ipsilateral heel strike. Three walking trials (one stride per trial) were then randomly selected for kinematic analysis (Mullineaux et al., 2001). Following the recording of video footage, digital images were captured via a video capture card (Adaptec FireConnect for Notebooks, Adaptec Inc., Milpitas, California, USA) and appropriate joints were identified and named with digitising software (SiliconCoach Ltd, Dunedin, New Zealand) operating on a laptop computer (Toshiba PIV, Toshiba Australia, North Ryde, Australia).

Two markers were placed 1 m apart on the floor in the direction of travel in order to calibrate the digitising software. The first author performed all digitising of the digital video images in order to prevent intraindividual variability in anatomical marker identification. The intraclass correlation coefficient (ICC) values for the digitized X and Y coordinate data ranged from 0.9-0.95. The ICC data for within-subject gait kinematic measures ranged from 0.8–0.85.

Data points were used to calculate gait kinematic parameters including peak displacements, velocities and acceleration (Winter 1984) for the ipsilateral lower limb joints using Microsoft® Office Excel (Microsoft Corporation, North Ryde, Australia). Figure 1 outlines the joint angle conventions used to determine the kinematic variables. Graphical representations of the angular kinematics of the trunk, hip, knee and ankle joints were normalized (100 points) for the gait cycle using a cubic spline routine to determine a mean ensemble curve and 95% confidence intervals (Kurz et al., 2003). Temporal-spatial gait parameters determined included stride length, stride cadence, contact time, swing time,

initial double support time, ipsilateral leg support time, final double support time, contralateral leg support time, total time and speed using the video footage and digitising software. For the purpose of this study stride length was calculated as the distance from successive initial ground contacts of the ipsilateral foot.

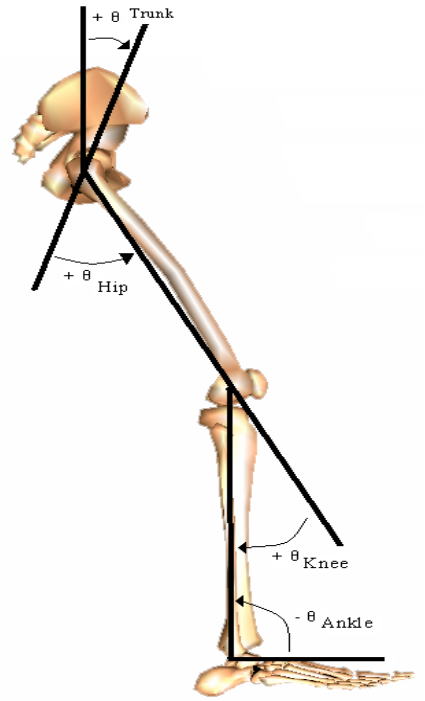

Figure 1. Joint angle conventions

Treadmill testing

Following collection of the digital imagery, subjects undertook a graded exercise test on a treadmill (Trackmaster TMX55, Full Vision, Kansas, USA) for determination of walking performance and physiological responses to exercise. The physiological responses obtained at peak exercise included oxygen uptake (VO_{2peak}), respiratory exchange ratio (RER_{peak}), ventilation (VE_{peak}) and heart rate (HR_{peak}). The physiological responses were determined

via indirect calorimetry using a metabolic cart (Power lab/8M Metabolic system, ADInstruments Pty Ltd, Castle Hill, Australia). The metabolic gas analysis system was switched on 30 min prior to each test and calibrated using a 3 L syringe, temperature (^{o}C), barometric pressure (mmHg), airflow (L), body mass (kg), room air (20.93% and 0.04% for O_2 and CO_2 respectively) and alpha gas composition (~10% O_2, ~7% CO_2) (BOC, Melbourne, Australia). Before the test began, the subject was fitted with a headpiece that held a rubber mouthpiece connected to a T shaped two-way non-rebreathing value (Hans Rudolph, Inc., Kansas City, Missouri, USA) which in turn was connected to the mixing chamber of the metabolic gas analysis system by 35 mm diameter smooth bore hosing. ECG electrodes (silver/silver chloride electrodes, 3M, Pymble, Australia) were positioned at the manubrium, 7th cervical vertebrae and 5th intercostal-axiliary line (lead II) for the recording of an electrocardiogram. All physiological responses were recorded continuously using Chart (v5.1, ADInstruments Pty Ltd, Castle Hill, Australia) sampling at 1000 Hz and were analyzed post test as 15 s averages.

The graded treadmill walking protocol consisted of a constant speed of 3.2 km·h^{-1} and an incline of 0% for the first 2 min which was then increased by 2% every 2 min (Gardner et al., 1991a). Subject perception of exercise intensity was determined every 60 s via Borg's (1970) Rating of Perceived Exertion (RPE) instrument while subjects perceptions of the distance to onset, moderate, intense and maximal claudication pain was determined via the 5-point (0=no pain, 1=onset of pain, 2= moderate pain, 3=intense pain, 4=maximal pain) Claudication Pain Scale (CPS)(American College of Sports Medicine, 2006). Walking performance (maximal walk distance, MWD) was assessed by the distance walked until

perceived maximal claudication pain, exhaustion or until 25 min of walking was achieved. Subjects were permitted to hold the treadmill handrail if they required support whilst walking and a number of common phrases (e.g. you can make it, keep walking) were used to encourage subjects and their use was standardized by noting the frequency and type of phrase used in pilot and preliminary testing. Exercise test termination criteria included voluntary exhaustion, claudication pain or abnormal ECG rhythm.

Physical activity level

Following laboratory testing subject physical activity levels (number of steps, distance walked and calories expended during walking) were determined from 7 d pedometer (YAMAX DigiWalker SW-700, YAMAX Corporation, Tokyo, Japan) recordings.

Statistical analyses

Statistical analysis was performed using the SPSS (SPSS Inc, release 14.0, Chicago, Illinois, USA) for Windows® (Microsoft Corp, Redmond, Washington, USA) software program. Descriptive statistics were expressed as mean (±SD). Box-plot analyses were performed to identify extreme and outlier data. Data were analyzed using one-way ANCOVA with one between-subjects factor (PAD-IC vs. CON) and age as covariate (Vincent, 2005). An alpha level of .05 was adopted for this study.

Results

Subjects

Subjects in both groups were similar in age, height, mass, BMI and body fat (%). ABI for both the right and left leg was higher in the CON compared to PAD-IC ($P < .001$). PAD-IC subjects included a higher proportion of current ($P = .007$) and former smokers ($P < .001$) and a higher percentage of diabetes ($P = .007$), ischaemic heart disease ($P < .001$), and Beta-blocker prescription ($P < .001$) (Table 1). No changes in the results of this study were found when age was controlled using multivariate statistical technique.

Table 1. Mean (±SEM) descriptive characteristics of intermittent claudication (IC) and healthy age and mass matched control (CON) subjects (N=53)

Variable	IC (n = 28)	CON (n = 25)	P
Age (yr)	69.9 (±1.5)	66.2 (±1.5)	.642
Height (cm)	166.3 (±1.6)	167.6 (±1.5)	.678
Mass (kg)	79.3 (±3.1)	74.6 (±2.4)	.224
Body fat (%)	32.2 (±1.6)	33.6 (±1.5)	.550
BMI	28.5 (± 0.9)	26.5 (±0.7)	.095
ABI left leg	0.73 (±0.05)	1.16 (±0.03)	.000
ABI right leg	0.71 (±0.04)	1.16 (±0.03)	.000
Gender (% male)	50	40	.333
Current smoker (%)	25	0	.007
Former smoker (%)	64	32	.000
Type II diabetes (%)	25	0	.007

Hypertension (%)	43	24	.154
Ischaemic heart disease (%)	35.7	0	.000
Arthritis (%)	18	16	.861
Beta-blocker prescription (%)	28.6	0	.000

Values are mean (±SEM) or %
ABI = Ankle/brachial index; BMI = Body mass index.

Gait

All temporal-spatial gait parameters were significantly different between the IC and CON groups except for single support ipsilateral limb time (P = .128) (Table 2). The IC subjects walked at a slower pace (20%) and took longer (7%) to complete a gait cycle, which was characterized by a smaller (12%) stride length and lower (7%) cadence. IC subjects spent longer (7%) completing a stride, as a result of a longer (7%) ipsilateral leg contact and swing time (7%). The IC subjects spent longer (5%) in the single and double support (14%) stance phases. Significant percentage differences between PAD-IC and control temporal-spatial gait parameters found in this study ranged from 7-20%. Research has shown that normal age effect on most gait characteristics is in the magnitude of 4%-9% for ages 60 – 80 yr (Murray, Drought, & Kory, 1964; Murray et al., 1969). Diseases other than PAD such as Parkinson's or Multiple Sclerosis demonstrate greater percentage difference (11%-40%) for temporal-spatial gait parameters, but these neurological diseases are far more extreme then PAD (Murray et al., 1978). Compared to previous PAD research, Gardner, Forrester & Smith (2001) found significant differences in gait characteristics such as stride length (13%), contact time (2%), percentage of time spent in single support (4%)

percentage of time spent in double support (9%) and speed (17%) which is similar to this current study.

Joint kinematic analysis determined significant between-group differences for joint motion angles with ankle plantar flexion (20%), knee ROM (6%) and hip extension (23%) significantly reduced for IC compared with CON subjects (Table 3). Figure 2 presents graphical representation of the significant ROM differences for IC and CON subjects normalized (100 points) over the gait cycle.

Table 2. Mean (±SEM) temporal-spatial gait parameters of intermittent claudication (IC) and healthy age and mass matched control (CON) subjects (N=53)

Variable	IC (n = 28)	CON (n =25)	P
Stride length (m)	1.20 (±0.03)	1.35 (±0.03)	.001
Cadence (steps·min^{-1})	106.9 (±1.4)	115.1 (±1.1)	.000
Stride time (s)	1.13 (±0.02)	1.05 (±0.01)	.000
Contact time (s)	0.70 (±0.01)	0.65 (±0.01)	.000
Swing time (s)	0.43 (±0.01)	0.40 (±0.01)	.004
Single support contralateral (s)	0.43 (±0.01)	0.40 (±0.01)	.004
Single support ipsilateral (s)	0.41 (±0.01)	0.40 (±0.01)	.077
Double support 1 (s)	0.15 (±0.01)	0.13 (±0.01)	.001
Double support 2 (s)	0.14 (±0.01)	0.12 (±0.01)	.025
Speed (m·s^{-1})	1.08 (±0.03)	1.30 (±0.03)	.000

Stride length = distance either foot moves during the gait cycle; Cadence = number of steps taken in a min; Stride time = time taken to produce a stride; Contact time = time that the ipsilateral foot is in contact with the floor; Swing time= time that the ipsilateral foot is not

in contact with the floor; Single support = time that each foot is spent in contact with the floor by itself. Double support = time that is spent with both feet on the floor; Speed = calculation of stride length and stride time.
Values are mean (±SEM)

Table 3. Mean (±SEM) peak and ROM angular kinematics of intermittent claudication (IC) and healthy age and mass matched control (CON) subjects (N=53)

Variable	IC (n=28)	CON (n=25)	P
Ankle ROM (º)	22.31 (±0.59)	24.28 (±0.92)	.151
Ankle plantar flexion (º)	-10.03 (±0.43)	-12.52 (±0.95)	.036
Ankle dorsiflexion (º)	12.21 (±0.65)	11.75 (±0.60)	.570
Knee ROM (º)	56.84 (±1.22)	60.29 (±0.70)	.048
Knee flexion (º)	57.56 (±1.05)	59.19 (±0.66)	.365
Knee extension (º)	0.69 (±0.82)	-1.14 (±0.49)	.072
Hip ROM (º)	33.53 (±1.08)	36.03 (±1.02)	.081
Hip flexion (º)	21.00 (±0.96)	19.55 (±0.96)	.459
Hip extension (º)	-12.67 (±1.01)	-16.49 (±1.16)	.027
Trunk ROM (º)	8.17 (±0.38)	9.12 (±0.47)	.235
Trunk flexion (º)	3.37 (±0.54)	2.66 (±0.67)	.591
Trunk extension (º)	-4.80 (±0.53)	-6.46 (±0.67)	.157

Values are mean (±SEM)

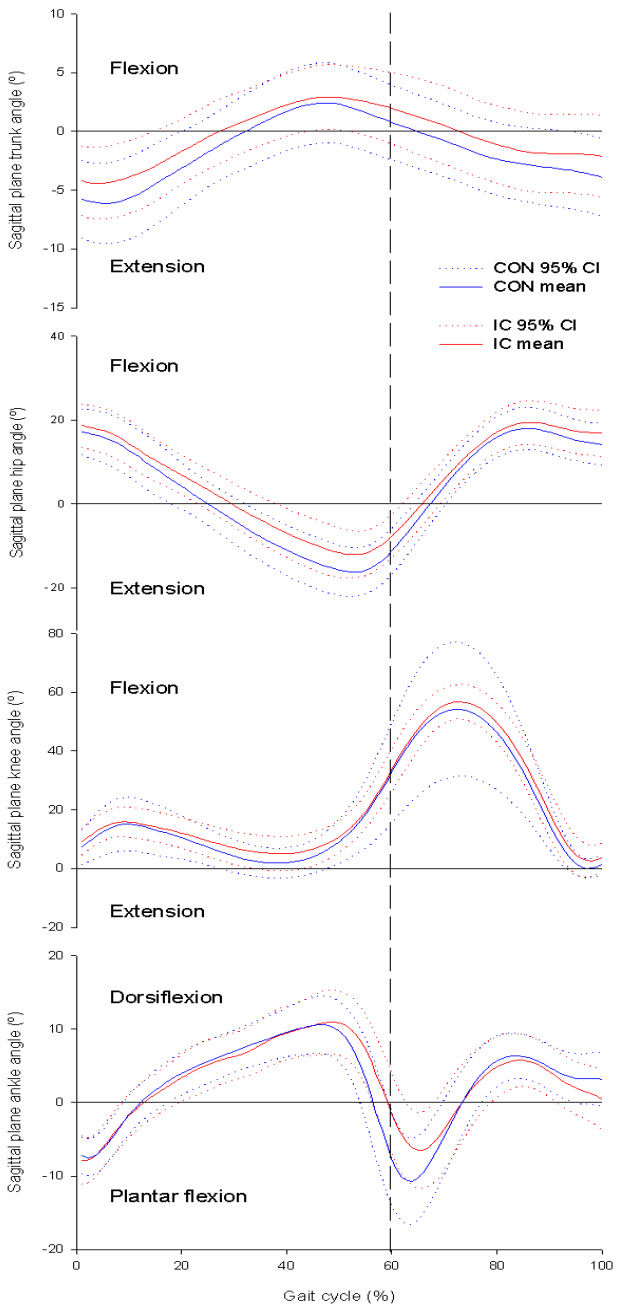

Figure 2. Trunk, hip, knee and ankle kinematics in the sagittal plane for IC and CON subjects; the dashed line indicates toe-off at ~60% gait cycle (with 0-60% representing stance; 60-100% representing swing)

The IC subjects demonstrated significantly smaller minimum and maximum joint angular velocities and accelerations for all variables compared with the CON subjects except ankle joint angular acceleration maximum and hip joint angular acceleration minimum (Table 4).

Table 4. Mean (±SEM) peak angular velocity and acceleration values for intermittent claudication (IC) and healthy age and mass matched control (CON) subjects (N=53)

Variable	IC (n=28)	CON (n=25)	P
Ankle velocity min ($^{o}\cdot s^{-1}$)	-133.23 (±4.09)	-161.63 (±7.47)	.004
Ankle velocity max ($^{o}\cdot s^{-1}$)	191.02 (±7.41)	243.31 (±11.39)	.001
Knee velocity min ($^{o}\cdot s^{-1}$)	-295.04 (±8.76)	-326.31 (±6.15)	.005
Knee velocity max ($^{o}\cdot s^{-1}$)	350.59 (±11.56)	393.23 (±7.92)	.010
Hip velocity min ($^{o}\cdot s^{-1}$)	-156.88 (±5.12)	-178.66 (±5.95)	.014
Hip velocity max ($^{o}\cdot s^{-1}$)	108.18 (±4.22)	121.28 (±4.28)	.018
Ankle acceleration min ($^{o}\cdot s^{-2}$)	-4102.43 (±150.48)	-5446.83 (±267.84)	.000
Ankle acceleration max ($^{o}\cdot s^{-2}$)	3202.36 (±123.37)	3596.84 (±145.82)	.059
Knee acceleration min ($^{o}\cdot s^{-2}$)	-5445.02 (±298.33)	-6254.65 (±211.05)	.048
Knee acceleration max ($^{o}\cdot s^{-2}$)	3590.18 (±88.25)	4008.82 (±90.63)	.002
Hip acceleration min ($^{o}\cdot s^{-2}$)	-2077.14 (±72.91)	-2279.39 (±110.26)	.139
Hip acceleration max ($^{o}\cdot s^{-2}$)	1888.80 (±55.65)	2109.52 (±74.51)	.035

Values are mean (±SEM)

Treadmill testing

Treadmill walking performance (MWD) and physiological responses (HR_{peak}, VO_{2peak} and VE_{peak}) were significantly greater for the CON compared to the IC subjects (Table 5). The CON subjects that were unable to complete the treadmill test (n=17) complained only of general fatigue and not claudication pain.

Table 5. Mean (±SEM) walking performance and physiological responses of intermittent claudication (IC) and healthy age and mass matched control (CON) subjects (N=53)

Variable	IC (n=28)	CON (n=25)	P
MWD (m)	271.8 (±34.8)	941.4 (±70.2)	.000
HR_{peak} (beats·min^{-1})	111 (±3.5)	140 (±3.5)	.000
VO_{2peak} (ml·kg^{-1}·min^{-1})	18.3 (±1.3)	34.5 (±1.7)	.000
VE_{peak} (L·min^{-1})	39.1 (±3.8)	63.7 (±5.3)	.001
RER_{peak}	0.90 (±0.03)	0.97 (±0.02)	.050

MWD = maximal walking distance, HR = heart rate, VO_2 = oxygen uptake, VE = ventilation, RER = respiratory exchange ratio
Values are mean (±SEM)

Physical activity level

CON subjects took a significantly greater number of steps, walked greater distances and burnt more calories than the IC subjects over the 7 d post-test period (Table 6).

Table 6. Mean (±SEM) seven day physical activity levels of intermittent claudication (IC) and healthy age and mass matched control (CON) subjects (N=53)

Variable	IC (n=28)	CON (n=25)	P
Steps	29093 (±4008)	47038 (±3524)	.016
Distance (km)	16.9 (±2.3)	30.4 (±2.3)	.001
Calories (kcal)	1148.8 (±169.9)	1847.4 (±153.5)	.023

Values are mean (±SEM)

Discussion

Temporal-spatial gait parameter results indicated that PAD-IC subjects compared to healthy age and mass matched controls spent a greater percentage of time in gait support phases, took longer to complete a stride and had reduced stride length and walking speeds during the gait cycle. These results confirm research indicating that PAD-IC results in reduced temporal-spatial gait parameters (Gardner et al., 2001a; Scherer et al., 1998) but contradicts other research that showed no significant gait changes (McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006). Research that has failed to find a significant effect of PAD-IC on temporal-spatial gait parameters compared to age-mass matched controls have used control subjects with comorbidities such as coronary artery, diabetes and lung disease (Scherer et al., 2006), PAD-IC subjects without intermittent claudication (McDermott et al., 2001), PAD-IC subjects that were engaged in regular medically supervised exercise programs (McCully et al., 1999) and different techniques of gait analysis (e.g. stop watches, which produce more human error)(McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006). These factors may explain the failure of significant effect of PAD-IC on temporal-spatial gait parameters in previous studies and why the use of subjects without these factors as shown in the current study demonstrate

significant effect of PAD-IC on temporal-spatial gait parameters, gait kinematics, walking performance, exercise capacity and physical activity level.

The kinematic descriptors of the temporal-spatial gait parameters were reduced peak hip extension (~55% gait cycle, Figure 4), knee ROM (~40% & 75% gait cycle, Figure 3), and peak ankle plantarflexion (~65% gait cycle, Figure 2). These reduced joint angular displacements occurred around the time of pre-swing and initial swing of the ipsilateral limb indicating a shuffling gait pattern much like the gait pattern evident in Parkinson's disease (Murray et al., 1978). The reduced joint angular displacements were accompanied by reduced peak minimum and maximum joint angular velocity and acceleration values clearly demonstrating reduced lower limb mobility in PAD-IC compared to control subjects.

As indicated by the gait kinematics, mobility is reduced in this population therefore it would be expected that walking capacities and physical activity levels would also be reduced compared to age and mass matched controls. The graded treadmill test results and 7 d pedometer recordings confirmed this assumption. These findings reinforce the view that individuals with PAD-IC are at greater risk of future lower limb mobility loss and reduced capacity to perform activities of daily living resulting in decreased quality of life and poorer health outcomes (Daley & Spinks, 2000; Hausdorff et al., 1997). It should be noted that some of the PAD-IC subjects (n=7) were current smokers and this can cause a limitation of the walking performance test, as PAD-IC subjects have been shown to have reduce PFWD, MWD and peak oxygen uptake compared to PAD-IC former smokers

(Anton et al., 2006; Gardner, 1996; Gardner et al., 2004). However, the aim of this study was to examine the relationship between gait kinematics, walking performance, exercise capacity and physical activity level in healthy controls and a typical population of PAD-IC patients, which will include smokers.

The results of this study demonstrated that individuals with PAD-IC walk with a shuffling gait pattern indicated by reduced joint angular displacement, velocities and accelerations compared with healthy age and mass matched controls. The causes of this gait disturbance are likely multi-factorial. Possible mechanisms include adaptation to the pain association with lower limb ischaemia, myopathy associated with ischaemia or diabetes and cardiac impairment due to associated coronary artery disease. The later is unlikely since patients were excluded if they were thought to be unable to tolerate a treadmill test.

Research has indicated that supervised exercise rehabilitation programs lead to significant improvement in walking performance, physical activity and perceived quality of life in PAD-IC individuals (Gardner et al., 2005; Gardner & Poehlman, 1995). Future research should examine the effects of these supervised exercise rehabilitation programs on temporal-spatial gait parameters and the gait kinematics of PAD-IC patients. This may provide a better understanding of how PAD-IC affects gait as well as providing new insights into the formulation of exercise rehabilitation treatment plans for PAD-IC.

Acknowledgments

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Chapter 4

Intralimb coordination variability in peripheral arterial disease

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Abstract

Background: Increased variability has been traditionally associated with decreased movement performance due to disease and aging. However, recent research indicates that variability may be of functional importance in motor control. Thus the purpose of this study was to determine whether individuals with peripheral arterial disease and suffering from intermittent claudication have reduced intralimb joint coordination variability compared to individuals without peripheral arterial disease. A further aim was to examine the efficacy of various techniques used to describe intralimb joint coordination variability.

Methods: Participants with peripheral arterial disease and suffering from intermittent claudication (n=28) were selected based on an appropriate history of peripheral arterial disease and intermittent claudication, ankle brachial pressure index <0.9 in at least 1 leg and a positive Edinburgh claudication questionnaire response. A further group of participants (n=25) free of peripheral arterial disease (ankle brachial pressure index >0.9) and who were non regular exercisers were recruited from the community to act as age and mass matched controls. All participants underwent 2D angular kinematics analysis during normal walking. Intralimb coordination variability was measured using parameterization, vector coding and normalized root mean square techniques applied to relative motion plots of various joint couplings. Differences between groups were examined by one-way ANOVA.

Findings: Participants with peripheral arterial disease and suffering from intermittent claudication displayed significantly greater intralimb joint coordination variability than age and mass matched controls participants for all joint couplings using all intralimb joint coordination variability techniques.

Interpretation: These findings suggest that higher levels of intralimb joint coordination variability of the lower limbs in participants with peripheral arterial disease and suffering from intermittent claudication may be an adaptation of the motor control system to deal with perturbations associated with the gradual onset of claudication pain.

Introduction

Increased movement variability has been traditionally associated with decreased movement performance due to disease and aging. However, more recent research from a dynamical systems viewpoint indicated that variability may be of functional importance in motor control (Van Emmerik et al., 2005). Dynamical systems theory proposes that movements 'emerge' or self-organise from a dynamical interaction of numerous organismic, environmental and task related variables. These variables impose constantly changing constraints upon movement and the movement pattern that emerges is a function of these constraints (Newell, 1986). A stable movement pattern is a behavioural state that is reproducible & independent of others and equates to low variability. When variability increases the system becomes unstable. Loss of stability represents a system in transition (e.g. when progressing from crawling to walking or from normal walking to affected walking due to injury or disease). Thus patterns of change in movement can be attributed to changes in one or more constraints which can lead to an increase in variability (Clark, 1995; Handford et al., 1997; Williams et al., 1999).

Disease or illness may be seen as organismic constraints that influence the way individuals accomplish locomotion as a task constraint. Variability may be functional in helping individuals adapt to changing task constraints in dynamic environments (Clark & Phillips, 1993; Hamill et al., 1999; Holt, Jeng, Rr, & Hamill, 1995). However, it should be noted that higher or lower joint coordination variability is relative due to the differential impact of constraints on individuals and research is yet to determine levels of variability that might reflect injury, disease states or positively influence locomotion (Van Emmerik et al., 2005).

Based on the constraints led model of motor control (Newell, 1986) it is unlikely that there will be an exact level of variability that might reflect an injured or diseased state.

Variability provides flexibility when adjusting to perturbations in the environment and is fundamental to changing coordination patterns during locomotion, thus higher variability may be beneficial (Heiderscheit et al., 2002; Van Emmerik et al., 2005; Van Emmerik et al., 1999). On the other hand, pain or injury may result in reduced intralimb joint coordination variability (Hamill et al., 1999; Heiderscheit et al., 2002; Pollard et al., 2005). Therefore, the assessment of variability in human walking using either temporal-spatial gait parameters or joint coordination patterns would provide distinctly opposing information about individual motor control during locomotion (Heiderscheit, 2000).

Research on the variability of human temporal-spatial gait parameters such as stride length, stride width, stride time and cadence, has shown that higher variability in these parameters is associated with an increased risk of falling due to lower limb mobility problems such as poor stability and reduced obstacle avoidance ability (Hausdorff et al., 1998; Webster et al., 2006; Weerdesteyn, Nienhuis, & Duysens, 2005). Hausdorff et al. (1998) reported that compared to healthy controls, individuals with Parkinson's and Huntington's disease displayed significantly increased variability in all temporal parameters during the gait cycle, even though the average stride time between the groups was equal. Thus calculation of temporal-spatial gait parameter variability has been suggested as a tool for assessing human walking ability in various gait pathologies. However, by limiting analysis to temporal-spatial gait parameters, the variability in the locomotion pattern is ignored

(Heiderscheit, 2000). Analysis of intralimb joint coordination variability using biomechanical degrees of freedom (joint angular kinematics) may provide more information about the level of variability during locomotion. This information will represent how individuals interact with the unique range of task, organismic and environmental constraints impinging upon them and has implications for the choice of movement variability assessment techniques.

There are a number of different techniques used to calculate intralimb joint coordination variability. These include parameterization, normalized root mean square (NoRMS) and vector coding (VC) (Goswami, 1998; Sidaway et al., 1995; Tepavac & Field-Fote, 2001). None of these techniques has been considered superior at assessing intralimb joint coordination variability in either the elderly or for those with pathologies that can affect locomotion.

Peripheral arterial disease (PAD) affects physical activity by causing inadequate blood flow to the lower limbs which may result in various levels of ischemic pain referred to as intermittent claudication (IC) (Aronow, 2004b; Bick, 2003; Hankey et al., 2006). Research on temporal-spatial gait parameters in PAD-IC individuals has produced conflicting results. Some studies have shown reduced lower limb temporal-spatial gait parameters and joint angular kinematics (Crowther, Spinks, Leicht, Quigley, & Golledge, 2007; Gardner et al., 2001a; Scherer et al., 1998) while others have shown that PAD-IC has no effect on lower limb gait characteristics (McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006).

The purpose of this investigation was to compare the intralimb joint coordination variability of individuals with and without PAD-IC. As research has shown that individuals with lower limb pain demonstrate lower intralimb coordination variability it was hypothesized that individuals with PAD-IC would display lower intralimb joint coordination variability compared to individuals without PAD-IC. A further aim was to determine the extent to which the data derived from different techniques of calculating intralimb joint coordination variability provide information of value to clinicians.

Methods

Participants

Participants (n=28) presenting with PAD-IC volunteered based on an appropriate history of PAD-IC, absence of significant peripheral neuropathy after assessment by a consultant vascular physician. PAD-IC was confirmed by absence of peripheral leg pulses, imaging confirmed lower limb artery stenosis or occlusion, ankle-brachial pressure index (ABI) <0.9 and positive Edinburgh Claudication Questionnaire responses (Leng & Fowkes, 1992). Participants medical history and prescribed medications were recorded as previously described (Golledge et al., 2006). A further group of participants (n=25) free of PAD-IC (ABI >0.9) and who were non regular exercisers were recruited from the community via email bulletin boards, local newspaper and television coverage to act as age and mass matched controls (CON). Participants were excluded from the study if they required mobility aids, had observable gait abnormalities (e.g. Steppage, vaulting, circumduction and hip hiking) or medical conditions which influenced gait (e.g. orthopedic conditions and neurological impairment). Body mass index (BMI), percentage body fat and ABI were

measured as previously described (Crowther et al., 2007). Co-morbidities and smoking history was determined via questionnaire. All participants volunteered and gave written informed consent to participate in this study. The study was approved by the institutional ethics committee. The descriptive characteristics of the participants are outlined in Table 1.

Table 1. Descriptive characteristics of peripheral arterial disease (PAD-IC) and healthy age and mass matched control (CON) participants (N=53)

Variable	PAD-IC (n = 28)	CON (n = 25)
Age (yr)	69.9 (±7.7)	66.2 (±7.5)
Height (cm)	166.3 (±8.3)	167.6 (±7.3)
Mass (kg)	79.3 (±16.5)	74.6 (±12.1)
Body fat (%)	32.2 (±8.2)	33.6 (±7.5)
BMI	28.5 (±4.6)	26.5 (±3.6)
ABI left leg	0.73 (±0.24)	1.16 (±0.16)**
ABI right leg	0.71 (±0.22)	1.16 (±0.14)**
Gender (% male)	50	40
Current smoker (%)	25	0*
Former smoker (%)	64	32**
Type II diabetes (%)	25	0*
Hypertension (%)	43	24
Ischaemic heart disease (%)	35.7	0**
Arthritis (%)	18	16
Beta-blocker prescription (%)	28.6	0**

Values are mean (±SD) or %

ABI = Ankle/brachial index; BMI = Body mass index.
* P < .05; ** P < .001 vs. PAD-IC

Apparatus

Kinematics

Joint angular kinematics were determined via 2D motion analysis using a high-speed digital video camera (Canon MV550i, Mini DV Digital Camcorder, Canon, Australia) set at a frame rate of 50 Hz and placed 3 m perpendicular to the line of motion providing an uninterrupted video field. Digital images were captured via a video capture card (Adaptec FireConnect for Notebooks, Adaptec Inc., Milpitas, California, USA) and appropriate joints were identified and named with digitising software (SiliconCoach Ltd, Dunedin, New Zealand) operating on a laptop computer (Toshiba PIV, Toshiba Australia, North Ryde, Australia). Angular kinematics were determined using the digitising software and Microsoft® Office Excel (Microsoft Corporation, North Ryde, Australia). Two markers were placed 1 m apart on the floor in the direction of travel in order to calibrate the digitising software. The first author performed all digitising of the digital video images in order to prevent intra-individual variability in anatomical marker identification. Figure 1 outlines the joint angle conventions used to determine the joint kinematic variables.

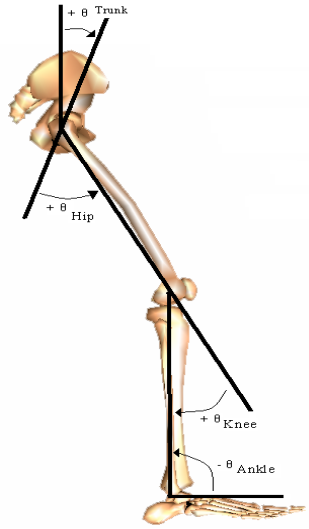

Figure 1 Sagittal plane angle convention

Parameterization

Parameterization is used to examine the variability of the area and perimeter of the shape of an angle-angle plot (joint coupling). This technique presents a quantitative characterization of normal gait and allows for clinical identification of pathological conditions and for patient progress through rehabilitation programs (Goswami, 1998).

NoRMS

The NoRMS technique utilises angle-angle plots to quantify joint coordination variability and stability changes in human movement. The root mean square of a series of angle-angle cycles is calculated and then normalized with respect to the number of cycles and excursion of the mean plot (Equation 1) (Sidaway et al., 1995). A high NoRMS value for an angle-angle plot indicates a greater variability in the joint coordination pattern.

$$NoRMS = 100 * \left(\frac{\sum_{j=1}^{k} \sqrt{\sum_{j=1}^{n} (\bar{x}_A - x_{Ai})^2 + (\bar{x}_B - x_{Bi})^2 / n_j}}{R} \right) \quad (1)$$

A & B denote the two variable, *k* is the number of cycles, *n* is the number of data points, R is the resultant excursion of the mean angle-angle curve over the entire cycle (estimated using the hip and knee corresponding to the maximum and minimum values at either the two joints), $\bar{x}$ is the mean position of a given variable at the *i*th data point and x is the position of a given variable at the *i*th data point on the *j*th cycle (Wheat & Glazier, 2006).

Although the NoRMS technique provides a measure of joint-joint coupling limb coordination variability that takes into account changes in magnitude and shape it however, gives no clue of the coordination between the segments of concern (Wheat & Glazier, 2006).

VC

VC also referred to as Encoded Chain Technique was first employed by Freeman (1974) and later modified by Tepavac & Field-Fote (2001), involves placing an image of an angle-angle plot on a grid and the perimeter of the image is then encoded using an eight point scale based on the direction of the line between two consecutive data points (frame-frame interval) (Figure 2). The magnitude and direction of the vector connecting the two points of the angle-angle plot is then calculated. The VC data are then used to identify high or low variability of the angle (a), magnitude (m) and vector (r) during cycles over multiple cycles. Higher mean (r) values indicate a more consistent (less variable) intersegmental

relationship (Tepavac & Field-Fote, 2001). The advantage of the VC technique is that there is no requirement to normalize the data, thereby maintaining true spatial information. The technique also provides both shape, magnitude and vector information which is more suitable for clinicians (Wheat & Glazier, 2006). However, the disadvantage is that VC provides spatial information only, with no consideration of temporal data (Hamill et al., 2000), which may reduce the sensitivity to variability in intra joint coordination.

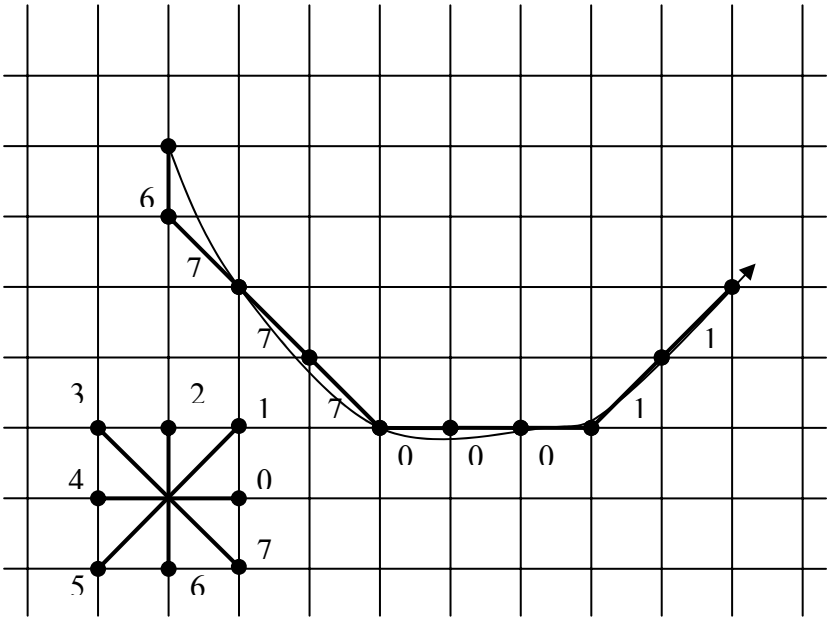

Figure 2 Vector coding technique

Procedure

All testing was conducted in the Human Performance Laboratory, Institute of Sport and Exercise Science, James Cook University, Townsville campus. Participants were assessed early in the morning to ensure no physical activity was undertaken. After completing informed consent reflective markers were placed on the right side of the participant's body on five landmarks, the shoulder (acromion), hip (greater trochanter of femur), knee (lateral

epicondyle of femur), ankle (lateral malleolus of fibula) and head of the 5th metatarsal. Participants then underwent 2 dimensional video recording while walking along a 10 m walkway marked at 1 cm intervals. Five complete trials were achieved. A walking trial was deemed to be complete and suitable for analysis if all anatomical markers were visible at the first and last ipsilateral heel strike. Three walking trials (one stride per trial) were then randomly selected for kinematic analysis (Mullineaux et al., 2001).

Data analysis

A combination of linear multi-joint analysis techniques were performed on the angular kinematic data to determine lower limb joint coordination variability in PAD-IC patients compared to CON. Data were analysed using custom software written in Matlab (Matlab 7 Release 14, The MathWorks, Inc. Natick, Massachusetts, USA). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc, release 14.0, Chicago, Illinois, USA) for Windows® (Microsoft Corp, Redmond, Washington, USA) software program. Descriptive statistics were expressed as mean (±SD). Box-plot analyses were performed to identify extreme and outlier data. Data were analyzed using one-way ANOVA with one between-subjects factor (PAD-IC vs. CON) (Vincent, 2005). An alpha level of .05 was adopted for this study.

Results

Mean values for age, height, mass, BMI and (%) body fat, were similar for both groups of participants (Table 1). ABI values for the right and left leg were higher in the CON compared to PAD-IC participants ($P < .001$). There was a higher percentage of both current

($P < .05$) and former ($P < .001$) smokers and a higher percentage of individuals prescribed Beta-blockers ($P < .001$) and diagnosed with diabetes ($P < .05$) and ischaemic heart disease ($P < .001$) in the PAD-IC group.

Intralimb joint coordination variability

Parameterization

Cycle perimeter was found to be significantly smaller for the PAD-IC participants compared CON for all angle-angle plots ($P < .05$) (Figure 3 – 5). The angle-angle plot cycle area was significantly smaller for the hip-knee and knee-ankle plots ($P < .05$) (Figures 3 - 4).

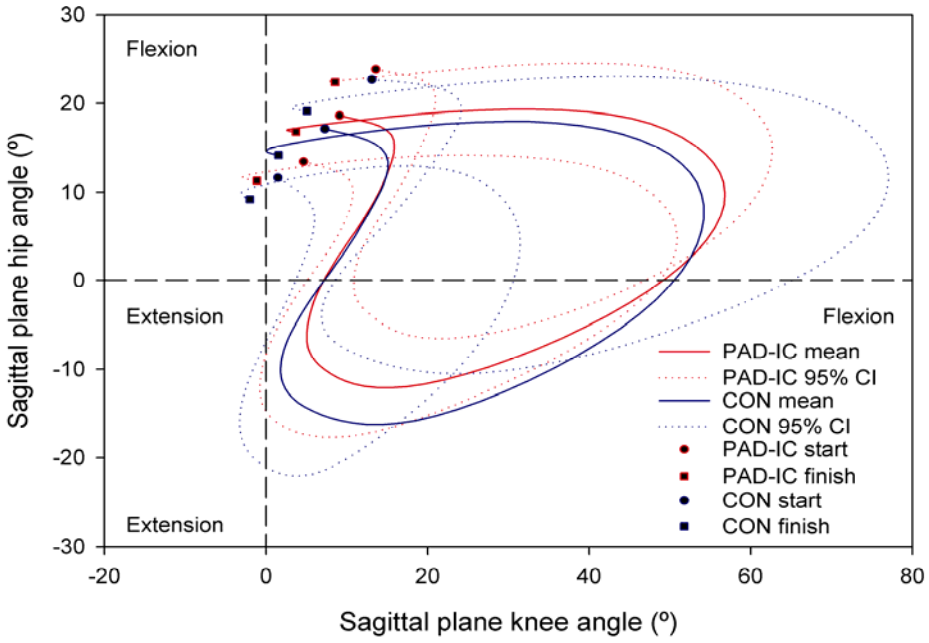

Figure 3 Joint-joint angular kinematics plot of the hip-knee during the gait cycle in the sagittal plane for PAD-IC and CON participants

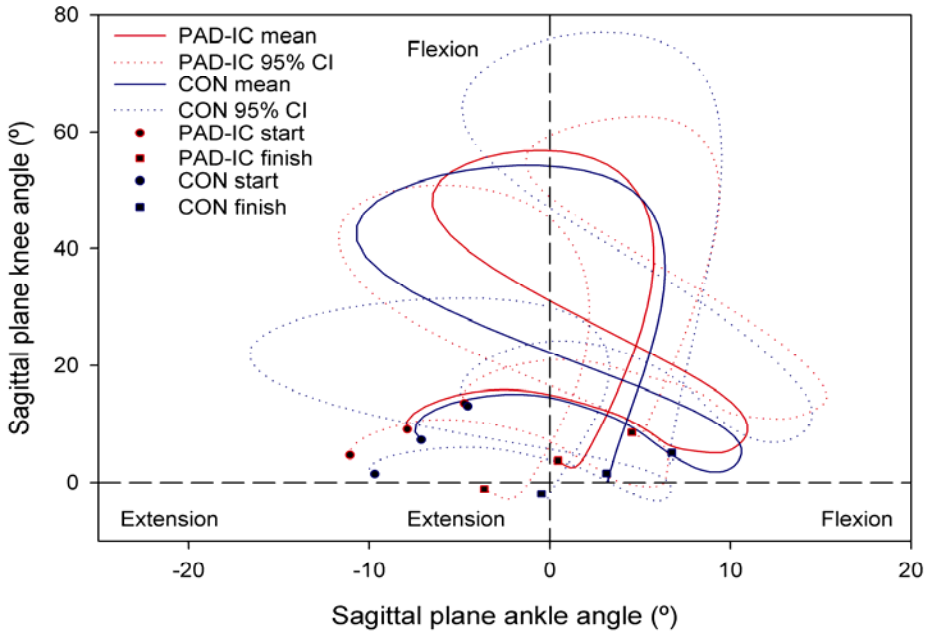

Figure 4 Joint-joint angular kinematics plot of the knee-ankle during the gait cycle in the sagittal plane for PAD-IC and CON participants

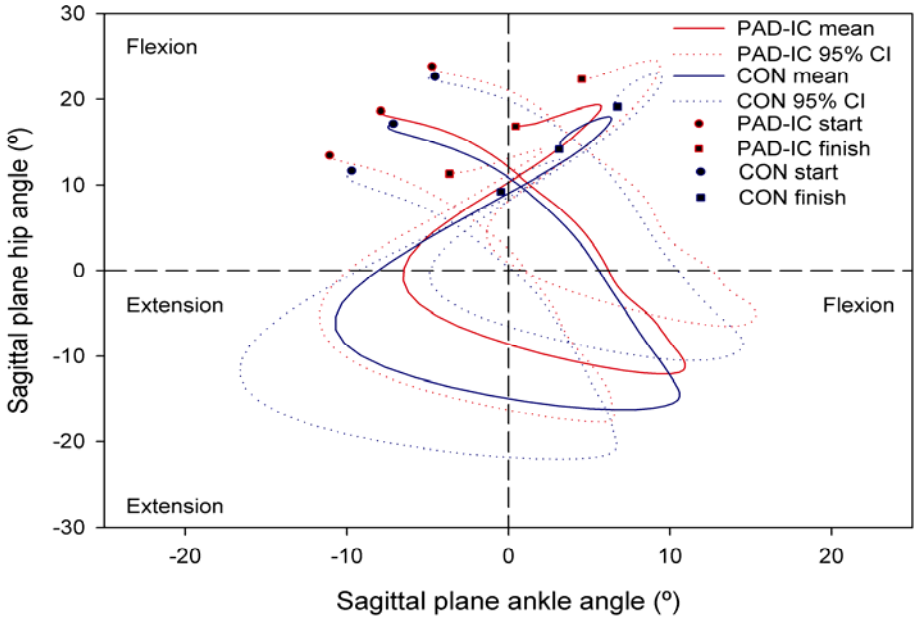

Figure 5 Joint-joint angular kinematics plot of the hip-ankle during the gait cycle in the sagittal plane for PAD-IC and CON participants

NoRMS & VC

The PAD-IC participants demonstrated significantly higher variability for all NoRMS angle-angle plots compared with the CON participants (Table 2). VC (a) was significantly lower for the hip-knee plot of the PAD-IC participants only. VC (m) and (r) variables were significantly lower in the angle-angle plots for the PAD-IC participants compared to the CON participants (Table 3).

Table 2. Mean (±SD) NoRMS values for peripheral arterial disease (PAD-IC) and control (CON) participants (N=53)

Variable	PAD-IC (n = 28)	CON (n = 25)
Hip – Knee	4.22 (± 1.19)	3.31 (± 1.11)**
Knee – Ankle	7.36 (± 2.68)	5.68 (± 1.50)**
Hip - Ankle	5.00 (± 1.22)	3.96 (± 1.14)**

**$P < 0.01$ vs. PAD-IC

Table 3. Mean (±SD) vector coding values for peripheral arterial disease (PAD-IC) and control (CON) participants (N=53)

Variable		PAD-IC (n = 28)	CON (n = 25)
Vector coding (a)	Hip – Knee	0.96 (± 0.03)	0.98 (± 0.02)*
	Knee – Ankle	0.96 (± 0.04)	0.93 (± 0.08)
	Hip - Ankle	0.89 (± 0.04)	0.91 (± 0.07)
Vector coding (m)	Hip – Knee	0.61 (± 0.05)	0.69 (± 0.08)***
	Knee – Ankle	0.60 (± 0.05)	0.65 (± 0.06)**
	Hip - Ankle	0.54 (± 0.06)	0.58 (± 0.06)*
Vector coding (r)	Hip – Knee	0.60 (± 0.06)	0.68 (± 0.08)***

Knee – Ankle	0.56 (± 0.06)	0.63 (± 0.06)***
Hip - Ankle	0.50 (± 0.07)	0.55 (± 0.06)**

a = angle; m = magnitudes; r = mean vector
*P < .05, **P < 0.01, ***P < .001 vs. PAD-IC

Discussion

The purpose of this study was to compare the variability of intralimb joint coordination between individuals with and without PAD-IC and to compare different techniques used to calculate variability. The NoRMS and VC results demonstrated that intralimb joint coordination variability was significantly higher in the PAD-IC participants compared to the CON participants which is contrary to the stated hypothesis. This may indicate that individuals with PAD-IC do not have reduced stability or poor obstacle avoidance ability however, this requires further research. These findings differ from research that determined that intralimb coordination variability is lower in populations with disease or reduced mobility (Heiderscheit et al., 2002; Pollard et al., 2005; Van Emmerik et al., 1999). However, PAD-IC individuals have reduced temporal-spatial gait parameters and joint angular kinematics compared to age and mass matched controls and adopt a shuffling style of walking characteristic of Parkinson's disease (Crowther et al., 2007).

Higher levels of intralimb joint coordination variability of the lower limbs may be an adaptation of the motor control system to deal with perturbation(s) associated with the gradual onset of claudication pain. The extent to which this adaptation is beneficial or detrimental (i.e. preventing or causing falls) to human locomotion is yet to be determined. The constraints imposed by the adoption of a Parkinson's style of walking may allow

individuals with PAD-IC to vary locomotion dynamics to accommodate increasing pain associated with reduced blood supply to the lower limbs.

A further purpose of this study was to compare the techniques used to calculate intralimb joint coordination variability. Parameterization was used to determine that PAD-IC individuals displayed a reduced angular kinematic pattern thereby demonstrating reduced movement patterns compared to healthy controls. This finding was in agreement with our previous research on joint angular kinematics in PAD-IC individuals (Crowther et al., 2007). While parameterization is not a true indication of intralimb joint coordination variability it still allows analysis of the joint coupling relationship thus providing information about movement patterns. Both intralimb joint coordination variability techniques (NoRMS, VC) resulted in higher measures of variability in the PAD-IC relative joint couplings. This result demonstrates that both techniques may be used in the assessment of intralimb joint coordination variability in this population. Although these techniques of determine intralimb joint coordination variability are useful, precisely at which joint in the joint-joint coupling is demonstrating higher measures of variability can not be determined. Therefore single joint techniques should also be used in conjunction with intralimb to determine which lower limb joint/s is producing the variability during gait.

Conclusions

Further research should consider the extent to which higher intralimb joint coordination variability is detrimental or beneficial for individuals with PAD-IC to determine if the

intralimb joint coordination variability results can be used as a clinical assessment of risk of falls and intervention improvements. Further research should also examine joint movement variability in individuals with PAD-IC using single joint analysis including non-linear dynamics and coefficient of variation.

Chapter 5

Lower limb movement variability in patients with peripheral arterial disease

Authors: Robert G. Crowther, Warwick L. Spinks, Anthony S. Leicht, Frank Quigley and Jonathan Golledge

Journal of Biomechanics - under review

Abstract

Peripheral arterial disease (PAD) is a chronic obstructive disease of the arteries of the lower limb caused by atherosclerosis. The resultant decrease in blood flow can result in symptoms of pain in the lower limb on exercise known as intermittent claudication (PAD-IC). Exercise induced pain is experienced in the calves, thigh or buttocks restricting activities of daily living and thus reducing quality of life. This study investigated lower limb movement variability in individuals with PAD-IC (n=28) compared to individuals without PAD-IC (CON, n=25). A further aim was to examine the efficacy of various techniques used to describe single joint movement variability. All participants underwent 2D angular kinematics analysis of the lower limb during normal walking. Single joint movement variability was measured using linear (Spanning Set and Coefficient of Variation) techniques. Between group differences were examined by one-way ANOVA. The PAD-IC participants displayed significantly higher levels of lower limb movement variability in all joints when assessed using the Coefficient of Variation technique. There were no significant between group differences using the Spanning Set technique. Individuals with PAD-IC have higher levels of lower limb movement variability and reduced walking speed compared to healthy age and mass matched controls. This variability may be an adaptation to the gradual onset of ischaemic pain in this population.

Introduction

The Dynamical Systems theory of human motor control posits that human movement variability, previously thought to be "noise" and thus to be unfavorable is a fundamental element in normal and healthy functioning humans (Hamill et al., 2006; Newell & Corcos, 1993). As such, the noisy element of the measured signal may reveal important information about the motor control system that produced it. However, the extent to which higher or lower movement variability is beneficial or detrimental to human gait is still not clear (Hamill et al., 2006). Movement variability is lower in the lower limb joint coupling of individuals that suffer from pain and injury (Hamill et al., 1999; Heiderscheit et al., 2002; Pollard et al., 2005). Research in our laboratory however, has shown that individuals with intermittent claudication resulting from peripheral arterial disease (PAD-IC) demonstrate higher intralimb joint coordination (joint-joint couplings) variability of the lower limbs.

PAD-IC is a lower limb pathology that causes inadequate blood flow to the lower limb which may result in various levels of ischemic pain during activity (Aronow, 2004b; Bick, 2003; Hankey et al., 2006). This disease affects mobility by reducing temporal-spatial gait parameters and gait kinematics (Crowther et al., 2007; Gardner et al., 2001a; Scherer et al., 1998).

Although intralimb joint coordination techniques are useful in describing movement variability in injury and pathological conditions, they are imprecise in determining the joint(s) where the movement variability exists. Therefore, analysis of movement variability involving single joint techniques (spanning set and coefficient of variation) should also be

utilized. The coefficient of variation techniques have shown that the elderly have higher movement variability in the lower limbs compared to younger adults (Winter, 1991).

The purpose of this study was to quantify single joint movement variability in the lower limb gait kinematics of individuals with and without PAD-IC using both spanning set and coefficient of variation techniques.

Methods

Participants

Participants (n = 28) presenting with PAD-IC were selected based on an appropriate history demonstrating occlusive PAD with absence of significant peripheral neuropathy and a physical examination by a consultant vascular physician. PAD-IC was confirmed by absence of peripheral leg pulses, lower limb artery stenosis or occlusion via imaging, ankle-brachial pressure index (ABI) <0.9 and positive Edinburgh Claudication Questionnaire responses (Leng & Fowkes, 1992). Participant medical history and prescribed medications were recorded as previously described (Golledge et al., 2006). A further group of participants (n=25) free of PAD-IC (ABI >0.9 & positive questionnaire responses) and who were non regular exercisers were recruited from the general community via email bulletin boards, local newspaper and television coverage to act as age and mass matched controls (CON). Participants were excluded from the study if they required mobility aids, had observable gait abnormalities (e.g. Steppage, vaulting, circumduction and hip hiking) or medical conditions which influenced gait (e.g. orthopedic conditions and neurological impairment). Body mass index (BMI), percentage body fat and

ABI were measured as previously described (Crowther et al., 2007). All participants volunteered and gave written informed consent to participate in this study. The study was approved by the institutional ethics committee. The descriptive characteristics of the participants are outlined in Table 1.

Apparatus

Kinematics

Joint angular kinematics in the sagittal plane were determined via 2D motion analysis using a high-speed digital video camera (Canon MV550i, Canon Australia, North Ryde, Australia) set at a frame rate of 50 Hz and placed 3 m perpendicular to the line of motion providing an uninterrupted video field. Digital images were captured via a video capture card (Adaptec FireConnect for Notebooks, Adaptec Inc., Milpitas, California, USA) and appropriate lower limb joints (hip, knee and ankle) were identified and named with digitising software (SiliconCoach Ltd, Dunedin, New Zealand) operating on a laptop computer (Toshiba PIV, Toshiba Australia, North Ryde, Australia). Angular kinematics were determined using the digitising software and Microsoft® Office Excel (Microsoft Corporation, North Ryde, Australia). Two markers were placed 1 m apart in the middle of recording space on the laboratory floor in the direction of travel in order to calibrate the digitising software. The first author performed all digitising of the digital video images in order to prevent inter-individual variability in anatomical marker identification. Figure 1 outlines the joint angle conventions used to determine the joint kinematic variables. Walking speed was calculated as the distance from successive initial ground contacts of the ipsilateral foot by the time of successive initial ground contacts.

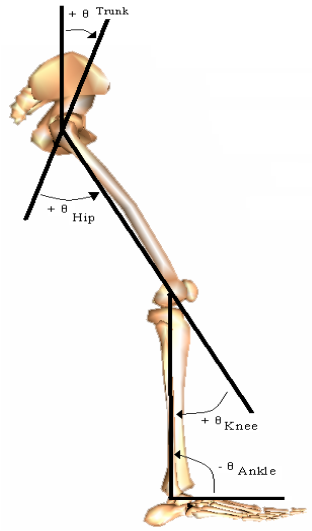

Figure 1 Sagittal plane angle convention

Coefficient of variation

Winter (1984) calculated the coefficient of variation (CV) in a single joint mean ensemble curve in order to determine gait cycle movement variability. This calculation is an adaptation of the CV equation used in many fields of research (CV = (standard deviation/mean)*100%). The CV is calculated as follows:

$$CV = \frac{\sqrt{\frac{1}{N}\sum_{i=1}^{N} S_i^2}}{\frac{1}{N}\sum_{i=1}^{N}|X_i|} \quad (1)$$

Where S is the standard deviation of the mean gait cycle, x is the ith point on the mean gait cycle, and N is the number of points in the mean gait cycle. The higher the CV the more variable the mean gait cycle curve (Winter, 1984).

Spanning set

The spanning set was developed by Lay (2000) and is composed of vectors that describe the possible linear combinations for a system of equations for a single joint mean curve. The larger the number of possible linear combinations of the vectors, the greater the variations in the possible solutions (Kurz & Stergiou, 2004). The span of the plane is dependant on the distance between the vectors (edges of the plane) that define the spanning set. Greater variability in the possible solutions of the two vectors is indicated by increased distance between the vectors and a greater span. A spanning set is created by a least-square method that fits a seventh-order polynomial to the standard deviation curves of the mean joint curve. Coordinate mapping introduces a familiar coordinate system that is used to describe the properties of the polynomials in R^n (Kurz & Stergiou, 2004; Lay, 2000). Coefficients from the respective polynomials are then used to map a vector space which in turn is used to define vectors in the spanning set. The magnitude of each spanning set indicates that movement variability results from the norm of the difference between the two vectors (Kurz & Stergiou, 2004).

Procedure

Participants were assessed early in the morning to ensure low levels of pretest physical activity. Upon arrival at the laboratory reflective markers were placed on five landmarks on the right side of the participant's body namely, the shoulder (acromion), hip (greater trochanter of femur), knee (lateral epicondyle of femur), ankle (lateral malleolus of fibula) and head of the 5^{th} metatarsal. Participants then underwent 2D video recording while walking at self-selected speed along a 10 m walkway marked at 1 cm intervals. Five

complete trials were achieved. A walking trial was deemed to be complete and suitable for analysis if all anatomical markers were visible at the first and last ipsilateral heel strike. Three walking trials (one stride per trial) were then randomly selected for kinematic analysis (Mullineaux et al., 2001).

Data analysis

A combination of single joint analysis techniques was performed on the angular kinematic data to determine lower limb movement variability. Data were calculated using custom software written in Matlab (Matlab 7 Release 14, The MathWorks, Inc. Natick, Massachusetts, USA). Statistical analysis was performed using the SPSS (SPSS Inc, release 14.0, Chicago, Illinois, USA) software program. Descriptive statistics were expressed as mean (±SD). Box-plot analyses were performed to identify extreme and outlier data. Data were analyzed using one-way ANOVA with one between-subjects factor (PAD-IC vs. CON). Medication and comorbidities data was analyzed using nonparametric Friedman test and post hoc comparison using Nemenyi's test. An alpha level of .05 was adopted for this study (Vincent, 2005).

Results

Mean values for age, height, mass, (%) body fat and BMI were similar for both groups of participants (Table 1). ABI values for the left and right leg were greater in the CON compared to PAD-IC participants ($P < .001$). PAD-IC participants also demonstrated reduced walking speed (Table 1).

Table 1. Descriptive characteristics of peripheral arterial disease-intermittent claudication (PAD-IC) and healthy age and mass matched control (CON) participants (N=53)

Variable	CON (n = 25)	PAD-IC (n = 28)
Age (yr)	66.2 (±7.5)	69.9 (±7.7)
Height (cm)	167.6 (±7.3)	166.3 (±8.3)
Mass (kg)	74.6 (±12.1)	79.3 (±16.5)
Body fat (%)	33.6 (±7.5)	32.2 (±8.2)
Gender (% male)	50	40
BMI	26.5 (±3.6)	28.5 (±4.6)
ABI left leg	1.16 (±0.16)	0.73 (±0.24)**
ABI right leg	1.16 (±0.14)	0.71 (±0.22)**
Walking Speed ($m \cdot s^{-1}$)	1.08 (±0.03)	1.30 (±0.03)**

Values are mean (±SD) or %
ABI = Ankle/brachial index; BMI = Body mass index.
* P < .05; ** P < .001 vs. CON

Lower limb movement variability

CV and spanning set

The PAD-IC participants demonstrated significantly higher CV for the hip, knee and ankle compared to CON. No significant between group differences were found using the spanning set technique (Figure 2) (Table 2).

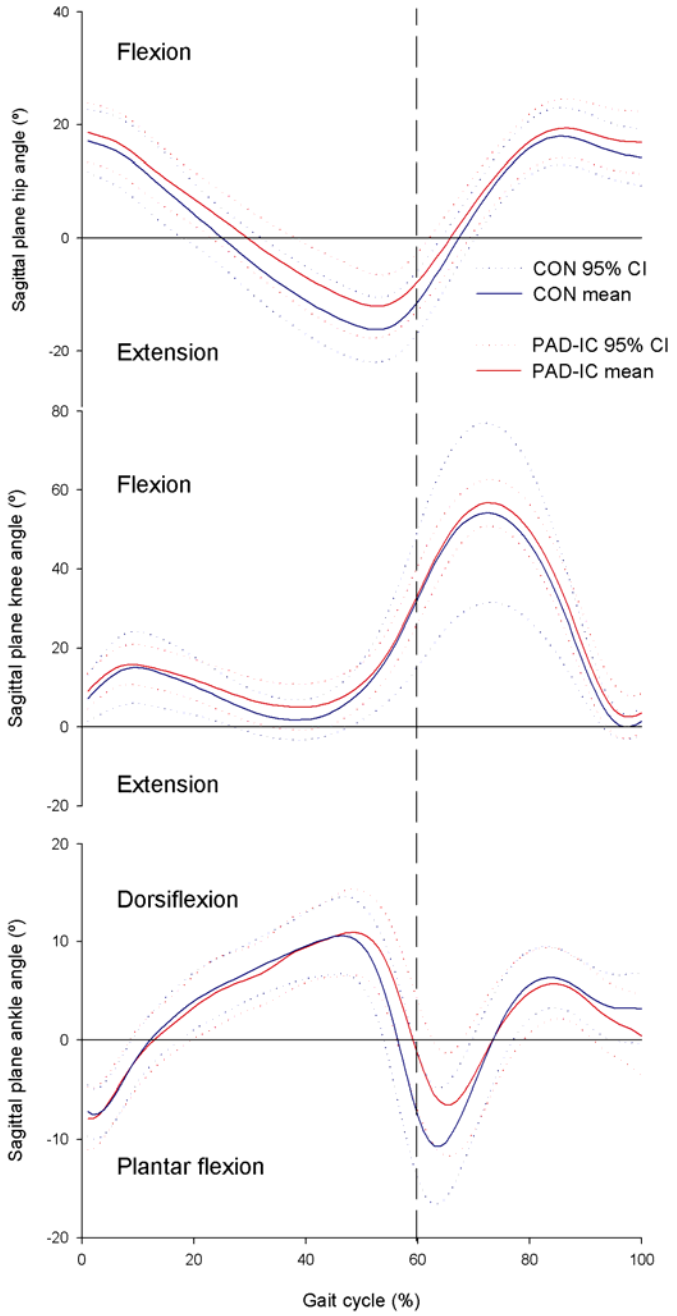

Figure 2 Hip, knee and ankle kinematics in the sagittal plane for PAD-IC and CON subjects; the dashed line indicates toe-off at ~60% gait cycle (with 0-60% representing stance; 60-100% representing swing)

Table 2. Coefficient of variation (CV) and spanning set values for peripheral arterial disease-intermittent claudication-intermittent claudication (PAD-IC) and control (CON) participants (N=53)

Variable		CON (n =25)	PAD-IC (n = 28)
Hip	CV (%)	9 (± 3)	12 (± 5)*
	Spanning set (º)	5.99 (± 3.23)	7.14 (± 3.48)
Knee	CV (%)	7 (± 2)	9 (± 3)*
	Spanning set (º)	10.89 (± 8.09)	11.09 (± 5.52)
Ankle	CV (%)	26 (± 7)	32 (± 10)**
	Spanning set (º)	11.20 (± 5.38)	9.46 (± 4.00)

Values are mean (±SD)
*P < .05, ** P < .01 vs. CON

Discussion

The purpose of this study was to quantify single joint variability in the sagittal plane between individuals with and without PAD-IC using both spanning set and CV techniques. Single joint variability determined via the CV technique was significantly higher for the PAD-IC participants for all joints (hip, knee and ankle). Research in our laboratory, individuals with PAD-IC demonstrated higher intralimb coordination variability in joint couplings (hip-knee, knee-ankle and hip-ankle) and the current study confirms that higher movement variability does exist in all of the joints when assessed using the CV technique.

Research using the CV technique has indicated that higher levels of single joint variability is associated with unstable gait (Buzzi et al., 2003; Winter, 1984). However, while the

results of this study demonstrate that individuals with PAD-IC have higher levels of movement variability the variability may not be reflective of gait pattern instability but may indicate adaptation of the motor control system to perturbation(s) associated with the gradual onset of claudication pain. Furthermore in this study PAD-IC participant were shown to have reduced waking speed. This reduced walking speed in PAD-IC patients could be described as a strategy to avoid/minimize pain onset. Research has shown that walking speed can influence stride-stride fluctuations (Jordan, Challis, & Newell, 2007) and may effect the lower limb movement variability in individuals. However, the extent to which this adaptation is beneficial or detrimental to human locomotion (i.e. preventing or causing falls) is yet to be determined. The constraints imposed by the adoption of variable lower limb biomechanics may allow individuals with PAD-IC to vary locomotion dynamics to accommodate increasing pain associated with reduced blood supply to the lower limbs.

On reflection the non-significant results for the spanning set technique are not surprising as the technique was initially developed to assess movement variability during the stance phase of the gait cycle. However, the technique was utilized in this study to determine if it could be apply to the whole gait cycle to provide additional information regarding movement variability over the whole gait cycle in the PAD-IC population but it failed to provide any relevant information.

Further research should consider the extent to which higher movement variability of the lower limbs is detrimental or beneficial (i.e. instability (fall risk) or dealing with

claudication pain) for individuals with PAD-IC. Research should also examine the effects of exercise intervention programs on lower limb movement variability in individuals with PAD-IC.

In conclusion, single joint movement variability analysis techniques have shown that individuals with PAD-IC demonstrate higher movement variability of the lower limbs and this may be an adaptation of the motor control system to perturbation(s) associated with the gradual onset of claudication pain.

Chapter 6

Effects of a long term exercise program on lower limb mobility, physiological responses, walking performance and physical activity levels in patients with peripheral arterial disease

Authors: Robert G. Crowther, Warwick L. Spinks, Anthony S. Leicht, Kunwarjit Sangla, Frank Quigley and Jonathan Golledge.

Journal of Vascular Surgery, 47(2), 303-309

Abstract

Objective: The purpose of the study was to examine the effects of a 12 month exercise program on lower limb mobility (temporal-spatial gait parameters and gait kinematics), walking performance, peak physiological responses and physical activity levels in individuals with symptoms of intermittent claudication due to peripheral arterial disease (PAD-IC).

Method: Participants (n = 21) with an appropriate history of PAD-IC, ankle brachial pressure index (ABI) <0.9 in at least 1 leg and a positive Edinburgh claudication questionnaire response were prospectively recruited. Participants were randomly allocated to either a control PAD-IC group (CPAD-IC) (n = 11) which received standard medical therapy and a treatment PAD-IC group (TPAD-IC) (n = 10), which also took part in a 12 month supervised exercise program. A further group of participants (n = 11) free of PAD (ABI >0.9) and who were non regular exercisers were recruited from the community to act as age and mass matched controls (CON). Lower limb mobility was determined via 2D video motion analysis. A graded treadmill test was used to assess walking performance and peak physiological responses to exercise. Physical activity levels were measured via a 7 day pedometer recording. Differences between groups were analyzed via repeated measures ANOVA.

Results: The 12 month supervised exercise program had no significant effect on lower limb mobility, peak physiological responses or physical activity levels in TPAD-IC compared to CPAD-IC participants. However, the TPAD-IC participants demonstrated significantly greater walking performance (171% improvement in pain free walking time and 120% improvement in maximal walking time compared with baseline).

Conclusion: The results of this study confirm that a 12 month supervised exercise program will results in improved walking performance, but does not have an impact on lower limb mobility, peak physiological responses or physical activity levels of PAD-IC patients.

Clinical Relevance

Presently the mechanisms underlying the benefit of supervised exercise in patients with intermittent claudication are poorly understood. We postulated that they result from improved lower limb mobility characteristics. We confirmed that a 12 month supervised exercise program improves walking performance however, this was not as a results of improved lower limb mobility or physiological responses.

Introduction

Patients with symptoms of intermittent claudication due to peripheral artery disease (PAD-IC) have reduced walking performance, peak physiological responses, lower limb mobility (temporal-spatial gait parameters and gait kinematics), physical activity levels and perceived health related quality of life (QOL) compare to healthy age matched controls (Breek et al., 2005; Breek et al., 2001; Crowther et al., 2007; Gardner et al., 2001a; McDermott et al., 2006). PAD-IC is usually treated conservatively with medications to reduce cardiovascular disease risk-factors however, patients often continue to have impaired QOL. For severe PAD-IC surgery is often the most appropriate treatment for QOL outcomes (Comerota, 2001; Lumsden & Rice, 2006). Regardless of the initial treatment, PAD-IC patients are encouraged to increase their physical activity levels, thereby reducing the risk factors associated with the condition (Hankey et al., 2006).

PAD-IC patients have been reported to walk significantly further following a 3 month supervised exercise program consisting of intermittent walking (Gardner & Poehlman, 1995). Although exercise programs have demonstrated improved walking performance (Gardner & Poehlman, 1995; Mika et al., 2005; Savage et al., 2001), the exact mechanisms for the improvement have not been demonstrated. Increased cardiac output, development of collateral lower limb arteries improved efficiency of oxygen delivery, adaptation of muscle metabolism and changes in lower limb mobility (Lumsden & Rice, 2006; Womack et al., 1997) have been suggest as contributors to improved walking performance but, there is no consensus as to the major contributing factors.

Most PAD-IC studies have employed short term exercise programs (Degischer et al., 2002b; Gardner & Poehlman, 1995; Mika et al., 2005; Savage et al., 2001). To date there has been only two studies that has investigated the effects of a longer (12 month) term exercise program on walking performance in PAD-IC patients (Gardner et al., 2002). Important factors such as the duration and intensity of the exercise may be central to improved walking performance. Also there has been no long term examination of the lower limb mobility of individuals with PAD-IC in order to determine if the reduced lower limb mobility in this population can be modified to more closely resemble healthy age matched controls. Gardner et al. (2001) speculated that the reduced temporal-spatial gait parameters could be modified to resemble that of age matched controls through the use of an exercise program.

Therefore, the aim of this study was to examine the effects of a 12 month supervised exercise program on the lower limb mobility of individuals with PAD-IC during pain free walking. A further aim was to examine the extent to which lower limb mobility contributes to long term exercise induced changes in walking performance, peak physiological responses and physical activity levels in PAD-IC patients. It was hypothesized that a long term supervised exercise program would result in improved lower limb mobility during pain free walking which in turn, would be reflected in improved functional capacity that is, improved walking performance, increased peak physiological responses to acute exercise and augmented levels of physical activity.

Methods

Participants

Between January 2003 and 2006 patients referred to the Vascular Department at the Townsville Hospital with symptoms of intermittent claudication were considered for inclusion in the study. Entry criteria included an appropriate history of intermittent claudication, imaging confirmation of PAD on lower limb duplex or computed tomographic angiograph (CTA), and ability and willingness to attend for regular supervised exercise. Approximately 50% of patients attending our Vascular Department live >200 km away. Thus the main reason for excluding patients was inability to attend the program (n=48). Other reasons for exclusion included selection for surgical or endovascular intervention (n=30), patient preference (n=20) and requirement for mobility aids, obvious gait abnormalities (e.g. Circumduction) or medical conditions which influenced gait (e.g. orthopedic conditions and neurological impairment) (n=20). All patients were assessed by a consultant vascular physician. PAD-IC was confirmed by absence of peripheral pulses, lower limb artery stenosis or occlusion on duplex or CTA, ankle-brachial pressure index (ABI) <0.9 and positive Edinburgh Claudication Questionnaire response (Leng & Fowkes, 1992). Five participants withdrew from the study following baseline testing citing health, changed address and personal motivation reasons. Participants were randomly allocated using a single blind protocol to either a control (CPAD-IC, n = 11) or treatment group (TPAD-IC, n = 10). All participants were reviewed by a vascular surgeon and consultant physician to optimize their atherosclerosis risk factor management which included recommendations to modify smoking habits, diet, medication, and to undertake regular physical activity. Patients randomized to the TPAD-IC experimental condition also

undertook a 12 moth supervised exercise program. A third group of participants (n = 11) free of PAD based on normal ABI and peripheral pulses and who were non regular exercisers were recruited from the general community via email bulletin boards, local newspaper and television coverage to act as age and mass matched controls (CON). Co-morbidity, medication and smoking history were determined at consultation by a vascular physician. All participants volunteered and gave written informed consent to participate in this study as approved by the institutional ethics committee. The descriptive characteristics of the participants are outlined in Table 1.

Procedure

Participants arrived at the laboratory in the early morning whilst in a fasting state (12 h) and underwent, body composition, resting ABI, gait and exercise performance testing at 0 and 12 months.

Anthropometry

Participant height was determined by a wall mounted stadiometer (Seca, model 220, Seca Scales, Hamburg, Germany). Body mass and composition (%body fat) were determined via bioelectrical impedance scales (TANITA TBF 521, TANITA Corporation, Arlington heights, Illinois, USA). Body mass index (BMI) was calculated as (mass in kg/[(height in $m)^2$]).

Ankle/brachial index (ABI)

Blood pressure measurements were taken by a qualified sonographer using a handheld bidirectional Doppler instrument (MD6, Hokanson, Bellevue, Washington, USA) with a 5-MHz transducer and standard blood pressure cuffs after the participant had rested in the supine position for 10 mins. ABI was calculated as the highest systolic blood pressure in the posterior tibial artery or dorsalis pedis artery divided by the highest systolic blood pressure in the left or right brachial artery (Caruana et al., 2005).

Lower limb mobility

Major joint segments were identified using reflective markers placed on five landmarks on the ipsilateral (right side) of the participant's body. The landmarks were determined via palpation and the markers were positioned at the shoulder (acromion), hip (greater trochanter of femur), knee (lateral epicondyle of femur), ankle (lateral malleolus of fibula) and head of the 5th metatarsal.

Participants were instructed to walk normally without shoes along a 10 m walkway which was marked at 1 cm intervals whilst the participant was in a pain free state. Digital imagery was obtained via a high-speed digital video camera (Canon MV550i, Canon Australia, North Ryde, Australia) set at a frame rate of 50 Hz and placed 3 m perpendicular to the line of motion providing an uninterrupted video field. Five complete trials were achieved. A walking trial was deemed to be complete and suitable for analysis if all anatomical markers were visible at the first and last ipsilateral heel strike. Three walking trials (one stride per trial) were then randomly selected for kinematic analysis (Mullineaux et al., 2001). During

the recording of video footage, digital images were captured via a video capture card (Adaptec FireConnect for Notebooks, Adaptec Inc., Milpitas, California, USA) and appropriate lower limb joints were identified and named with digitising software (SiliconCoach Ltd, Dunedin, New Zealand) operating on a laptop computer (Toshiba PIV, Toshiba Australia, North Ryde, Australia).

Two markers were placed 1 m apart on the floor in the direction of travel in order to calibrate the digitising software. The first author performed all digitising of the digital video images in order to prevent inter-individual variability in anatomical marker identification. The intraclass correlation coefficient (ICC) values for the digitized X and Y coordinate data ranged from 0.9-0.95. The ICC data for within-participant gait kinematic measures ranged from 0.8–0.85.

Data points were used to calculate gait kinematic parameters including peak displacements, velocities and acceleration for the ipsilateral lower limb joints. Figure 1 outlines the joint angle conventions used to determine the kinematic variables. Graphical representations of the angular kinematics of the trunk, hip, knee and ankle joints were normalized (100 points) for the gait cycle using a cubic spline routine to determine a mean ensemble curve and 95% confidence intervals (Kurz et al., 2003). Temporal-spatial gait parameters determined included stride length, stride cadence, contact time, swing time, initial double support time, ipsilateral leg support time, final double support time, contralateral leg support time, total time and speed. Stride length was calculated as the distance from successive initial ground contacts of the ipsilateral foot.

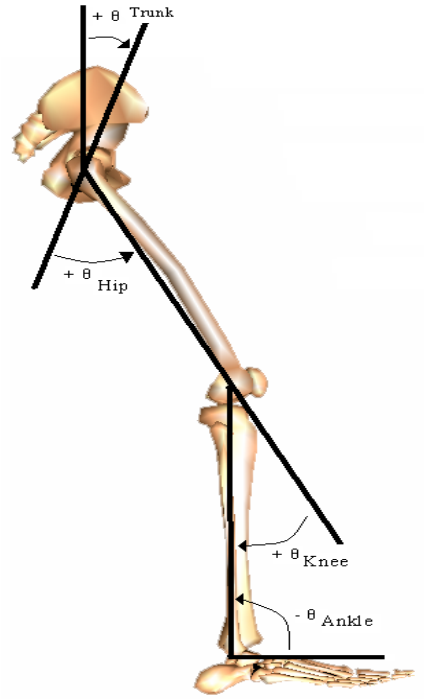

Figure 1 Sagittal plane angle convention

Treadmill testing

Following lower limb mobility assessment, participants undertook a graded exercise test on a treadmill (Trackmaster TMX55, Full Vision, Kansas, USA) for determination of walking performance and physiological responses to acute exercise. The peak physiological responses included oxygen uptake (VO_{2peak}), respiratory exchange ratio (RER_{peak}), ventilation (VE_{peak}) and heart rate (HR_{peak}). The physiological responses were determined via indirect calorimetry using a metabolic cart (Power LAB/8M Metabolic system, ADInstruments Pty Ltd, Castle Hill, Australia). The metabolic gas analysis system was calibrated with a 3 L syringe, temperature (^{o}C), barometric pressure (mmHg), airflow (L), body mass (kg), room air (20.93% and 0.04% for O_2 and CO_2 respectively) and alpha gas

composition (~10% O_2, ~7% CO_2) (BOC, Melbourne, Australia). Before the test began, the participant was fitted with a headpiece that held a rubber mouthpiece connected to a T shaped two-way non-rebreathing value (Hans Rudolph, Inc., Kansas City, Missouri, USA) which in turn was connected to the mixing chamber of the metabolic gas analysis system by 35 mm diameter smooth bore hosing. ECG electrodes (silver/silver chloride electrodes, 3M, Pymble, Australia) were positioned at the manubrium, 7^{th} cervical vertebrae and 5^{th} intercostal-axiliary line (lead II) for the recording of an electrocardiogram. All physiological responses were recorded continuously using Chart (v5.1, ADInstruments Pty Ltd, Castle Hill, Australia) sampling at 1000 Hz and were analyzed post test as 15 s averages.

The graded treadmill walking protocol consisted of a constant speed of 3.2 $km \cdot h^{-1}$ and an incline of 0% for the first 2 min which was then increased by 2% every 2 min(Gardner et al., 1991a). Participant perception of exercise exertion was determined every 60 s via Borg's(1970) Rating of Perceived Exertion (RPE) instrument while participant perception of claudication pain was determined via a 5-point (0=no pain, 1=onset of pain, 2= moderate pain, 3=intense pain, 4=maximal pain) Claudication Pain Scale (CPS)(American College of Sports Medicine, 2006). Walking performance was assessed as pain free walking time (PFWT) and maximal walk time (MWT) either by perceived maximal pain, volitional exhaustion or until 25 min of walking was achieved. Participants were permitted to hold the treadmill handrail if they required support whilst walking and a number of common motivational phrases (e.g. you can make it, keep walking) were used to encourage participants. Motivational phrase usage was standardized by noting the frequency and type

of phrase used in pilot and preliminary testing. Exercise test termination criteria included voluntary exhaustion and significant abnormal ECG rhythm.

Physical activity level

Following laboratory testing, participant physical activity levels were determined from 7 day pedometer (YAMAX DigiWalker SW-700, YAMAX Corporation, Tokyo, Japan) recordings. Physical activity level was determined as number of steps, distance walked and calories expended during walking. The TPAD-IC participants did not wear a pedometer during supervised exercise sessions in order to allow between group comparison of physical activity levels outside the laboratory.

Supervised exercise program

The exercise program initially consisted of supervised treadmill walking 3 $d \cdot wk^{-1}$ for 25 mins at 3.2 $km \cdot hr^{-1}$. Participants were required to walk until the pain level was perceived as being 3 or 4 on the CPS. Exercise intensity (via treadmill grade and walking speed) and duration (25 up to 40 mins) was progressively increased once the participant could walk without stopping for 25 mins below the pain CPS levels of 3 or 4. This exercise progression strategy was continued over the 12 month period.

Statistical analyses

Statistical analysis was performed using the SPSS (SPSS Inc, release 14.0, Chicago, Illinois, USA) software program. Descriptive statistics were expressed as mean (±SD). Box-plot analyses were performed to identify extreme and outlier data. Data were analyzed

using repeated measures ANOVA with one between-subjects factor (CON vs. CPAD-IC vs. TPAD-IC) and one within subject factor (Time - 0 vs. 12 month). Post hoc analysis was performed using the Tukey HSD test. Medication and comorbidities data were analyzed using the nonparametric Friedman test and post hoc comparison using Nemenyi's test. An alpha level of .05 was adopted for this study (Vincent, 2005).

Results

Participants

The groups were similar in age, height, mass, % body fat and BMI at baseline and no significant changes occurred over the 12 month study period (Table 1). As expected ABI values were higher in the CON group ($P < .001$) than both PAD-IC groups (Table 1). ABI measures indicated an equal number of right and left side index (worst) legs. Both PAD-IC groups included a higher proportion of former smokers ($P < .05$) compared to the CON group. The CPAD-IC group contained a higher proportion of patients who had been prescribed beta-blocker medication ($P < .05$) compared to the TPAD-IC and CON groups (Table 1).

Table 1 Descriptive characteristics of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Age (yr)	68.1 (±6.8)	69.4 (±6.9)	67.1 (±6.8)	68.1 (±6.8)	71.3 (±8.5)	72.3 (±8.5)
Height (cm)	167.8 (±8.2)	167.9 (±8.1)	165.6 (±8.7)	165.4 (±8.9)	165.7 (±8.9)	165.7 (±9.5)
Mass (kg)	70.7 (±8.4)	68.9 (±8.0)	74.5 (±18.9)	74.5 (±18.8)	80.7 (±15.3)	81.3 (±15.3)
Body fat (%)	31.6 (±9.5)	29.0 (±8.5)	30.4 (±8.6)	32.7 (±8.9)	33.1 (±9.0)	35.1 (±6.5)

BMI	25.2 (±3.2)	24.5 (±2.8)	26.9 (±5.3)	27.0 (±5.2)	29.2 (±4.1)	29.5 (±4.3)
ABI left leg#	1.18 (±0.16)	1.18 (±0.10)	0.64 (±0.22)	0.64 (±0.23)	0.72 (±0.22)	0.68 (±0.17)
ABI right leg#	1.16 (±0.13)	1.12 (±0.16)	0.69 (±0.27)	0.60 (±0.21)	0.71 (±0.23)	0.67 (±0.21)
Gender (% male)	45		45		50	
Current smoker (%)	0		27		10	
Former smoker (%)	27		64*		70*	
Type II diabetes (%)	0		27		10	
Hypertension (%)	9		36		30	
Ischaemic heart disease (%)	0		27		20	
Arthritis (%)	27		18		10	
Beta-blocker prescription (%)	0		45*		10	

Values are mean (±SD) or %
CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients; ABI, Ankle/brachial index; BMI, Body mass index.
# $P < .01$ between group CON vs. CPAD-IC & TPAD-IC
* $P < .01$ vs. CON

Lower limb mobility

There were significant between group differences for stride length, cadence, stride time, contact time, speed and reduced double support time (1 and 2) for the CON group compared to the CPAD-IC and TPAD-IC groups (Table 2). There were no significant differences between the CPAD-IC and TPAD-IC groups at 0 and 12 months for all temporal-spatial gait parameters and gait kinematics. The 12 month supervised exercise program had no significant impact on the temporal-spatial gait parameters or gait kinematics of the TPAD-IC participants (Tables 2-4 & Figure 2-5).

Table 2 Mean (±SD) temporal-spatial gait parameter values of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Stride length (m) #	1.37 (±0.15)	1.35 (±0.13)	1.20 (±0.16)	1.20 (±0.17)	1.19 (±0.16)	1.23 (±0.11)
Cadence (steps·min^{-1}) #	116.1 (±3.1)	114.8 (±4.3)	108.9 (±6.7)	107.9 (±8.3)	107.6 (±7.4)	109.6 (±6.1)
Stride time (s) #	1.04 (±0.03)	1.05 (±0.04)	1.11 (±0.06)	1.11 (±0.09)	1.12 (±0.08)	1.10 (±0.06)
Contact time (s) #	0.63 (±0.02)	0.65 (±0.02)	0.69 (±0.05)	0.70 (±0.06)	0.70 (±0.05)	0.69 (±0.04)
Swing time (s)	0.41 (±0.02)	0.40 (±0.02)	0.42 (±0.04)	0.41 (±0.04)	0.42 (±0.04)	0.41 (±0.03)
Single support contralateral (s)	0.41 (±0.02)	0.39 (±0.02)	0.42 (±0.04)	0.41 (±0.04)	0.42 (±0.04)	0.41 (±0.03)
Single support ipsilateral (s)	0.40 (±0.02)	0.39 (±0.03)	0.41 (±0.03)	0.41 (±0.04)	0.40 (±0.04)	0.40 (±0.02)
Double support 1 (s) #	0.12 (±0.02)	0.14 (±0.01)	0.15 (±0.02)	0.15 (±0.02)	0.15 (±0.03)	0.15 (±0.02)
Double support 2 (s) #	0.11 (±0.01)	0.13 (±0.02)	0.13 (±0.03)	0.14 (±0.03)	0.15 (±0.03)	0.14 (±0.02)
Speed (m·s^{-1}) #	1.3 (±0.2)	1.3 (±0.1)	1.1 (±0.2)	1.1 (±0.2)	1.1 (±0.2)	1.1 (±0.1)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients; Stride length, distance either foot moves during the gait cycle; Cadence, number of steps taken in a min; Stride time, time taken to produce a stride; Contact time, time that the ipsilateral foot is in contact with the floor; Swing time, time that the ipsilateral foot is not in contact with the floor; Single support, time that each foot is spent in contact with the floor by itself. Double support, time that is spent with both feet on the floor; Speed, calculation of stride length and stride time

# $P < .01$ between group CON vs. CPAD-IC & TPAD-IC

Table 3 Mean (±SD) angular kinematics values of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Ankle ROM (º)	24.5 (±5.6)	21.7 (±6.5)	21.9 (±3.2)	21.4 (±3.0)	22.7 (±3.4)	23.3 (3.2)
Ankle plantar flexion (º)	-12.7 (±6.0)	-12.4 (±4.5)	-10.2 (±2.2)	-10.0 (±2.8)	-9.4 (±2.5)	-10.7 (±2.4)
Ankle dorsiflexion (º)	11.8 (±3.6)	11.3 (±3.6)	11.5 (±3.0)	11.5 (±3.4)	13.3 (±4.5)	13.0 (±2.9)

Knee ROM (º)	59.0 (±3.6)	59.9 (±3.3)	58.5 (±6.6)	60.1 (±5.1)	56.4 (±6.2)	58.1 (±5.6)
Knee flexion (º)	58.0 (±2.9)	58.4 (±2.7)	58.7 (±6.4)	59.7 (±4.0)	57.4 (±4.7)	58.5 (±6.3)
Knee extension (º)	-1.6 (±1.9)	-1.6 (±3.1)	0.2 (±3.5)	-0.4 (±4.2)	1.0 (±5.8)	0.4 (±4.8)
Hip ROM (º)	35.5 (±5.8)	35.3 (±7.0)	34.2 (±6.0)	34.6 (±6.0)	33.2 (±6.3)	34.2 (±7.1)
Hip flexion (º)	20.0 (±5.4)	20.4 (±5.0)	20.7 (±5.9)	21.1(±3.4)	21.4 (±4.2)	21.2 (±6.8)
Hip extension (º)	-15.6 (±6.4)	-15.0 (±8.6)	-13.5 (±6.4)	-13.5 (±6.4)	-11.8 (±6.6)	-13.0 (±5.8)
Trunk ROM (º)	9.3 (±2.0)	9.2 (±2.0)	7.9 (±1.6)	8.5 (±1.8)	8.5 (±2.6)	8.3 (±2.7)
Trunk flexion (º)	3.1 (±3.6)	3.5 (±3.9)	3.0 (±3.3)	2.7 (±2.9)	4.1 (±2.6)	3.6 (±2.5)
Trunk extension (º)	-6.2 (±3.2)	-5.9 (±3.8)	-4.9 (±3.4)	-5.8 (±2.7)	-4.5 (±2.1)	-4.7 (±3.2)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients.

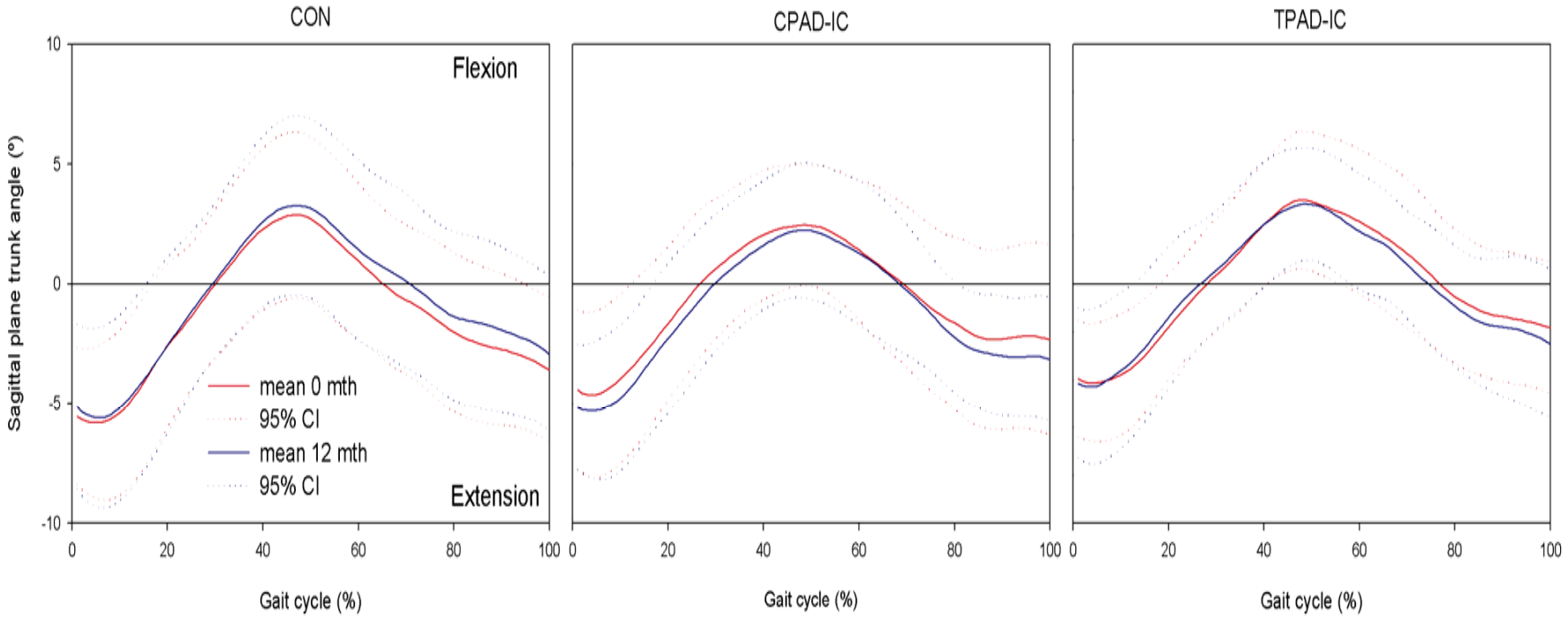

Figure 2 Participant trunk kinematics in the sagittal plane (CON = healthy age and mass matched controls, CPAD-IC = control peripheral arterial disease-intermittent claudication patients, TPAD-IC = treatment peripheral arterial disease-intermittent claudication patients)

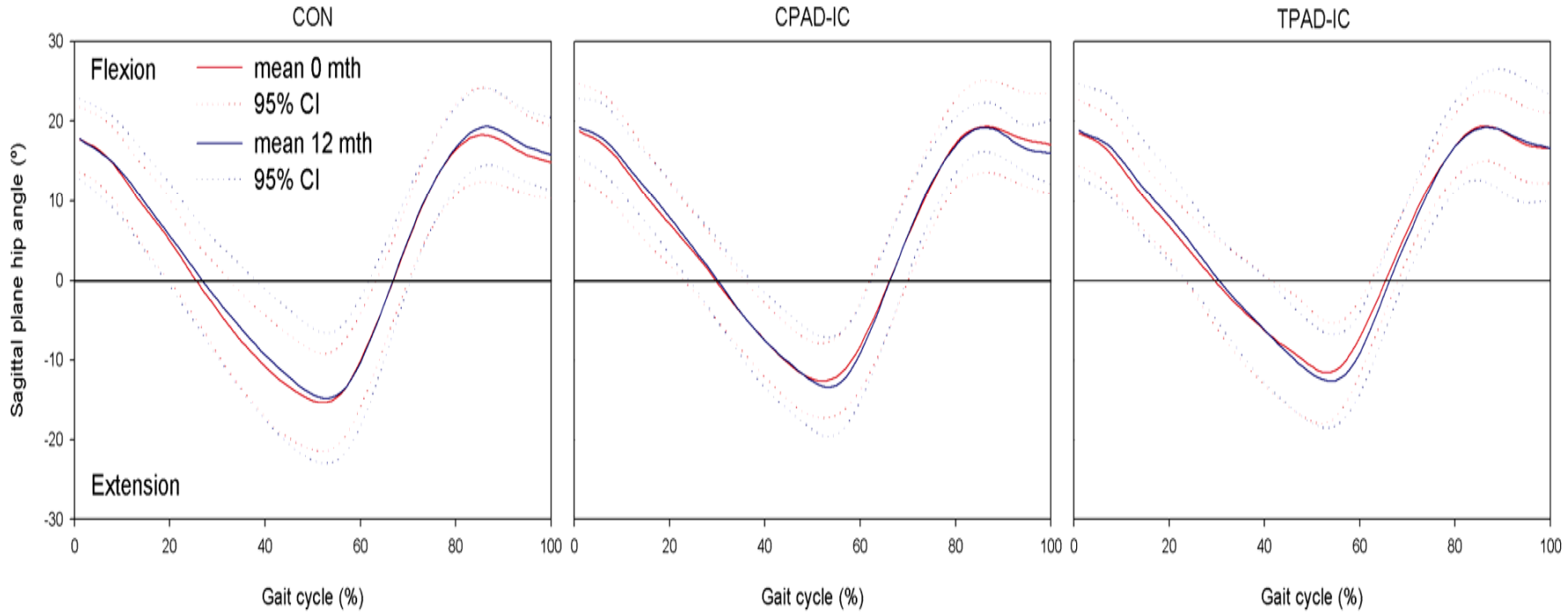

Figure 3 Participant hip kinematics in the sagittal plane (CON = healthy age and mass matched controls, CPAD-IC = control peripheral arterial disease-intermittent claudication patients, TPAD-IC = treatment peripheral arterial disease-intermittent claudication patients)

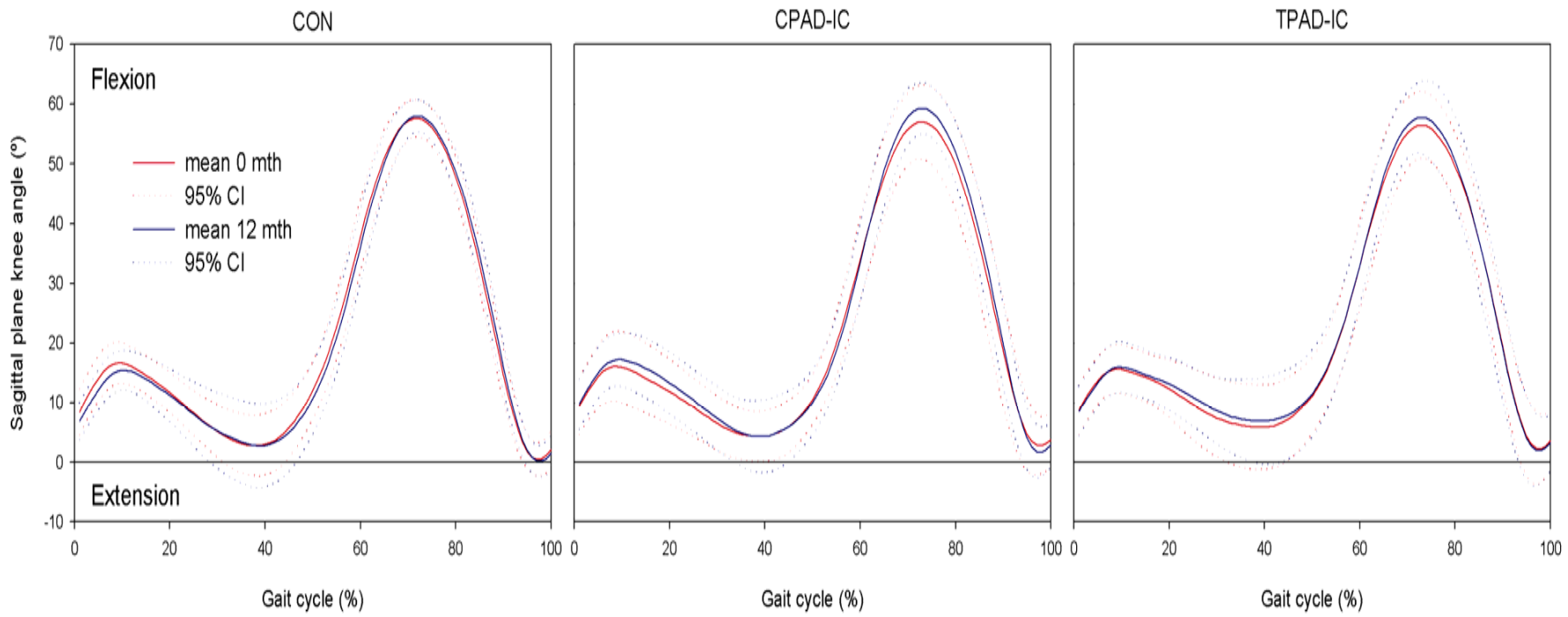

Figure 4 Participant knee kinematics in the sagittal plane (CON = healthy age and mass matched controls, CPAD-IC = control peripheral arterial disease-intermittent claudication patients, TPAD-IC = treatment peripheral arterial disease-intermittent claudication patients)

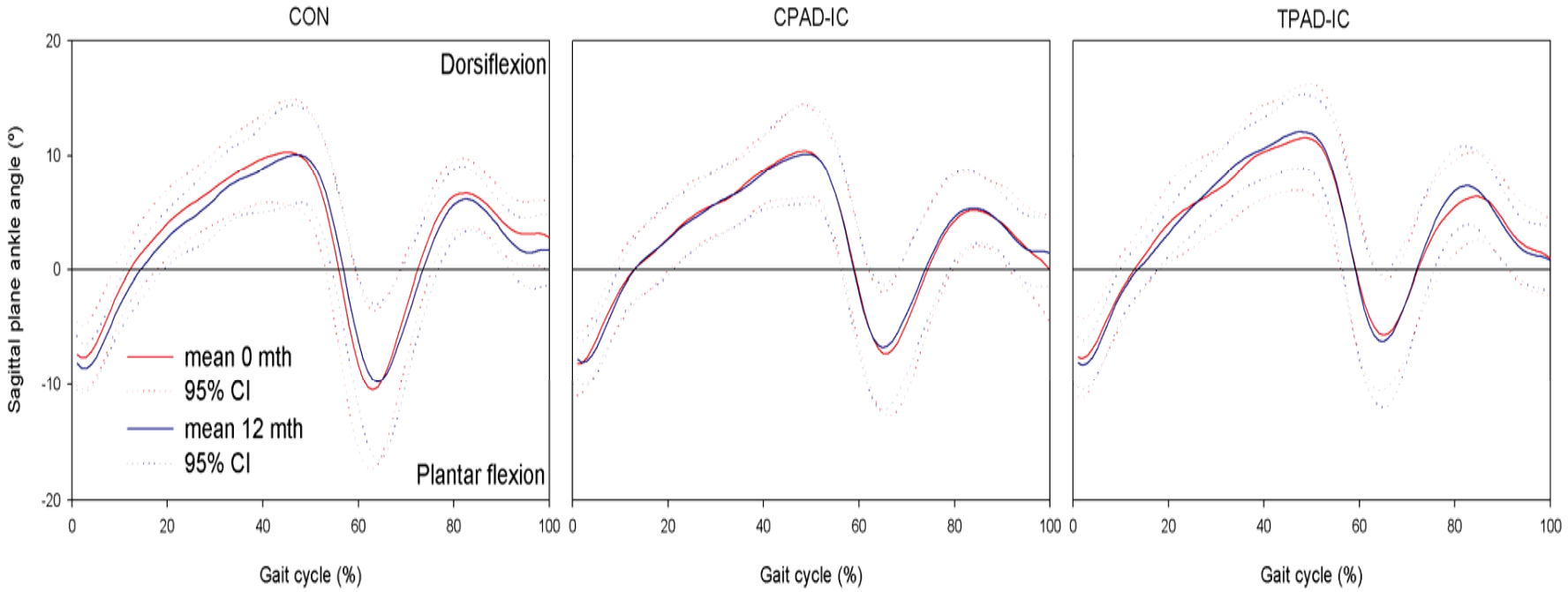

Figure 5 Participant ankle kinematics in the sagittal plane (CON = healthy age and mass matched controls, CPAD-IC = control peripheral arterial disease-intermittent claudication patients, TPAD-IC = treatment peripheral arterial disease-intermittent claudication patients)

Table 4 Mean (±SD) peak angular velocity and acceleration values of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	**12 mth**	**0 mth**	**12 mth**	**0 mth**	**12 mth**
Ankle velocity min ($^{o}\cdot s^{-1}$)	-160.7 (±49.4)	-157.8 (±47.4)	-132.6 (±22.6)	-129.2 (±26.2)	-130.5 (±26.6)	-145.8 (±32.3)
Ankle velocity max ($^{o}\cdot s^{-1}$)	238.9 (±71.3)	217.4 (±58.6)	199.0 (±48.1)	185.1 (±41.6)	179.5 (±33.3)	213.4 (±40.8)
Knee velocity min ($^{o}\cdot s^{-1}$)	-318.9 (±29.5)	-320.0 (±23.2)	-307.1 (±40.6)	-316.0 (±40.5)	-296.1 (±51.5)	-301.5 (±55.6)
Knee velocity max ($^{o}\cdot s^{-1}$)	378.3 (±31.5)	409.0 (±104.4)	367.6 (±71.0)	381.6 (±63.1)	352.6 (±39.1)	368.4 (±51.3)
Hip velocity min ($^{o}\cdot s^{-1}$)	-174.0 (±30.9)	-169.6 (±34.4)	-156.7 (±24.5)	-161.2 (±27.9)	-155.4 (±27.6)	-161.4 (±33.9)
Hip velocity max ($^{o}\cdot s^{-1}$)	123.8 (±25.9)	302.1 (±618.1)	106.3 (±27.9)	105.6 (±19.9)	112.8 (±19.5)	104.1 (±22.9)
Ankle acceleration min ($^{o}\cdot s^{-2}$)	-5349.2 (±1682.3)	-4884.3 (±1682.0)	-4089.2 (±952.1)	-3953.1 (±793.0)	-3940.7 (±724.3)	-4751.0 (±1084.7)
Ankle acceleration max ($^{o}\cdot s^{-2}$)	3689.4 (±891.5)	3460.6 (±521.8)	3263.8 (±718.4)	3010.2 (±455.1)	3071.7 (±655.5)	3129.9 (±421.3)
Knee acceleration min ($^{o}\cdot s^{-2}$)	-5827.1 (±1007.0)	-5523.4 (±1346.6)	-5873.9 (±2082.6)	-5950.9 (±1801.4)	-5358.8 (±1089.1)	-5651.0 (±1132.2)
Knee acceleration max ($^{o}\cdot s^{-2}$)	3888.5 (±310.1)	3810.5 (±548.0)	3569.1 (±587.8)	3613.4 (±545.2)	3617.7 (±342.2)	3722.5 (±529.7)
Hip acceleration min ($^{o}\cdot s^{-2}$)	-2118.0 (±231.2)	-2385.5 (±1052.6)	-2000.0 (±396.0)	-1992.85 (±418.4)	-2160.4 (±319.4)	-1994.5 (±286.5)
Hip acceleration max ($^{o}\cdot s^{-2}$)	2067.9 (±265.8)	1685.3 ± (367.7)	1818.5 (±321.0)	2102.0 (±505.8)	1953.9 (±342.6)	1735.8 (±483.2)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients.

Treadmill testing

The CON group demonstrated significantly greater MWT compared to the TPAD-IC and CPAD-IC groups. PFWT and MWT were significantly greater for the TPAD-IC group following the 12 month supervised exercise program compared to the CPAD-IC group (Table 5). The TPAD-IC group also demonstrated significantly improved PFWT and MWT at 12 month compared to baseline. Significantly higher VO_{2peak} and HR_{peak} values were determined for CON group compared to the PAD-IC groups. The 12 month supervised exercise program had no significant effect on any of the physiological responses (HR_{peak}, VO_{2peak}, VE_{peak} and RER_{peak}) for the TPAD-IC group compared to the CPAD-IC and CON groups (Table 5).

Physical activity level

The CON group demonstrated significantly greater physical activity levels (number of steps, walk distance and calorie expenditure) compared to the PAD-IC groups over the seven day pedometer recording period (Table 6). The 12 month supervised exercise program had no significant effect on the physical activity levels of the TPAD-IC participants compared to the CPAD-IC and CON participants outside the supervised training sessions. However, at the end of the 12 month exercise program the TPAD-IC participants walked an additional 3.9 – 6.9 $km \cdot wk^{-1}$.

Table 5 Mean (±SD) walking performance and physiological responses values of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	**12 mth**	**0 mth**	**12 mth**	**0 mth**	**12 mth**
PFWT (sec)			115.9 (±99.5)	166.3 (±89.4)	132.8 (±61.1)	360.0 (±188.3)*†
MWT (sec)	1191.1 (±436.1)	1180.9 (±411.2)	283.2 (±183.3)‡	347.7 (±206.1)‡	335.5 (±140.2)‡	739.4 (±311.2)**‡††
HR_{peak} (beats·min^{-1})#	141.4 (±20.0)	131.7 (±18.7)	119.4 (±15.4)	108.6 (±12.8)	117.5 (±18.4)	116.4 (±19.7)
VO_{2peak} (ml·kg^{-1}·min^{-1})#	35.3 (±6.8)	29.5 (±6.3)	19.8 (±7.1)	19.7 (±4.3)	18.3 (±6.5)	18.5 (±7.2)
VE_{peak} (L·min^{-1})	58.6 (±22.5)	46.0 (±8.9)	38.3 (±14.6)	39.7 (±12.3)	45.4 (±23.3)	43.9 (±21.6)
RER_{peak}	0.93 (±0.07)	0.94 (±0.07)	0.88 (±0.14)	0.87 (±0.09)	0.95 (±0.16)	0.94 (±0.09)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients; PFWT, pain free walking time; MWT, maximal walking time; HR, heart rate; VO_2, oxygen uptake; VE, ventilation; RER, respiratory exchange ratio.
*P < .05, ** P < .01 vs. 0 mth
† < .05, †† vs. CPAD-IC 12 mth
‡P < .01 vs. CON
# P < .01 between group CON vs. CPAD-IC & TPAD-IC

Table 6 Mean (±SD) seven day physical activity levels values of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Steps#	45603 (±13157)	53037 (±22473)	31008 (±14637)	30131 (±15851)	18554 (±17519)	22657 (±15851)
Distance (km)#	30.2 (±9.3)	36.2 (±15.5)	16.3 (±7.9)	16.3 (±7.9)	9.9 (±10.4)	14.2 (±14.8)
Calories (kcal)#	1954.2 (±693.7)	2044.6 (±938.7)	1065.1 (±517.6)	1008.9 (±528.5)	653.2 (±575.6)	899.3 (±549.8)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients.
# $P < .01$ between group CON vs. CPAD-IC & TPAD-IC

Discussion

The purpose of this study was to investigate the effects of a 12 month supervised exercise program on individuals with PAD-IC. To our knowledge this study was the first to examine the lower limb mobility characteristics (temporal-spatial gait parameters and gait kinematics) of individuals with PAD-IC over a 12 month period. Because lower limb mobility characteristics have been shown to predict functional decline (Brach et al., 2002; Gill et al., 1995; Guralnik et al., 1995; Spirduso & Cronin, 2001) and fall risk (Daley & Spinks, 2000; Prince et al., 1997; Rubenstein et al., 2001; Sadeghi et al., 2002) it is very important to understand how PAD-IC affects patient lower limb mobility. The results of this study demonstrated that a 12 month supervised exercise program did not alter the lower limb mobility characteristics of PAD-IC patients. Gardner et al. (2001) speculated that exercise programs could be used to improve lower limb mobility in individuals with PAD-IC to the extent that their mobility characteristics more closely resemble that of healthy age matched controls. However, this view was not supported by our data. Studies that have reported increased lower limb mobility in healthy aged populations were exercise intensity and dosage dependant (Lopopolo, Greco, Sullivan, Craik, & Mangione, 2006). Thus, the exercise intensity and dosage adopted for the current study may not have been sufficient to elicit improved lower limb mobility in the PAD-IC patients. However, a more frequent or intense exercise program is unlikely to be feasible in practice. As in other studies we were only able to recruit a small proportion of the population of patients presenting with intermittent claudication and a more intense exercise program would potentially have made recruitment even more problematic. Temporal-spatial gait parameters and gait kinematics power values for this study ranged from low to moderate

for this sample size. This may demonstrate that the sample size was too small to show any significant changes in lower limb mobility.

Although lower limb mobility was not altered in TPAD-IC participants, the 12 month supervised exercise program produced significantly higher treadmill walking performance compared with baseline and the CPAD-IC participants at 12 months. This result is similar to previous studies on the effects of exercise programs on walking performance in this population (Ambrosetti, Salerno, Tramarin, & Pedretti, 2002; Gardner & Poehlman, 1995; Menard et al., 2004). However, there was no improvement in the physical activity levels (outside the supervised exercise sessions) of patients undergoing supervised exercise as assessed by 7 day pedometer measurements, although there was a trend in this direction (Table 6). We also found no changes in physiological responses (HR_{peak}, VO_{2peak}, VE_{peak} and RER_{peak}) for either of the intervention groups. The lack of improvement in physiological responses especially VO_{2peak} may have been due to the intermittent nature of the exercise program undertaken by the TPAD-IC patients. These participants were advised to cease walking when they reached a pain intensity of 3-4 on the CPS. This exercise regime would have had a limited impact on central adaptation processes underlying peak oxygen consumption.

The results of this study show that lower limb mobility and physiological responses may not be the mechanism underlying improved walking performance in PAD-IC patients following a supervised exercise program. The mechanism may be peripheral in nature for example, improved blood flow, mitochondrial oxidative capacity, skeletal muscle diffusive

capacity, capillary growth, and/or improved oxygen perfusion in the area of the arterial obstruction (Ernst & Matrai, 1987; Gardner et al., 2000; Lumsden & Rice, 2006; Slordahl et al., 2005). In our view another plausible mechanism could be the impact of adaptation to claudication pain with PAD-IC patients becoming more tolerant of claudication pain due to the progressive nature of exercise programs. Also lower limb mobility characteristics were only measured during pain free walking. Lower limb mobility may alter during the gradual onset of claudication pain and/or at maximal claudication pain levels.

Conclusion

The results of this study demonstrated that a 12 month supervised exercise program results in improved walking performance in PAD-IC patients but does not alter central physiological characteristics during exercise, reported physical activity levels or lower limb mobility during pain free walking. Power values for the temporal-spatial gait parameters ranged from low to moderate for this sample size. Future research should use larger sample sizes to increase the power for these variables. The improved walking performance may be due to peripheral physiological mechanisms and the effects of intensity and dosage of exercise.

Chapter 7

Effects of a long term exercise program on lower limb movement variability and walking performance in patients with peripheral arterial disease

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Journal of Biomechanics – under review

Abstract

The purpose of the study was to examine the effects of a 12 mth exercise program on walking performance and lower limb movement variability in patients suffering from intermittent claudication of the lower limbs resulting from peripheral arterial disease (PAD-IC). Participants (n = 21) with an appropriate history of PAD-IC, ankle brachial pressure index (ABI) <0.9 in at least 1 leg and a positive Edinburgh claudication questionnaire response volunteered for this study. Participants were randomly allocated to either a control group (CPAD-IC) (n = 11) which received normal medical therapy and a treatment group (TPAD-IC) (n = 10), which received normal medical therapy treatment and a 12 mth supervised exercise program. A further group of participants (n = 11) free of PAD (ABI >0.9) and who were non regular exercisers were recruited from the community to act as age and mass matched controls (CON). All participants underwent 2D joint angular kinematic analysis during normal walking to assess lower limb movement variability and walking speed. Intralimb coordination variability was measured using parameterization, vector coding and normalized root mean square techniques applied to relative motion plots of various joint couplings. Single joint movement variability was assessed using coefficient of variation. A graded treadmill test was used to assess walking performance. Between-group differences were analyzed via repeated measures ANOVA. The 12 mth supervised exercise program made no significant impact on the lower limb movement variability or walking speed of the TPAD-IC group as determined by either intralimb joint coordination or single joint analysis techniques. However, the TPAD-IC participants demonstrated significantly greater walking performance (171% improvement in pain free walking time and 120% improvement in maximal walking time). This study

demonstrated that lower limb movement variability is not related to walking performance of PAD-IC patients. Long term supervised exercise programs do not influence the lower limb movement variability of PAD-IC patients.

Introduction

Research concerning lower limb movement variability using joint angular kinematics of human locomotion is relatively incomplete compared to research involving lower limb mobility characteristics such as temporal-spatial gait parameters and gait kinematics in disease populations. The majority of lower limb movement variability research has examined factors such as age, risk of falls and the effects of lower limb injury (Buzzi et al., 2003; Hausdorff, 2005; Hausdorff et al., 1997; Heiderscheit et al., 2002; Pollard et al., 2005). However, research on populations with conditions such as diabetes induced neuropathy and multiple sclerosis is increasingly evident. This research has found that individuals with diabetes neuropathy multiple sclerosis and other conditions demonstrate higher levels of movement variability of the lower limbs which may be due to reduced walking speed (Crenshaw, Royer, Richards, & Hudson, 2006; Dingwell & Cavanagh, 2001; Dingwell & Cusumano, 2000; Jordan et al., 2007). However, Dingwell et al., (2001) pointed out that the gait movement pattern (i.e. speed) of patients with diabetes neuropathy may not only reflect the presence and level of neuropathy but may also indicate the motor control strategies that patients develop to compensate for sensory loss. Data collected in our laboratory on lower limb movement variability in patients presenting with symptoms of intermittent claudication caused by peripheral arterial disease (PAD-IC), indicates higher levels of movement variability in the lower limbs in this population. This movement variability may be due to adaptations of the motor control system in order to deal with perturbation(s) associated with the gradual onset of claudication pain.

PAD-IC is a common circulatory problem resulting from decreased blood flow and atherosclerosis in the lower limb arteries (Buzzi et al., 2003). The most common presenting symptom of PAD-IC is intermittent claudication with exercise induced pain experienced in the calves, thighs or buttocks that is relieved with rest (Beebe, 2001; Bendermacher et al., 2005). Compared to healthy age matched individuals, patients with PAD-IC demonstrate reduced lower limb mobility, walking performance, exercise induced physiological characteristics, physical activity levels, and perceived quality of life (QOL) (Crowther et al., 2007; Gardner et al., 2005; Gardner & Poehlman, 1995; Killewich, 2006; Regensteiner et al., 1997; Serracino-Inglott et al., 2007).

PAD-IC patients are usually treated conservatively with medications to reduce cardiovascular disease risk factors such as high blood pressure and cholesterol. For severe PAD-IC surgery is often the most appropriate treatment for QOL outcomes (Beebe, 2001; Dormandy & Rutherford, 2000; Regensteiner, 2004). Regardless of the initial treatment, PAD-IC patients are encouraged to increase their physical activity levels, thereby reducing the risk factors associated with the condition (Aronow, 2006; Collinson & Donnelly, 2004; Comerota, 2001; Lumsden & Rice, 2006).

Supervised exercise programs have been shown to be beneficial in improving walking performance and QOL in patients with PAD-IC (Ambrosetti et al., 2002; Gardner & Poehlman, 1995; Menard et al., 2004; Serracino-Inglott et al., 2007). To date there has been no research examining the effects of a long term exercise program on lower limb movement variability in any disease population. Furthermore there are many assessment

techniques used to determine lower limb movement variability, with no single method being classed as superior. These techniques include intralimb joint coordination (parameterization, normalized root mean square and vector coding) and single joint (coefficient of variation) techniques.

Therefore, the aim of this study was to examine the effects of a 12 mth exercise program on lower limb movement variability and walking performance in individuals with PAD-IC using both intralimb joint coordination and single joint techniques.

Methods

Participants

Patients referred to the Vascular Department at the Townsville Hospital with symptoms of intermittent claudication between January 2003 and June 2006 were screened for inclusion in the study. Participant selection criteria included an appropriate history of intermittent claudication, imaging confirmation of PAD on lower limb duplex or computed tomographic angiograph (CTA), and ability and willingness to attend for regular supervised exercise. Approximately 50% of patients attending our Vascular Department live >200 km away. Thus the main reason for excluding patients was inability to attend the program (n=48). Other reasons for exclusion included selection for surgical or endovascular intervention (n=30), patient preference (n=20) and requirement for mobility aids, obvious gait abnormalities (e.g. Steppage, vaulting, circumduction and hip hiking) or medical conditions which influenced gait (e.g. orthopedic conditions and neurological impairment) (n=20).

All patients were assessed by a consultant vascular physician. PAD-IC was confirmed by absence of peripheral pulses, lower limb artery stenosis or occlusion on duplex or CTA, ankle-brachial pressure index (ABI) <0.9 and positive Edinburgh Claudication Questionnaire response (Leng & Fowkes, 1992). Five participants withdrew from the study following baseline testing citing health, changed address and personal motivation reasons. Participants were randomly allocated using a single blind protocol to either a control (CPAD-IC, n = 11) or treatment group (TPAD-IC, n = 10). All participants were reviewed by a consultant physician to optimize their atherosclerosis risk factor management. Patients randomized to the TPAD-IC experimental condition also undertook a 12 mth supervised exercise program. A third group of participants (n = 11) free of PAD based on normal ABI and peripheral pulses and who were non regular exercisers were recruited from the general community via email bulletin boards, local newspaper and television coverage to act as age and mass matched controls (CON). Co-morbidity, medication and smoking history were determined at consultation by the vascular physician. All participants volunteered and gave written informed consent to participate in this study as approved by the institutional ethics committees. The descriptive characteristics of the participants are outlined in Table 1.

Procedure

Kinematics

Reflective markers were placed on the right side of the participant's body on five landmarks, the shoulder (acromion), hip (greater trochanter of femur), knee (lateral epicondyle of femur), ankle (lateral malleolus of fibula) and head of the 5th metatarsal. Participants then walked along a 10 m walkway while being filmed via a high-speed digital

video camera (Canon MV550i, Canon Australia, North Ryde, Australia) set at a frame rate of 50 Hz and placed 3 m perpendicular to the line of motion providing an uninterrupted video field. Joint angular kinematics were determined using SiliconCoach digitising software (Figure 1)(SiliconCoach Ltd, Dunedin, New Zealand) and Microsoft® Office Excel (Microsoft Corporation, North Ryde, Australia). Walking speed was calculated as the distance from successive initial ground contacts of the ipsilateral foot by the time of successive initial ground contacts.

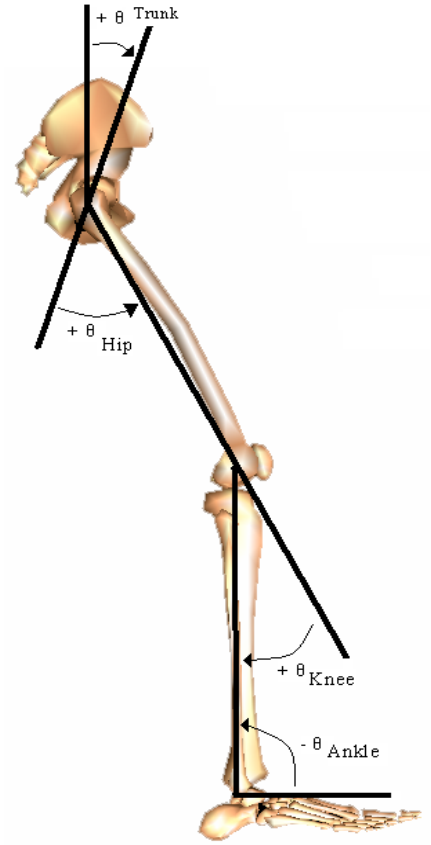

Figure 1 Sagittal plane angle convention

Treadmill testing

Following kinematics, participants undertook a graded exercise test on a treadmill (Trackmaster TMX55, Full Vision, Kansas, USA) for determination of walking performance. The graded treadmill walking protocol consisted of a constant speed of 3.2 $km \cdot h^{-1}$ and an incline of 0% for the first 2 min which was then increased by 2% every 2 min (Gardner et al., 1991a). Participant perception of exercise exertion was determined every 60 s via Borg's (1970) Rating of Perceived Exertion (RPE) scale while participant perception of claudication pain was determined via the 5-point (0=no pain, 1=onset of pain, 2= moderate pain, 3=intense pain, 4=maximal pain) Claudication Pain Scale (CPS)(American College of Sports Medicine, 2006). Walking performance was assessed as pain free walking time (PFWT) and maximal walk time (MWT) either by perceived maximal pain, volitional exhaustion or until 25 min of walking was achieved. Participants were permitted to hold the treadmill handrail if they required support whilst walking and a number of common motivational phrases (e.g. "you can make it", "keep walking") were used to encourage participants. Motivational phrase usage was standardized by noting the frequency and type of phrase used in pilot and preliminary testing. Exercise test termination criteria included voluntary exhaustion and significant abnormal ECG rhythm.

Data analysis

Combinations of intralimb joint and single techniques were performed on the joint angular kinematic data to determine lower limb movement variability. Data were analysed using custom software written in Matlab (Matlab 7 Release 14, The MathWorks, Inc. Natick, Massachusetts).

Intralimb joint coordination variability techniques

Parameterization

Parameterization is used to examine the area and perimeter of the shape of an angle-angle plot (joint coupling). This technique presents a quantitative characterization of normal gait and allows for clinical identification of pathological conditions and for patient progress through rehabilitation programs (Goswami, 1998).

Normalized Root Mean Square (NoRMS)

The NoRMS technique uses angle-angle plots to quantify joint coordination variability and stability changes in human movement (Sidaway et al., 1995). NoRMS involves calculating the root mean square of a series of angle-angle cycles and then normalizing the result with respect to the number of cycles and excursion of the mean plot (Equation 1). A high NoRMS value for an angle-angle plot indicates a greater variability in the joint coordination pattern.

$$NoRMS = 100 * \left(\frac{\sum_{j=1}^{k} \sqrt{\sum_{j=1}^{n} (\bar{x}_A - x_{Ai})^2 + (\bar{x}_B - x_{Bi})^2 / n_j}}{R} \right) \quad (1)$$

A & B denote the two variable, *k* is the number of cycles, *n* is the number of data points, R is the resultant excursion of the mean angle-angle curve over the entire cycle (estimated using the hip and knee corresponding to the maximum and minimum values at either the two joints), $\bar{x}$ is the mean position of a given variable at the *i*th data point and x is the position of a given variable at the *i*th data point on the *j*th cycle (Wheat & Glazier, 2006).

Vector coding

Vector coding (VC) also referred to as Encoded Chain Technique (ECT) was first employed by Freeman (1974) and later modified by Tepavac & Field-Fote (2001), involves placing an image of an angle-angle plot on a grid and the perimeter of the image is then encoded using an eight point scale based on the direction of the line between two consecutive data points (frame-frame interval) (Figure 2).

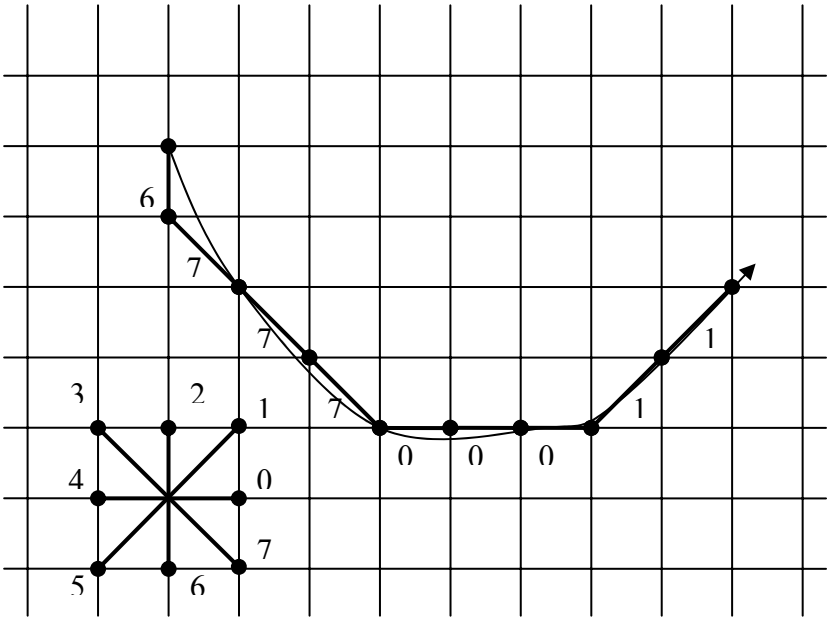

Figure 2 Vector coding technique

The magnitude and direction of the vector connecting the two points of the angle-angle plot is then calculated. The VC data is then used to identify high or low variability of the angle (a), magnitude (m) and vector (r) during cycles over multiple cycles. Higher mean (r) values indicate a more consistent (less variable) intersegmental relationship (Tepavac & Field-Fote, 2001). The advantage of the VC technique is that there is no requirement to normalize the data, thereby maintaining true spatial information. However, the

disadvantage is that VC only provides spatial information, with no consideration of temporal data (Hamill et al., 2000).

Single joint movement variability

Coefficient of variation

Winter (1984) calculated the coefficient of variation (CV) in a single joint mean ensemble curve in order to determine gait cycle movement variability. This calculation is an adaptation of the CV equation used in many fields of research (CV = (standard deviation/mean)*100%). The CV is calculated as follows:

$$CV = \frac{\sqrt{\frac{1}{N}\sum_{i=1}^{N} S_i^2}}{\frac{1}{N}\sum_{i=1}^{N}|X_i|} \quad (1)$$

Where S is the standard deviation of the mean gait cycle, x is the ith point on the mean gait cycle, and N is the number of points in the mean gait cycle. The higher the CV the more variable the mean gait cycle curve (Winter, 1984).

Supervised exercise program

The exercise program initially consisted of supervised treadmill walking 3 $d \cdot wk^{-1}$ for 25 mins at 3.2 $km \cdot hr^{-1}$. Participants were required to walk until the pain level was perceived as

being 3 or 4 on the CPS. Exercise intensity (via treadmill grade and walking speed) and duration (25 mins up to 40 mins) was progressively increased once the participant could walk without stopping for 25 mins below the pain CPS levels of 3 or 4. This exercise progression strategy was continued over the 12 mth period.

Statistical analyses

Statistical analysis was performed using the SPSS (SPSS Inc, release 14.0, Chicago, Illinois, USA) software program. Descriptive statistics were expressed as mean (±SD). Box-plot analyses were performed to identify extreme and outlier data. Data were analyzed using repeated measures ANOVA with one between-subjects factor (CON vs. CPAD-IC vs. TPAD-IC) and one within subject factor (Time - 0 vs. 12 mth). Post hoc analysis was performed using the Tukey HSD test. Medication and comorbidities data were analyzed using the nonparametric Friedman test and post hoc comparison using Nemenyi's test. An alpha level of .05 was adopted for this study.

Results

Participants

The groups were similar in age, height, mass, % body fat and BMI at baseline and no significant changes occurred over the 12 month study period (Table 1). As expected ABI values were higher in the CON group ($P < .001$) than both PAD-IC groups (Table 1). Both PAD-IC groups included a higher proportion of former smokers ($P < .05$) compared to the CON group. The CPAD-IC group contained a higher proportion of patients who had been prescribed beta-blocker medication ($P < .05$) compared to the TPAD-IC and CON groups

(Table 1). There were significant between group differences for walking speed for the CON group compared to the CPAD-IC and TPAD-IC groups (Table 1). There were no significant differences between the CPAD-IC and TPAD-IC groups at 0 and 12 months for walking speed. The 12 month supervised exercise program had no significant impact on walking speed of the TPAD-IC participants (Tables 1).

Table 1 Descriptive characteristics of participants

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Age (yr)	68.1 (±6.8)	69.4 (±6.9)	67.1 (±6.8)	68.1 (±6.8)	71.3 (±8.5)	72.3 (±8.5)
Height (cm)	167.8 (±8.2)	167.9 (±8.1)	165.6 (±8.7)	165.4 (±8.9)	165.7 (±8.9)	165.7 (±9.5)
Mass (kg)	70.7 (±8.4)	68.9 (±8.0)	74.5 (±18.9)	74.5 (±18.8)	80.7 (±15.3)	81.3 (±15.3)
Body fat (%)	31.6 (±9.5)	29.0 (±8.5)	30.4 (±8.6)	32.7 (±8.9)	33.1 (±9.0)	35.1 (±6.5)
BMI	25.2 (±3.2)	24.5 (±2.8)	26.9 (±5.3)	27.0 (±5.2)	29.2 (±4.1)	29.5 (±4.3)
ABI left leg#	1.18 (±0.16)	1.18 (±0.10)	0.64 (±0.22)	0.64 (±0.23)	0.72 (±0.22)	0.68 (±0.17)
ABI right leg#	1.16 (±0.13)	1.12 (±0.16)	0.69 (±0.27)	0.60 (±0.21)	0.71 (±0.23)	0.67 (±0.21)
Speed ($m \cdot s^{-1}$) #	1.3 (±0.2)	1.3 (±0.1)	1.1 (±0.2)	1.1 (±0.2)	1.1 (±0.2)	1.1 (±0.1)
Gender (% male)	45		45		50	
Current smoker (%)	0		27		10	
Former smoker (%)	27		64*		70*	
Type II diabetes (%)	0		27		10	
Hypertension (%)	9		36		30	
Ischaemic heart disease (%)	0		27		20	
Arthritis (%)	27		18		10	

Beta-blocker prescription (%)	0	45*	10

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients; ABI, Ankle/brachial index; BMI, Body mass index; Speed, calculation of stride length and stride time
Values are mean (±SD) or %
# P < .01 between group CON vs. CPAD-IC & TPAD-IC
* P < .01 vs. CON

Intralimb joint coordination

Parameterization, NoRMS & VC

Participants in all groups were analogous for all intralimb joint coordination techniques. The 12 mth exercise study had no effect on intralimb limb joint coordination variability in TPAD-IC compared to CPAD-IC and CON groups when assessed by NoRMS and VC techniques (Table 2 & 3). However, the NoRMS technique indicated a significant main effect differences for months at the hip-ankle and knee-ankle joint coupling. Parameterization also indicated no change in cycle area or perimeter of joint-joint couplings between the groups (Figure 3-5).

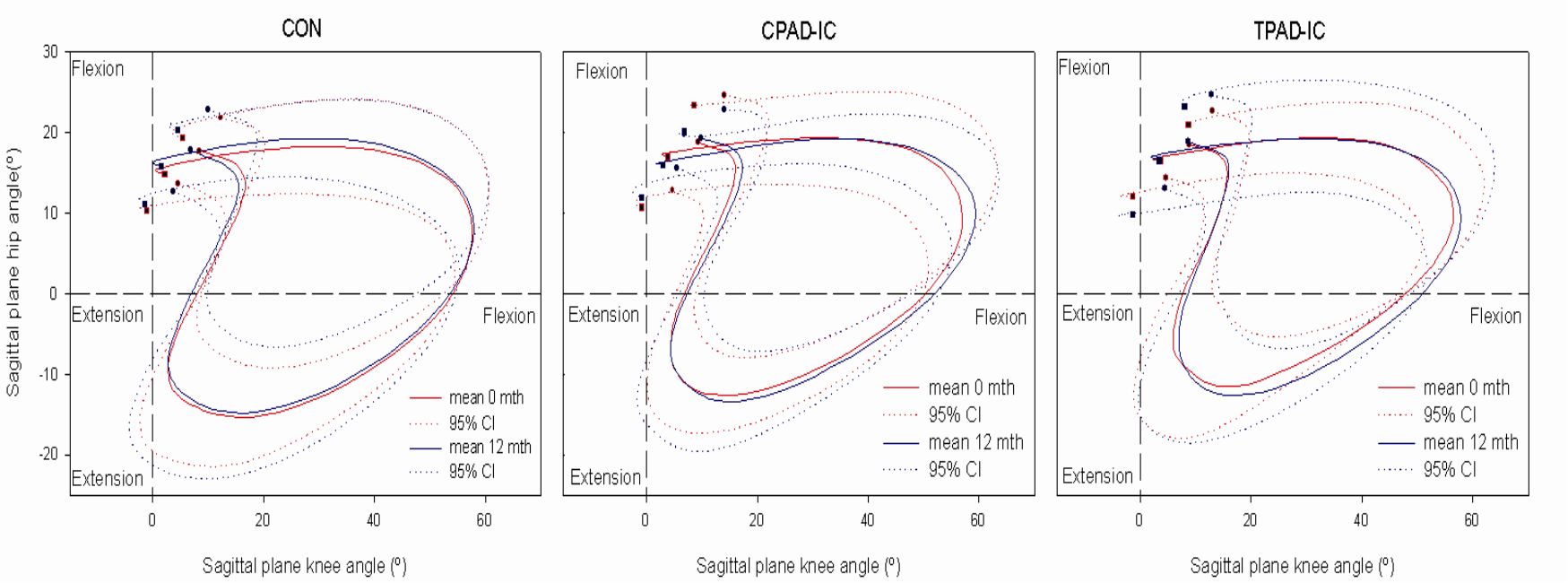

Figure 3 Hip-knee plot in the sagittal plane (CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients)

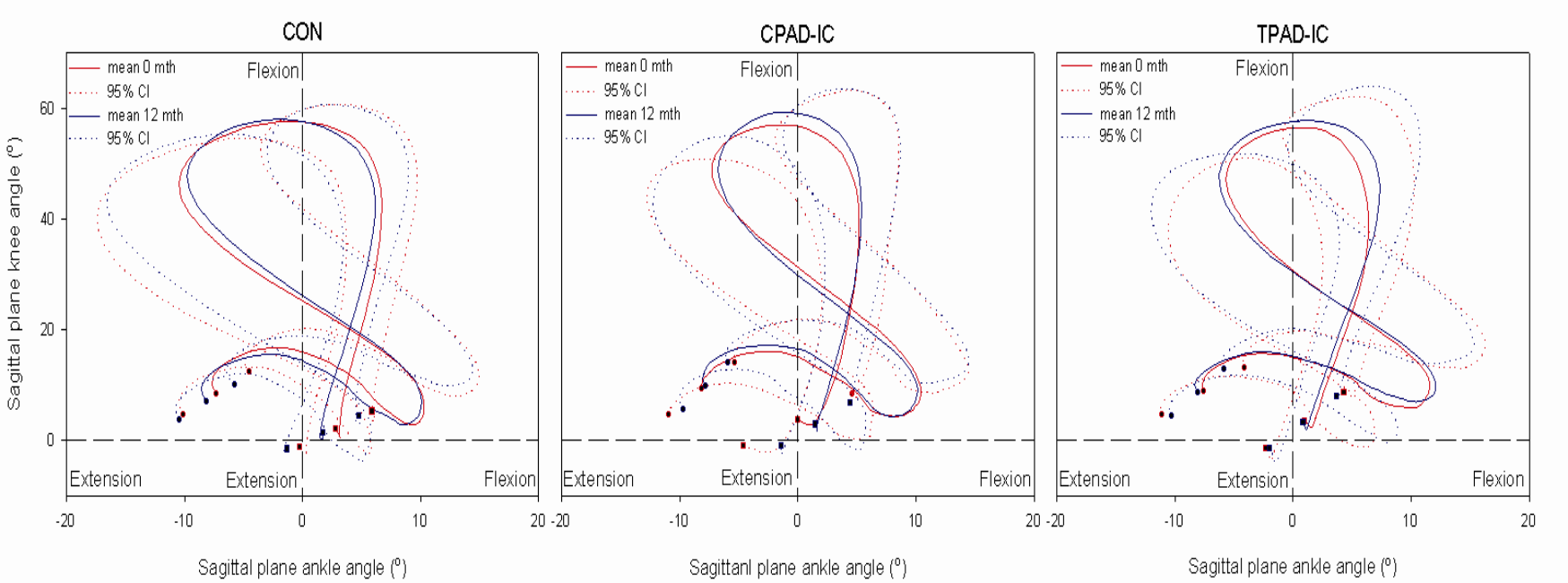

Figure 4 Knee-ankle plot in the sagittal plane (CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients)

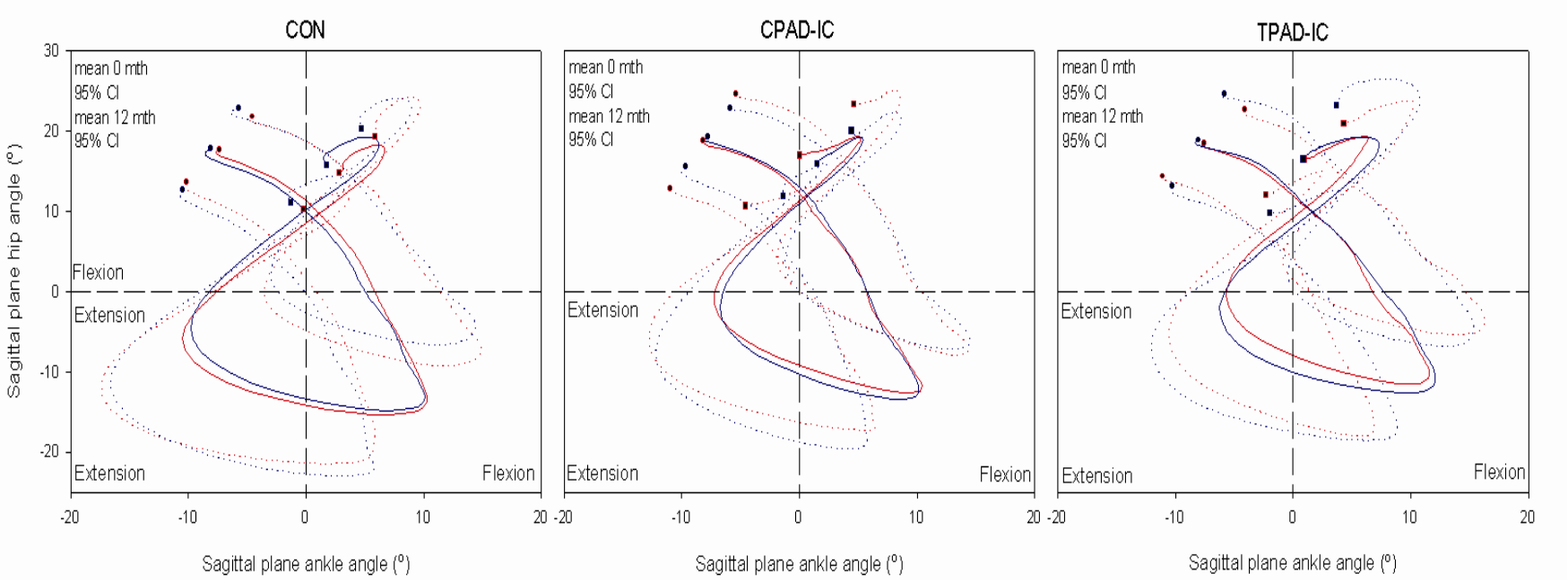

Figure 5 Hip-ankle plot in the sagittal plane (CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients)

Table 2 Mean (±SD) normalized root mean square values

Variable	CON (n =11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Hip – Knee	3.46 (±1.34)	3.14 (±0.90)	4.26 (±1.11)	3.88 (±1.48)	3.91 (±0.89)	3.58 (±1.12)
Knee – Ankle #	5.92 (±1.99)	5.49 (±1.00)	6.89 (±1.63)	5.36 (±1.01)	7.73 (±4.03)	5.60 (±2.16)
Hip – Ankle #	4.17 (±1.45)	3.72 (±0.96)	4.98 (±1.08)	4.12 (±1.26)	4.71 (±1.23)	3.95 (±1.01)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients
# P < .01 main effect months

Table 3 Mean (±SD) vector coding values

Variable	CON (n =11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
Hip – Knee	0.69 (±0.09)	0.69 (±0.07)	0.62 (±0.06)	0.63 (±0.10)	0.58 (±0.06)	0.64 (±0.05)
Knee – Ankle	0.63 (0.07)	0.61 (0.05)	0.57 (0.03)	0.60 (0.07)	0.58 (0.07)	0.59 (0.06)
Hip – Ankle	0.55 (0.07)	0.55 (0.07)	0.50 (0.05)	0.56 (0.07)	0.53 (0.10)	0.52 (0.06)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients

Single joint linear

CV

Single joint technique CV demonstrated not significant difference between the any of the groups for any of the lower limb joints (hip, knee and ankle). However, CV indicated a

significant main effect for months at the ankle. The 12 mth exercise program had no effect on single joint movement variability of the TPAD-IC group (Table 4).

Table 4 Mean (±SD) coefficient of variation values

Variable	**CON (n =11)**		**CPAD-IC (n = 11)**		**TPAD-IC (n = 10)**	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
(%) Hip	0.10 (±0.03)	0.09 (±0.03)	0.10 (±0.03)	0.09 (±0.03)	0.12 (±0.05)	0.10 (±0.05)
(%) Knee	0.07 (±0.03)	0.07 (±0.03)	0.09 (±0.03)	0.08 (±0.02)	0.07 (±0.02)	0.07 (±0.03)
(%) ankle #	0.26 (±0.09)	0.26 (±0.09)	0.34 (±0.10)	0.25 (±0.05)	0.30 (±0.11)	0.23 (±0.05)

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients
# $P < .01$ main effect months

Treadmill testing

The CON group demonstrated significantly greater MWT compared to the TPAD-IC and CPAD-IC groups. PFWT and MWT were significantly greater for the TPAD-IC group following the 12 month supervised exercise program compared to the CPAD-IC group (Table 5). The TPAD-IC group also demonstrated significantly improved PFWT and MWT at 12 month compared to baseline.

Table 5 Mean (±SD) walking performance values

Variable	CON (n = 11)		CPAD-IC (n = 11)		TPAD-IC (n = 10)	
	0 mth	12 mth	0 mth	12 mth	0 mth	12 mth
PFWT (sec)			115.9 (±99.5)	166.3 (±89.4)	132.8 (±61.1)	360.0 (±188.3)*†
MWT (sec)	1191.1 (±436.1)	1180.9 (±411.2)	283.2 (±183.3)‡	347.7 (±206.1)‡	335.5 (±140.2)‡	739.4 (±311.2)**‡††

CON, healthy age and mass matched controls; CPAD-IC, control peripheral arterial disease-intermittent claudication patients; TPAD-IC, treatment peripheral arterial disease-intermittent claudication patients; PFWT, pain free walking time; MWD, maximal walking time

*P < .05, ** P < .01 vs. 0 mth

† < .05, †† vs. CPAD-IC 12 mth

‡P < .01 vs. CON

Discussion

The purpose of this study was to investigate the effects of a 12 mth supervised exercise program on walking performance and lower limb movement variability in patients with PAD-IC using different methods of determining lower limb movement variability (intralimb joint coordination and single joint techniques). The results demonstrated that engaging in a supervised exercise program does not alter lower limb movement variability in patients with PAD-IC compared to PAD-IC patients undertaking typical medical treatment and healthy age matched controls. Furthermore, no significant differences were shown between the values derived by the different techniques used to calculate lower limb movement variability namely, intralimb joint coordination and single joint techniques.

Intralimb joint coordination assessment techniques are useful in describing movement variability in injury and pathology (Heiderscheit et al., 2002; Van Emmerik et al., 2005; Van Emmerik et al., 1999) however, they are imprecise in determining movement variability within joints. Therefore, single joint assessment techniques (e.g. coefficient of variation) should also be utilized to gain more specific information. Also, traditional linear techniques (single and intralimb coordination coupling) used to calculate movement variability may screen the structure of human motor variability, due to the use of average data masking variations in temporal data. However, in terms of the results of this study, the adoption of any one of these techniques may be problematic in the PAD-IC context.

PAD-IC patients who undertook the 12 mth exercise program demonstrated significantly improved walking performance in terms of PFWT and MWT. This result

is similar to previous studies on the effects of exercise programs on walking performance in this population (Ambrosetti et al., 2002; Gardner & Poehlman, 1995; Menard et al., 2004). However, walking speed was found to not change over the 12 mth period. The results of this study show that lower limb movement variability is not linked with improved walking performance in PAD-IC patients following a long term supervised exercise program. Research that has shown changes in lower limb movement variability has also shown changes in walking speed leading researchers to suggest that lower limb movement variability and walking speed are related (Crenshaw et al., 2006; Dingwell & Cavanagh, 2001; Dingwell & Cusumano, 2000; Jordan et al., 2007). The current study continues to validate this suggestion whereby both walking speed and lower limb variability did not alter due to a 12 mth exercise program.

These findings continue to support research conducted in our laboratory which showed that the lower limb mobility characteristics (temporal-spatial gait parameters and gait kinematics) of PAD-IC patients are not influenced by long-term exercise programs. Studies that have reported changes in lower limb mobility of healthy aged populations were exercise intensity and dosage dependant (Lopopolo et al., 2006). Thus, the exercise intensity and dosage adopted for the current study may not have been sufficient to elicit change in the lower limb movement variability of PAD-IC patients. However, a more frequent or intense program is unlikely to be feasible in practice and would potentially have made participant recruitment even more problematic due to the small proportion of the population (~6%) that this disease affects.

Conclusion

This study demonstrated that a 12 mth supervised exercise program will result in improved walking performance but has no effect on lower limb movement variability or walking speed in patients with PAD-IC. Future research should investigate the effects of varied intensity and duration of exercise on lower limb movement variability in PAD-IC patients and what this might mean for functional capacity and risk of injury (such as falls) in this population. Additionally research should investigate lower limb movement variability in other disease populations to improve understanding of the effects of chronic disease on lower limb movement characteristics. The choice of techniques used to assess lower limb movement variability appears to be dependant on the nature of the research question(s) being addressed.

Chapter 8

Summary, conclusions and recommendations

Summary

Peripheral arterial disease (PAD) is a common circulatory problem resulting from decreased blood flow and atherosclerosis in the lower limb arteries (Beebe, 2001; Bendermacher et al., 2005). Reduced blood flow to the lower limb muscles may result in leg pain/cramp at rest (indicative of severe PAD) or during exercise in PAD individuals. This pain, commonly called intermittent claudication (IC) usually subsides when the individual ceases physical activity (Meru et al., 2005). Research has shown that individuals with PAD-IC have reduced walking performance, peak physiological responses to exercise, lower limb mobility, physical activity levels and perceived health related quality of life (QOL) compared to healthy age matched controls (Breek et al., 2005; Breek et al., 2001; Gardner et al., 2001a; McDermott et al., 2006).

Previously only five studies investigated the effects of PAD-IC on lower limb mobility characteristics. These studies have led to conflicting results, with some research determining that individuals with PAD-IC walk slower, have slower cadence rates and smaller stride lengths due to an increase in double limb support and stride time (Gardner et al., 2001a; Scherer et al., 1998) while other studies have indicated no effect of PAD-IC on temporal-spatial gait parameters (McCully et al., 1999; McDermott et al., 2001; Scherer et al., 2006). However, none of these studies examined the mechanisms (i.e. joint angular kinematics) underlying the temporal-spatial gait parameters of

individuals with PAD-IC. Understanding of the interaction between temporal-spatial gait parameters and gait kinematics allows more precise classification of gait abnormality and its effects on lower limb mobility in any disease population. Gait kinematic analysis is becoming more commonly used as a clinical tool for evaluation of lower limb mobility in the elderly, lower limb disease populations and individual responses to exercise programs.

Increased movement variability in lower limb kinematics has been traditionally associated with decreased movement performance due to disease and aging. However, more recent research from a dynamical systems perspective has indicated that movement variability may be of functional importance in motor control and may provide flexibility when adjusting to movement constraints imposed by disease.

Gardner et al. (2001) speculated that the temporal-spatial gait parameters of individuals with PAD-IC could be improved by participation in exercise programs. To date there has been no attempt to determine the validity of this proposition. Therefore, for the purposes of this thesis, a series of studies were undertaken to investigate 1) the temporal-spatial gait parameters, gait kinematics, lower limb movement variability, walking performance, physiological responses and physical activity levels of individuals with and without PAD-IC and 2) the effects of a long term exercise program on these same variables in individuals with PAD-IC compared to individuals with and without PAD-IC.

Study 1 (Chapter 3)

The first study examined the lower limb mobility (temporal-spatial gait parameters and gait kinematics) of individuals with PAD-IC and the relationship between lower limb mobility, walking performance, exercise capacity and physical activity level in this population.

Lower limb mobility was determined via 2D motion analysis. A graded treadmill test was used to assess walking performance (pain free walking distance/time (PFWD/T) and maximal walking distance/time (MWD/T)) and peak physiological responses (VO_{2max}, HR_{peak} etc.) to exercise. Physical activity levels were measured via a 7 d pedometer recording following motion analysis.

The results showed that individuals with PAD-IC demonstrated reduced temporal-spatial gait parameters ($P < .05$), except for ipsilateral limb single support time. PAD-IC participants spent a greater percentage of time in gait support phases, took longer to complete a stride and had reduced stride length and walking speed during the gait cycle. The joint angular kinematics of the PAD-IC participants showed significantly reduced ankle plantar flexion ($P = .017$), knee ROM ($P = .021$) and hip extension ($P = .016$) compared to control (CON) participants during the gait cycle. All joint minimum and maximum angular velocities and accelerations, walking performance, physiological responses and physical activity levels were significantly lower for PAD-IC compared to the CON participants.

Study 2 (Chapters 4 & 5)

The purpose of this investigation was to compare lower limb movement variability through the use of intralimb joint coordination (Chapter 4) and single joint movement (Chapter 5) in individuals with and without PAD-IC.

All participants underwent 2D angular kinematics analysis during normal walking. Intralimb coordination variability was measured using parameterization, vector coding and normalized root mean square techniques applied to relative motion plots of various joint couplings. Single joint movement variability was measured using spanning set and coefficient of variation techniques.

The results indicated that participants with PAD-IC displayed significantly greater intralimb joint coordination variability than CON participants for all joint couplings using all intralimb joint coordination variability techniques. PAD-IC participants displayed significantly higher levels of lower limb movement variability in all joints when assessed using the coefficient of variation technique. There were no significant between group differences using the spanning set technique.

Study 3 (Chapter 6)

The aim of this study was to examine the effects of a 12 mth exercise program on the lower limb mobility of individuals with PAD-IC. A further aim was to examine the extent to which lower limb mobility contributes to long term exercise induced changes in walking performance, peak physiological responses and physical activity levels in PAD-IC patients.

Lower limb mobility was determined via 2D video motion analysis. A graded treadmill test was used to assess walking performance and peak physiological responses to exercise. Physical activity levels were measured via a 7 d pedometer recording.

The 12 mth exercise program had no significant effect on lower limb mobility, peak physiological responses or physical activity levels in PAD-IC patients who received normal medical therapy treatment and a 12 mth exercise program (TPAD-IC) compared to PAD-IC patients who received normal medical therapy (CPAD-IC). However, the TPAD-IC participants demonstrated significantly greater walking performance (171% improvement in PFWT and 120% improvement in MWT) compared with baseline.

Study 4 (Chapter 7)

The purpose this study was to examine the effects of a 12 mth exercise program on walking performance and lower limb movement variability in individuals with PAD-IC using both intralimb joint coordination and single joint techniques.

All participants underwent 2D joint angular kinematics analysis during normal walking. Intralimb coordination variability was measured using parameterization, vector coding and normalized root mean square techniques applied to relative motion plots of various joint couplings. Single joint movement variability was assessed using coefficient of variation. The 12 mth supervised exercise program made no significant impact on the lower limb movement variability of the TPAD-IC group. However, the TPAD-IC participants demonstrated significantly greater walking performance (171% improvement in PFWT and 120% improvement in MWT compared with baseline).

Conclusions

Based on the results of the studies conducted for this thesis, the following general conclusions are made regarding the biomechanical, physiological and walking performance characteristics of individuals with PAD-IC before and after participation in a 12 mth exercise program:

(a) Individuals with PAD-IC demonstrate reduced lower limb mobility (temporal-spatial gait parameters). Specifically the push off (or toe off) of the gait cycle is significantly reduced compared to healthy age matched controls.

(b) Individuals with PAD-IC demonstrate reduced walking performance (PFWD & MWD), physiological responses to exercise (VO_{2peak} and HR_{peak}) and physical activity level (assessed by pedometer recordings) compared to healthy age matched controls.

(c) Individuals with PAD-IC have significantly higher levels of lower limb movement variability as assessed by intralimb joint coordination and single joint assessment techniques. This may be related to constraint adaptation leading to reduced walking speed in an attempt to delay the onset of claudication pain.

(d) A 12 mth exercise program consisting of intermittent treadmill walking has no impact on lower limb mobility, physical activity level, physiological responses to exercise and resting ABI measures in patients with PAD-IC.

(e) A treatment program of normal medical therapy combined with a 12 mth exercise program results in improved walking performance (PFWT and MWT) in PAD-IC patients compared to baseline and healthy age matched control subjects.

(f) A 12 mth exercise program has no influence on the lower limb movement variability characteristics of PAD-IC patients as assessed by both intralimb coordination and single joint techniques.

Recommendations for further study

The research findings indicate that future studies:

- Should examine the effects of different exercise program intensities and dosage on the lower limb mobility characteristics of individuals with PAD-IC.

- Should determine if there is a relationship between lower limb stability and lower limb movement variability in individuals with PAD-IC.

- Examine the extent to which improved walking performance in PAD-IC affected individuals is due to increased adaptation to claudication pain as a by-product of the progressive nature of exercise programs.

- Examine the in-motion effects of different levels of claudication pain (onset to maximal) on the lower limb mobility and lower limb movement variability of individuals with PAD-IC.

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Appendix A

Queensland Government
Queensland Health

Townsville Health Service District

Institutional Ethics Committee

PATIENT CONSENT FORM

PROTOCOL NAME: Effect of intensive medical therapy on health-related quality of life in intermittent claudication

INVESTIGATORS: Associate Professor Jonathan Golledge, MA Mchir FRCS FRACS
Dr Anthony Leicht,
Associate Professor Warwick Spinks,
Professor Justin LaBrooy,
Associate Professor Francis Quigley, FRACS MS DDU

1. The nature and purpose of the research project has been explained to me. I understand it, and agree to take part
2. I have been given an Information Sheet which explains the purpose of the study, the possible benefits, and the possible risks.
3. I understand that I may not directly benefit from taking part in the trial.
4. I understand that, while information gained during the study may be published, I will not be identified and my personal results will remain confidential.
5. I understand that I can withdraw from the study at any stage and that it will not affect my medical care, now or in the future.
6. ** I understand the statement concerning payment to me for taking part in this study, which is contained in the Information Sheet.
7. I have had the opportunity to discuss taking part in this investigation with a family member or friend.

NAME OF SUBJECT: _____

SIGNED: _____

DATED: _____

I certify that I have explained the study to the patient/volunteer and consider that he/she understands what is involved

SIGNATURE OF INVESTIGATORS: _____

Townsville Health Service District

Institutional Ethics Committee

PATIENT INFORMATION SHEET

PROTOCOL NAME: Effect of intensive medical therapy on health-related quality of life in intermittent claudication

INVESTIGATORS: Associate Professor Jonathan Golledge, MA Mchir FRCS FRACS
Dr Anthony Leicht, Phd
Associate Professor Warwick Spinks, Phd
Professor Justin LaBrooy, MRACS
Associate Professor Francis Quigley, FRACS MS DDU

You have been invited to enter a study to assess the benefit of exercise and intensive medical treatment for your blocked arteries. It is up to you to decide if you would like to take part in this study. You may take as long as you like to decide and may want to discuss this with your local doctor and family.

The study may involve you visiting the hospital for regular treatments including supervised exercise, check-up on your blood pressure, control of the fats in your blood and help with giving up smoking (if required). You will also be asked to fill in questionnaires regarding your symptoms and you will undergo a number of blood tests and scans.

The aim of the study is to clarify how effective these treatments are to the health related quality of life of patients such as yourself. You will not be paid for participating in this study.

Any further information you require can be obtained for Associate Professor Jonathan Golledge, telephone 4796 1417. The Ethics Committee has approved this study at the Townsville Hospital. Should you wish to discuss the study with someone not directly involved, in particular in relation to matters concerning policies, information about the conduct of the study, or your rights as a participant, you may contact Dr Andrew Johnson at the Townsville Hospital.

INVESTIGATOR CONTACT NAME: Associate Professor Jonathan Golledge

INVESTIGATOR CONTACT TELEPHONE NO. (07) 4796 1417

DATED:

SIGNATURE OF CONTACT INVESTIGATOR:

Appendix B

Conference presentations

1. **Crowther, R.G.**, Spinks, W.L., Leicht, A.S., Sangla, K., Quigley, F. & Golledge, J. (2007). Effects of exercise rehabilitation on gait and exercise responses in peripheral arterial disease individuals. Paper presented to the 6th Biennial Australian and New Zealand Society of Biomechanics Australasian Biomechanics Conference, Auckland, New Zealand, February 15-17.

2. **Crowther, R.G.**, Spinks, W.L., Leicht, A.S., Sangla, K., Quigley, F. & Golledge, J. (2007). Effects of a 12 week rehabilitation program on gait variability in peripheral arterial disease individuals. Paper presented to the 6th Biennial Australian and New Zealand Society of Biomechanics Australasian Biomechanics Conference, Auckland, New Zealand, February 15-17.

3. **Crowther, R.G.**, Spinks, W.L., Leicht, A.S., Sangla, K., Quigley, F. & Golledge, J. (2007). Effects of 6 month exercise rehabilitation on gait & exercise responses in peripheral arterial disease. Paper presented to the 4th International Biomechanics of the Lower Limb in Health Disease & Rehabilitation Conference, Salford, Manchester, United Kingdom, September 3-5.

4. **Crowther, R.G.**, Spinks, W.L., Leicht, A.S., Sangla, K., Quigley, F. & Golledge, J. (2007). Effects of 6 month rehabilitation program on joint coordination variability in peripheral arterial disease patients. Paper presented to the 4th International Biomechanics of the Lower Limb in Health Disease & Rehabilitation Conference, Salford, Manchester, United Kingdom, September 3-5.