THE UNIVERSITY OF HULL

# Adaptations in plantarflexor muscle-tendon properties and their impact on gait in claudicants with peripheral arterial disease

being a Thesis submitted for the Degree of Doctor of Philosophy

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by

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**Thesis summary**

Peripheral arterial disease (PAD) is a chronic atherosclerotic disease, primarily affecting the lower limbs. The associated intermittent claudication (IC) is a muscle pain/cramping sensation in the legs, primarily brought on by physical activity, such as walking, which can negatively affect daily function and quality of life. Poorer levels of lower-limb muscle strength are strong predictors for mortality and the plantarflexor muscles in particular are a frequent site of claudication pain, with previous literature also indicating their dysfunction during level gait. However, little is known about the size and architecture of these muscles, the quality of the in-series Achilles tendon or the factors that contribute to voluntary joint moments and how these relate to physical function in this population. The aim of this thesis was to determine the functional properties of the gastrocnemii muscles and Achilles tendon in order to make evidence-based clinical recommendations for specific exercise interventions for claudicants.

A total of 23 participants (13 claudicants and 10 controls) took part in the study. Muscle-tendon dimensions and architecture, tendon properties, activation patterns and muscle strength, power and quality (specific tension) were assessed be integrating ultrasound imaging, electromyography and dynamometry. Stair gait biomechanics were analysed using 3D motion capture as indicators of whole body physical function. Within the claudicant cohort, disease severity was determined using the ankle brachial pressure index and walking performance assessed by a modified six-minute walk test. Average post-exercise ankle brachial pressure index of the claudicating-limbs were 0.55±0.21 with initial (onset of claudication pain) and absolute (maximal claudication pain) walking distances of 105±45m and 265±136m, respectively.

The first study investigated the relationships between the resting architecture of the gastrocnemii and functional properties of the Achilles tendon with disease severity and walking endurance. Worse disease severity was significantly associated with longer fascicle: tendon length ratios in both lateral (R=-.789, P=.001) and medial (R=-.828, P=<.001) gastrocnemius, and increased tendon hysteresis (R=-.740, P=.006). This suggests that the Achilles tendon has undergone deleterious changes and the muscle has adopted a structure designed to compensate for this. However, the concomitant associations with poorer walking endurance indicate this mechanism is not effective. Walking endurance could also be explained by lateral and medial gastrocnemius pennation angle, maximum tendon force, tendon hysteresis and disease severity ($R^2$=~0.6). The direction of coefficients within these models suggests that improving tendon properties and increasing strength, but without increasing pennation angle, would be beneficial for walking endurance. Thus, eccentric resistance training may be an effective exercise intervention.

The second study investigated relationships between static and dynamic muscle quality with disease severity and walking endurance. The power-producing capabilities of claudicants' plantarflexors (both the claudicating/painful limb and asymptomatic limb) were impaired compared to healthy controls, particularly at high contraction velocities (24% difference at 180°/s). This could be explained by some reduction in gastrocnemii muscle quality and a greater reliance on the prominently type I fibred soleus muscle. As reduced dynamic capability of the plantarflexor muscles was associated with disease severity (R=.541, P=.037) and walking endurance (R=.689, P=.006), high velocity resistance training of the plantarflexor muscles appears important to maintain functional performance.

The third and fourth studies investigated the functionally challenging daily tasks of stair ascent and stair descent, respectively. During stair ascent, plantarflexor moments were similar in claudicants compared to healthy controls, indicating the muscle could meet the strength demands of this task. We also observed that ankle angular velocity at the instant of peak moment, peak ankle power generation, as well as propulsive and vertical forces, were all reduced during forward continuance in the claudicating-limb group. It seems that claudicants possess adequate levels of strength when moving more slowly but are unable to remain strong when moving more quickly, therefore it could be suggested that the slower walking speed is a means to allow claudicants to operate within safer limits relative to their maximal strength capacity. This provides further evidence, in a functional context, of the velocity-dependent limitations of the plantarflexors detected in study two. During stair descent we hypothesised that the task demands would be redistributed away from the affected plantarflexors towards the muscles surrounding the hips and knees. Instead, the claudicants placed a greater reliance on the plantarflexors compared to healthy controls (40% vs 28% of plantarflexor contribution to peak support moment). Additionally, a unique hip extensor strategy was exposed during weight acceptance that was adopted by 73% of the claudicating-limb group, which was also associated with increased disease severity. However this was not a mechanism to reduce the functional demands on the plantarflexors but rather to reduce demands on the knee musculature. These data indicate the claudicants were relying heavily on the functionally limited plantarflexors to absorb the falling body mass during weight acceptance in stair descent, which may pose an increased risk of falling.

This thesis has identified important changes in the structure and quality of the gastrocnemii muscles and the properties and function of the Achilles tendon, that appear to influence whole body function during demanding and risky physical activities (stair negotiation) that necessitate alternate strategies. Taken as a whole, it is clear that high-velocity and eccentric resistance training would likely improve the musculoskeletal characteristics of claudicants, increase walking endurance and facilitate safe stair negotiation.

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## Dissemination

The work described in this thesis has been published as:

### a) Papers

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## List of Abbreviations

ABPI – Ankle brachial pressure index

ACD – Absolute claudication distance

AT – Achilles tendon

BMI – Body mass index

CoM – Centre of mass

CSA – Cross-sectional area

EMG – Electromyography

GL – Gastrocnemius lateralis muscle

GM – Gastrocnemius medialis muscle

GRF – Ground reaction force

GS – Gastrocnemii (combined gastrocnemius lateralis and medialis)

IC – Intermittent claudication

ICD – Initial claudication distance

MA – Moment arm

MTJ – Musculo-tendinous junction

MTU – Muscle-tendon unit

MVC – Maximal voluntary contraction

PAD – Peripheral arterial disease

PCSA – Physiological cross-sectional area

PRT – Progressive resistance training

TA – Tibialis anterior muscle

TE – Tendon excursion

# Chapter 1. Introduction

The UK population is ageing rapidly with 50% of the population predicted to be ≥50 years of age by 2024 (H.M. Government, 2010a). Peripheral arterial disease and intermittent claudication (PAD-IC) primarily affects the older population (Ostchega et al., 2007, Savji et al., 2013), therefore the prevalence of PAD-IC and subsequent care costs will likely rise in the near future. PAD-IC is atherosclerotic in origin, narrowing the arteries in the lower legs which often results in muscular pain/discomfort (intermittent claudication) primarily in the calf during even during light exercise, such as walking. The disease can severely limit physical activity levels, the ability to accomplish typical activities of daily living and quality of life.

Supervised exercise interventions are recommended by the National Institute for Health and Care Excellence (NICE) as a treatment for all those diagnosed with PAD-IC (National Institute for Health and Care Excellence, 2012) and the American College of Cardiology/American Heart Association specifically recommend walking therapy (Hirsch et al., 2006, Norgren et al., 2007). However, whilst walking therapy may improve a number of clinical outcome measures, such as walking endurance, there may well be additional functional deficits present in the population that are currently unidentified. There is contradictory evidence as to whether claudicants are inherently weaker than those without the disease and this likely stems from inconsistent methodology to assess muscle strength (Scott-Okafor et al., 2001, , McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012). Similarly, there is conflicting evidence about the efficacy of progressive resistance training (PRT) as an exercise modality and this may be related to a paucity of research comparing traditional aerobic-based interventions with evidence-

based targeted PRT programmes. Therefore it seems there is a lack of understanding of the specific deficits in muscle function in this population, which prevents the design of optimal and timely training interventions.

Numerous factors contribute to muscle 'strength' that have not been quantified in PAD-IC including muscle activation capacity, antagonist co-activation, intrinsic muscle quality and in-series tendon properties. Whilst muscle size has been previously reported, the methodology employed fails to account for the architectural characteristics of the muscle, which can play a substantial role in the ability to generate force. Some functional deficits have been established during level gait analysis that specifically implicate the plantarflexor muscles (Scott-Pandorf et al., 2007, Chen et al., 2008, Koutakis et al., 2010a, Wurdeman et al., 2012a), however the musculoskeletal mechanisms causing the dysfunction are unclear.

Any weakness or dysfunction in the muscles will have important consequences for many tasks of daily living, such as stair negotiation, which place a substantially increased demand on the muscles, particularly the plantarflexors. Given the limitations evident in this muscle group during level gait, reports of impaired balance (Gohil et al., 2013, Mockford et al., 2011, Gardner and Montgomery, 2001) and a greater prevalence of falls (Gardner and Montgomery, 2001) in those with PAD-IC, it is likely that this population also makes biomechanical adaptations to meet the requirements of stair negotiation. It is imperative to understand the specific impairments in muscle function and the biomechanical strategies claudicants employ to achieve the demanding task of stair negotiation in order to design effective evidence-based interventions.

# Chapter 2. Literature review

This Chapter will provide a detailed underpinning of peripheral arterial disease, musculoskeletal factors pertaining to muscle strength and stair negotiation biomechanics and review relevant literature from the PAD-IC population. The first section will focus on the functional abilities of those with peripheral arterial disease and the current treatment practices, notably exercise interventions. The second section will discuss the roles of muscle and tendon properties on measures of strength, and the final section will outline gait biomechanics during stair ascent and descent.

## 2.1 Peripheral arterial disease

### *2.1.1 Background*

Peripheral arterial disease (PAD) refers to a chronic disease of the peripheral arteries, primarily in the legs, resulting in a chronic reduction in the diameter of the arterial lumen (Levy, 2002). Atherosclerosis is the predominant cause of PAD (Hirsch et al., 2006) with ~90% of arterial problems in the lower limbs stemming from these obstructive plaques (Cimminiello, 2002). Intermittent claudication (IC) is a classic manifestation of PAD and refers to the muscular pain and/or discomfort, primarily in the calf muscles (Norgren et al., 2007), that is brought on by even low-moderate activities such as walking. Indeed the distances claudicants can walk before pain becomes maximal and forces the individual to cease walking can be as little as ~300m (McDermott et al., 2007, King et al., 2012). The disease predominantly affects older individuals; prevalence increases further with advancing age (Ostchega et al., 2007, Savji et al., 2013) and negatively impacts on functional ability (McDermott et al., 2001), physical activity levels (Garg et al., 2006) and quality of life (Spronk et al., 2007). Within the USA, a reported 12-20% of the

population ≥65 years were diagnosed with PAD with ~10% displaying typical IC symptoms (Roger et al., 2011). Similar statistics were reported in a large-scale European study of six countries, where incidence varied (from 7-28%) depending on nationality (Sanna et al., 2011) with prevalence of approximately 20% reported in the UK in those aged 55-75 years (National Institute for Health and Care Excellence, 2011). The presence of PAD is associated with risk factors typical for cardiovascular disease: higher body mass index, diabetes mellitus, smoking, hypertension and hypercholesterolemia (see Table 2.1). Higher rates of myocardial infarction, angina, stroke and cardiovascular related deaths are also evident in those with PAD compared to their healthy counterparts (Leng et al., 1996). The UK population is ageing rapidly with estimates that 50% of the population will be ≥50 years of age by 2024 (H.M. Government, 2010a). The consequence will likely be a proportional increase in the prevalence of PAD and subsequent costs to the NHS.

**Table 2.1.** Summary of demographics according to previously reported risk factors in patients diagnosed with PAD and healthy counterparts. All data are expressed as %.

| Study | | # | Male (%) | BMI (%) | DM (%) | Past Smoker (%) | Present Smoker (%) | HypT (%) | HypC (%) |
|---|---|---|---|---|---|---|---|---|---|
| (Skalkidis et al., 1989) | PAD | 100 | 88 | *NR* | 42 | 21 | 66 | *NR* | *NR* |
| | CON | 100 | 87 | | 6 | 19 | 36 | | |
| (Fowkes et al., 1992) | PAD | 73 | 49 | *NR* | 10 | 80* | | *NR* | *NR* |
| | CON | 1080 | 53 | | 6 | 59* | | | |
| (Price et al., 1999) | PAD | 64 | 54 | *NR* | *NR* | 53* | | *NR* | *NR* |
| | CON | 1044 | 48 | | | 31* | | | |
| (Murabito et al., 2002) | PAD | 118 | 51 | *NR* | 28 | *NR* | 55 | 65 | 30 |
| | CON | 2960 | 49 | | 9 | | 14 | 40 | 28 |
| (Alzamora et al., 2010) | PAD | 286 | 62 | 37 | 33 | 38 | 26 | 68 | 59 |
| | CON | 3295 | 44 | 37 | 14 | 26 | 17 | 44 | 46 |
| (Félix-Redondo et al., 2012) | PAD | 105 | 62 | 31 | 33 | 67* | | 74 | 67 |
| | CON | 2726 | 45 | 29 | 13 | 53* | | 38 | 38 |

*NR* – not reported, # - number patients, BMI – Body Mass Index >30, DM – Diabetes Mellitus, HypT – Hypertension, HypC – Hypercholesterolemia. * indicates past and current smokers combined.

*2.1.2 Identification of disease and assessment of severity*

Current guidelines by the National Institute for Health and Care Excellence (NICE) (National Institute for Health and Care Excellence, 2012), the American College of Cardiology/American Heart Association (ACC/AHA) (Hirsch et al., 2006) and the Trans-Atlantic Inter-Society Consensus for the management of PAD (TASC) (Norgren et al., 2007) stipulate diagnosis of peripheral arterial disease should incorporate a subjective history of walking impairment and symptoms of intermittent claudication as well as the clinical assessment using the ankle brachial pressure index/ratio (ABPI). The ABPI is a simple non-invasive measure giving the ratio between the systolic pressure of the dorsalis pedis or posterior tibial arteries and the systolic brachial artery. The test has been shown to be sensitive and specific for PAD (Fowkes, 1988), and associated with increased relative risk of adverse cardiac events and mortality (for a comprehensive summary see Caruana *et al.* (2005). Furthermore, low ABPI is associated with greater functional decline (McDermott et al., 2004a) and reduced lower limb strength (McDermott et al., 2008b). Conversely, there are signs of disparity between ABPI and clinical symptoms of IC (Stein et al., 2006), with reports that ABPI does not show improvement post-exercise intervention despite significant increases in functional ability (walking endurance) (Watson et al., 2008, Lane et al., 2014). In spite of these omissions, ABPI is often used to classify disease severity (Hirsch et al., 2006, McDermott et al., 2008b, Potier et al., 2011) and remains a frequently reported outcome measure in intervention studies.

### *2.1.3 Current treatment practice*

Current treatment strategies for claudication include pharmacotherapy (Aung et al., 2007, Bedenis et al., 2014), exercise therapy (Bendermacher et al., 2006, Lane et al., 2014), percutaneous transluminal angioplasty (Chowdhury et al., 2014) and surgery (Kakkar and Abbott, 2015, Conte et al., 2015). A recent systematic review determined medical/pharmacological intervention was inferior to exercise therapy, angioplasty and open surgery (Malgor et al., 2015). However, surgery is often associated with lengthy hospitalisation (Malgor et al., 2015) and indicated primarily for those with significant disability that are unresponsive to previous exercise and/or pharmacotherapy (Hirsch et al., 2006). Whilst, revascularisation can illicit more immediate improvements in functional ability and quality of life, long-term effects are not necessarily sustained compared to exercise therapy (Fowkes and Gillespie, 2000, Spronk et al., 2009). Guidelines proposed by NICE state that a supervised exercise programme is offered to all individuals diagnosed with PAD-IC (National Institute for Health and Care Excellence, 2012), however it is clear from the literature that no gold standard exercise intervention protocol has been established (King et al., 2012).

### *2.1.4 Exercise therapy for PAD-IC*

The ACC/AHA and TASC recommend walking therapy for treatment for PAD-IC (Hirsch et al., 2006, Norgren et al., 2007) which is supported by meta-analyses (Gardner and Poehlman, 1995, Wind and Koelemay, 2007) and Cochrane reviews (Watson et al., 2008, Lane et al., 2014) advocating this mode of exercise. However, the vast majority of research focuses on aerobic exercise; 89% of trials reported in a recent systematic review investigated walking and lower extremity aerobic exercise with only three studies/trials comparing aerobic

exercise to progressive resistance training (PRT) and one investigating PRT alone (Parmenter et al., 2011). Whilst PRT is currently not viewed as effective as traditional walking therapy (Parmenter et al., 2011), this mode has been shown to improve knee extensor strength and quality of life (McDermott et al., 2009a), as well as walking endurance and capillary density (McGuigan et al., 2001a). More recently, a high-intensity PRT elicited substantial increases in walking distance and both calf and hip muscle strength and endurance (Parmenter et al., 2013a). The disparity in the literature between the effectiveness of PRT and bias towards investigation of aerobic-based interventions may stem from the inconsistent protocols employed in previous PRT studies, confounding the potential for consistent evaluations of this mode of exercise. The rationale for the selection of exercises within PRT protocols is also unclear, most likely because of the lack of knowledge of the musculoskeletal impairments regarding the ability to generate and transmit muscle force into functional strength.

### *2.1.5 Functional impact of PAD-IC*

The presence of PAD-IC has detrimental effects on a multitude of factors. It is well established that PAD-IC is associated with poorer quality of life (Chetter et al., 1997, Izquierdo-Porrera et al., 2005, Regensteiner et al., 2008), reduced daily physical activity levels (Garg et al., 2006, McDermott et al., 2011) and substantially reduced walking endurance (McDermott et al., 2002, McDermott et al., 2004a) with disease progression associated with further declines in physical function. There is also evidence for impaired peroneal nerve function (McDermott et al., 2004c, McDermott et al., 2006b), contradictory reports of fibre-type shifting in the plantarflexors towards more type II (McGuigan et al., 2001b, Askew et al., 2005, Gasparini et al., 2012) and conversely more type I fibres

(Regensteiner et al., 1993, Steinacker et al., 2000) as well as indications of intra-muscular fat infiltration in the calf (Raval et al., 2012).

However, despite these musculoskeletal adaptations and clear deteriorations in physical function, few studies have directly compared muscle strength between claudicants to healthy controls. Furthermore there are some disparities between the four studies that have made direct comparisons (Scott-Okafor et al., 2001, McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012). There are indications of reduced isometric and isokinetic dorsiflexor strength (Scott-Okafor et al., 2001, Camara et al., 2012), reduced isometric hip extensor and hip flexor strength (McDermott et al., 2004b) but inconsistencies regarding the strength of the plantarflexors (Scott-Okafor et al., 2001, McDermott et al., 2008b, Camara et al., 2012), and knee extensors (McDermott et al., 2008b, Camara et al., 2012). The ability to draw valid conclusions is further hampered by different strength testing techniques; isokinetic dynamometry (Scott-Okafor et al., 2001, Camara et al., 2012) and musculoskeletal strength chairs (McDermott et al., 2004b , McDermott et al., 2008b), as well as joint configurations; hip and knees flexed to 90° (Scott-Okafor et al., 2001), hip in neutral and knee flexed to 45° (Camara et al., 2012) and no joint configuration reported (McDermott et al., 2004b McDermott et al., 2008b).

Poorer levels of muscle strength are strong predictors of mortality (Singh et al., 2010, McDermott et al., 2012) with reduced lower limb strength also associated with faster functional decline (Herman et al., 2009). However, the underlying mechanism(s) explaining these possible disease induced strength losses have not been identified, and it is not known

if/how deleterious adaptations in the muscle and tendon properties occur and contribute to reduced functional ability. The understanding of these mechanisms is essential to design appropriately targeted exercise interventions specific to PAD-IC patients.

### 2.2 Factors influencing muscle strength and function

Muscle strength is dependent on multiple factors: muscle size and architecture, voluntary activation capacity, antagonist co-activation, muscle quality, moment arm length and the properties of the in-series tendon. The following section will discuss each individual variable based on the planometric musculoskeletal models depicted in Figures 2.1 and 2.3.

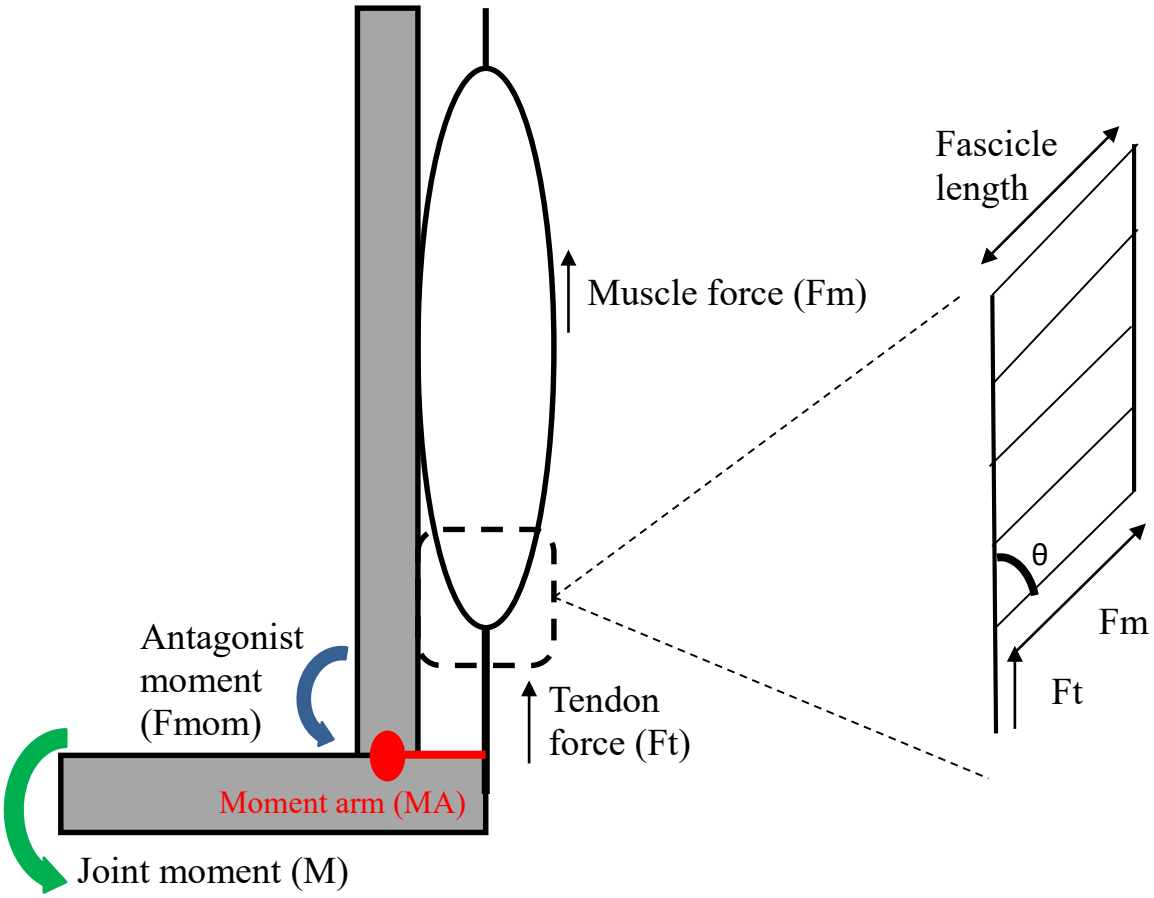


**Figure 2.1.** Musculoskeletal model schematic depicting the factors contributing to plantarflexion MVC

*2.2.1 Muscle size*

Broadly, the dimensions of a muscle are directly proportional to the maximum force and power it can exert. Power is dependent on the mass, or volume of the muscle (Lieber, 1992). However, maximal muscle force is more dependent on the arrangement of the material within the muscle (Lieber, 1992). The physiological cross-sectional area (PCSA) accounts for muscle volume, fascicle length and pennation angle (Figure 2.2). It is quantified as the sum of the cross-sectional areas (CSA) of all the muscle fibres and determines maximal force (Lieber & Friden, 2000). In functionally important anti-gravity muscles, such as the gastrocnemii, soleus and quadriceps, PCSA differs from the anatomical CSA (ACSA) measured in the transverse-plane as it accounts for the angle at which muscle fascicles insert to the force-generating axis (Figure 2.2) (Narici et al., 2003).

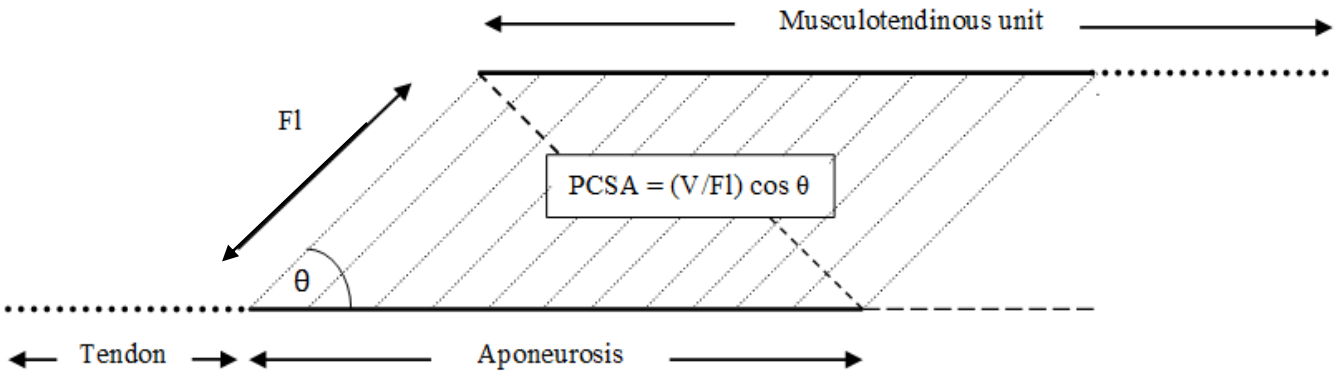


**Figure 2.2.** Musculoskeletal schematic depicting the calculation of muscle PCSA. *Fl* – fascicle length, *V* – muscle volume, $\theta$ – pennation angle

With healthy ageing, gastrocnemii PCSA reduces (Narici et al., 2003, Morse et al., 2005b, Stenroth et al., 2012) which is accompanied by corresponding reductions in plantarflexor strength (Morse et al., 2005b, Onambele et al., 2006, Thom et al., 2007, Stenroth et al., 2012). In PAD-IC, muscle anatomical CSA (ACSA) has been quantified using computed tomography to assess proportions of muscle, fat and bone from a single slice through the muscle belly (McDermott et al., 2007, Garg et al., 2011, McDermott et al., 2012, Raval et al., 2012). Those with low ABPI (high disease severity) possess calves with lower ACSA's, higher fat percentages and accordingly, reduced physical function (McDermott et al., 2007). A recent finite-element model analysis of intramuscular fat infiltration of the gastrocnemius demonstrated that fatty musculoskeletal models had reduced fibre stress, force generation and subsequently reduced muscle quality (Rahemi et al., 2015). This is congruent with previous investigations into obese claudicants. Raval et al. (2012) reported associations between claudicants with higher body mass index, lower calf muscle density and higher fat percentages indicate poorer muscle quality in obese participants due to intramuscular fat infiltration. However, to date muscle architecture or PCSA have not been quantified. Therefore, whilst previous CT technique have provided relationships between muscle and fat content within the calf, important information regarding the arrangement of the material content of the muscle is missed and the potential adaptations that may explain reductions in physical function remain unidentified.

### *2.2.2 Muscle architecture*

The "design" of a muscle plays an important role in its function. The pennation angle provides a mechanism for increasing PCSA without increasing the overall mass of the muscle by allowing room for 'fibre-packing' to occur (Gans & Gaunt, 1991) and can change in

response to training, disuse and ageing (Kawakami et al., 1995, Narici et al., 2003, Morse et al., 2005a, de Boer et al., 2007a, Seynnes et al., 2007).

During muscle contraction in a pennate muscle, fascicles shorten, rotate and pennation angle increases therefore only the vector resultant of the force produced by the fascicles to the line of action will contribute to the tendon force, and consequently joint moment (Gans & Gaunt, 1991, Narici et al., 1996). Fascicle length has a direct effect on the utilised portion of the force-length relationship of the sarcomeres, and therefore the force-producing capability of the muscle. For a given change in total muscle-tendon length, a sarcomere in a muscle-tendon unit possessing a longer fascicle: tendon length ratio will undergo less shortening. In the case of the gastrocnemii that operate on the ascending limb of the force-length curve (Maganaris, 2003, Winter & Challis, 2010), less sarcomere shortening places the sarcomere closer to the plateau region and therefore closer to optimal length for force production (Arnold & Delp, 2011). A longer fascicle also allows a greater force generation across larger ranges of motion and at higher contraction velocities, due to reduced individual sarcomere effort (Lieber & Friden, 2000).

With healthy aging, maximum velocity and maximum power both decrease compared to younger counterparts (for a comprehensive review see Raj et al., 2010). In both the force-velocity and power-velocity relationships, there is a rightward and downwards shift in the curve with ageing (Thom et al., 2007, Raj et al., 2010). Part of these reductions could be attributed to the associated alterations in muscle architecture seen in healthy ageing. As power generation is a function of the number of sarcomeres in parallel and in series, it is not

surprising that the summative effect of age-related reductions in both pennation angle and fascicle length results in substantial reductions in power. Investigations into the functional impact of age-related declines in power revealed associations between reduced power and the poorer performance in the short physical performance battery (Bean et al., 2002) and the 6-minute walk test (Puthoff and Nielson., 2007) as well as slower maximal and habitual walking speed (Suzuki et al., 2001). Whilst correlations do not necessarily imply causation, the growing body of evidence indicates a strong relationship between power and functional capacity. The force-velocity and power-velocity relationships in those with PAD-IC have not yet been explored. However, reductions in functional capacity have been documented (see section 2.1.5) and reductions in joint power observed during level walking (Wurdeman et al., 2012a), therefore alterations in these velocity-dependent parameters may exist in claudicants and offer some explanation for these previous findings.

The architecture of a muscle clearly has a substantial effect on the ability to generate maximal force. However, these variations in sarcomere behaviour during contraction can also affect the metabolic cost of muscle contraction, which is pertinent in the claudicant population. A longer fascicle, which results in smaller individual sarcomere length changes and shortening speeds, would allow for less energy consumption per unit of muscle force (Beltman et al., 2004). In an ischemic environment, where metabolic energy is at a premium, adaptations that may conserve energy will likely be beneficial. Currently, nothing is known about adaptations in muscle architecture in claudicants, and what the implications may be for force generation to maintain functional ability, or metabolic efficiency to allow for prolonged muscle activity.

*2.2.3 Intrinsic muscle quality (specific tension)*

The maximal force a muscle is capable of producing is equal to the product of its PCSA and the specific tension of the muscle. Specific tension is defined as the force producing potential per unit area of the muscle and is the index of intrinsic strength, i.e. muscle quality. Muscle quality is known to reduce with ageing (Morse et al., 2005b, Suetta et al., 2009), disuse (Suetta et al., 2009) and increase in response to resistance training (Reeves et al., 2004b, Morse et al., 2007, Suetta et al., 2009, Erskine et al., 2011). For optimum measures of muscle quality, information regarding each individual component that contributes towards maximum muscle force (MVC, activation capacity and antagonist co-activation) and muscle size (volume, fascicle length and pennation angle) must be quantified and accounted for. Currently, only plantarflexor MVC and single-site CSA has previously been quantified in those with PAD-IC, therefore the quality of claudicant plantarflexors is unknown, as are possible variations in the multiple factors that contribute to maximum muscle force.

*2.2.4 Muscle activation*

Muscles are rarely, if ever activated fully, and as such the level of neural activation modulates the actual muscle force produced. Agonist activation capacity, quantified through electrical stimulation (Rutherford et al., 1986, Behm et al., 2001) reduces with ageing (Morse et al., 2004, Morse et al., 2005b, Kubo et al., 2007b) and immobilisation (Suetta et al., 2009), and increases post-PRT intervention in the elderly (Reeves et al., 2004b, Reeves et al., 2004c, Morse et al., 2007) with these increases attributed to more motor units being activated and/or increases motor unit discharge rates (Patten et al., 2001).

Co-activation of the antagonist muscle group reduces the net joint moment. However the effect of ageing is less conclusive. There are indications that co-activation of the dorsiflexors is reduced (Simoneau et al., 2005) or comparable (Morse et al., 2004) in the elderly, and sex-specific reports of increased co-activation post-PRT intervention in elderly women (de Boer et al., 2007b) and comparable co-activation in males (Morse et al., 2007).

Neither agonist nor antagonist activation levels have previously been measured in claudicants, although neuropathies have been identified. With PAD-IC, peroneal nerve function is impaired (McDermott et al., 2004c, McDermott et al., 2006b), however this nerve primarily supplies the anterior aspect of the lower leg and may well offer explanations for reduced dorsiflexor strength observed in this population (Scott-Okafor et al., 2001, Camara et al., 2012). Despite not being previously reported, it may be that the tibial nerve that innovates the plantarflexors is also impaired. Furthermore, the alterations in peroneal nerve function may also impact on the co-activation of the dorsiflexors during plantarflexor contractions. Increased co-activation would result in reduced movement efficiency since agonist muscles would have to work harder to generate the required joint moments.

### *2.2.5 Tendon properties*

Work performed by the muscle is transferred via tendons to produce a resultant joint action, therefore the properties of the tendon play a key role in the appropriate transmission of force and movement (Figure 2.3). *In vitro* studies have established reductions in collagen fibril crimp angle, increases in elastin, reductions in extracellular water and increases in type V collagen, which all act to decrease the stiffness of the tendon in the ageing tendon (Narici &

Maganaris, 2006, Magnusson et al., 2008). *In vivo s*tudies have shown that strain (Kubo et al., 2003, Kubo et al., 2007a, Kubo et al., 2007b) stiffness (Kubo et al., 2003, Onambele et al., 2006, Stenroth et al., 2012) and Young's Modulus (Onambele et al., 2006, Stenroth et al., 2012) are significantly reduced in an aged tendon compared to younger counterparts. However these changes can be offset through training (Kubo et al., 2001, Kubo et al., 2003, Reeves et al., 2003a, Reeves et al., 2003b, Reeves et al., 2005b) due to the exercise stimulus imparting increased load and consequently strain onto the tendon.

When tendons are elongated they store elastic energy that is then recovered during shortening, or recoil, and contribute to the work required for the next joint action (Peltonen et al., 2013). However, tendons are not perfectly elastic and some energy is lost prior to recoil. This is known as hysteresis and the energy lost is expressed as a percentage of energy stored. Hysteresis values of in vivo human tendons have been observed to range between 18-32% (Kubo et al., 2003, Reeves et al., 2003b) and greater hysteresis has been observed in ageing populations (Reeves et al., 2006), as a result of disuse (Kubo et al., 2004) and following stroke (Zhao et al., 2009). Any deterioration of claudicant tendons may include increased hysteresis.

During muscle contraction the tendon lengthens and muscle shortens. However when tendon stiffness is low, the tendon stretches further and therefore the muscle shortens further (Figure 2.3). This modulates the fascicle length during contraction at any given joint angle and consequently alters the pattern of the force-length relationship for the whole muscle-tendon unit. Moreover, changes in tendon stiffness can also impact the shape of the force-velocity

relationship. First, peak force occurs at greater muscle-tendon lengths during isometric contractions than high velocity concentric contractions (Kawakami et al., 2002), and this effect is amplified when tendon stiffness is reduced. Second, when force is generated rapidly from rest the tendon elongates as load increases, this diminishes the transmission of muscle force to generate a joint moment. Associations between tendon stiffness, rate of force development and electro-mechanical delay have been documented in both older adults (Reeves et al., 2003a) and younger adults (Bojsen-Moller et al., 2005). It is clear that tendon stiffness is of particular importance in the ability to execute rapid tasks, such as absorbing the falling body weight during stair descent.

For PAD patients, operating in an ischemic environment, an Achilles tendon that does not utilise this mechanism to increase efficiency of movement would have adverse consequences on mobility. There appears to be some support for the likelihood of impaired tendon properties in claudicants, since previous case studies have reported spontaneous tendon rupture due to ischemia (Shukla, 2002, Jain & Dawson, 2007). Although the exact mechanisms responsible for these ruptures remain unclear, it is known that the most commonly injured region (mid-portion) of the tendon coincides with the primary area of reduced blood supply (van Dijk et al., 2011). Therefore, it could be postulated that PAD-IC causes changes in the tendon's structure and/or mechanical properties that predispose it to a greater risk of injury.

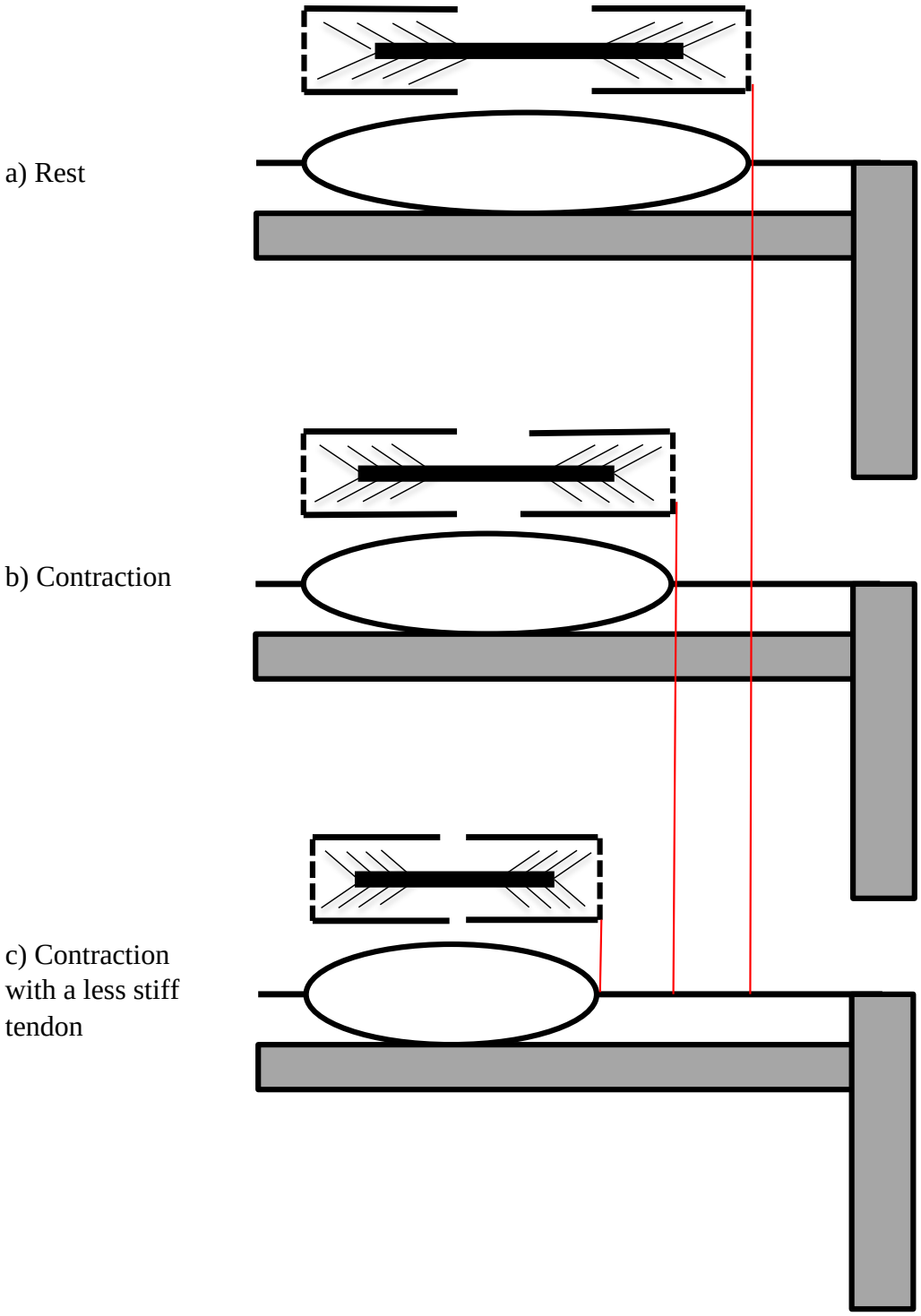


**Figure 2.3.** Influence of tendon stiffness on changes of a representative sarcomere length during contraction. During muscle contraction the tendon elongates, with a magnitude inversely proportional to its stiffness, and the muscle shortens (a-b). When stiffness is low (c) the tendon stretches further, meaning muscle shortens further. This alters the region of the force-length relationship utilised by the sarcomeres and therefore influences the force generation potential of the muscle.

*2.2.6 Moment arm*

Moment arm (MA) is defined as the perpendicular distance from the line of action of the tendon force to the centre of rotation (Hammill & Knutzen, 2009). Two techniques are frequently employed to assess MA length *in vivo.* The centre of rotation technique utilises MRI images to locate the centre of rotation (COR) for the perpendicular distance from it to the action line to be measured (Maganaris et al., 1998a, Maganaris et al., 2000, Maganaris, 2004, Fath et al., 2010). Alternatively, the tendon excursion (TE) method for estimating moment arm uses ultrasound imaging to derive the changes in tendon position in relation to changes in joint angle (Ito et al., 2000, Maganaris et al., 2000, Maganaris and Paul, 2002, Fath et al., 2010). Whilst the TE method generates MA lengths smaller than those obtained via COR techniques, there is good agreement between the two methods and the TE values are similar to those obtained via cadaver studies adopting a similar method to TE (Spoor et al., 1990), suggesting these values may be a closer representation to true Achilles MA length.

The magnitude of joint moment is tempered by the length of the MA; for a given tendon force, a longer moment arm would increase the resultant joint moment (Hammill & Knutzen, 2009). However a longer moment arm would also result in greater fascicle excursion, therefore resultant joint power will decrease at high contraction velocities (Nagano & Komura, 2003). Moment arm length is known to change as a function of joint angle and contraction state with MA length increasing when the ankle is more plantarflexed and during MVC (Maganaris et al., 1998a, Maganaris et al., 2000, Fath et al., 2013). The is no indication that MA length is affected by ageing (Morse et al., 2005b, Onambele et al., 2006) and there is no reason to believe that MA will alter due to the presence of PAD-IC, however this parameter is yet to be quantified.

## 2.3 Stair negotiation

Whilst the quantification of musculoskeletal adaptations in response to ageing/disease and intervention is essential to understand the mechanisms for alterations in muscle strength, it is vital to understand how these mechanisms influence whole body function and explore potential compensatory strategies during typical daily tasks. Within PAD-IC, gait mechanics during level walking has previously been investigated. There are clear signs of plantarflexor dysfunction with reduced ground reaction forces (GRF), plantarflexor moment and ankle power generation observed at push-off in both the absence and presence of claudication pain (Scott-Pandorf et al., 2007, Chen et al., 2008, Wurdeman et al., 2012a, Koutakis et al., 2010a). However, the muscular demands of level gait are reduced compared to other activities of daily living such as stair negotiation (Nadeau et al., 2003, Tiedemann et al., 2007). Therefore the ability of the plantarflexors to perform adequately during this more challenging task may also be impaired and consequently may impact on the risk for falling.

### *2.3.1 Stair ascent*

The task of stair ascent can be characterised by five phases depicted in Figure 2.4: weight acceptance, pull-up, forward continuance, foot clearance and foot placement (McFadyen & Winter, 1988).

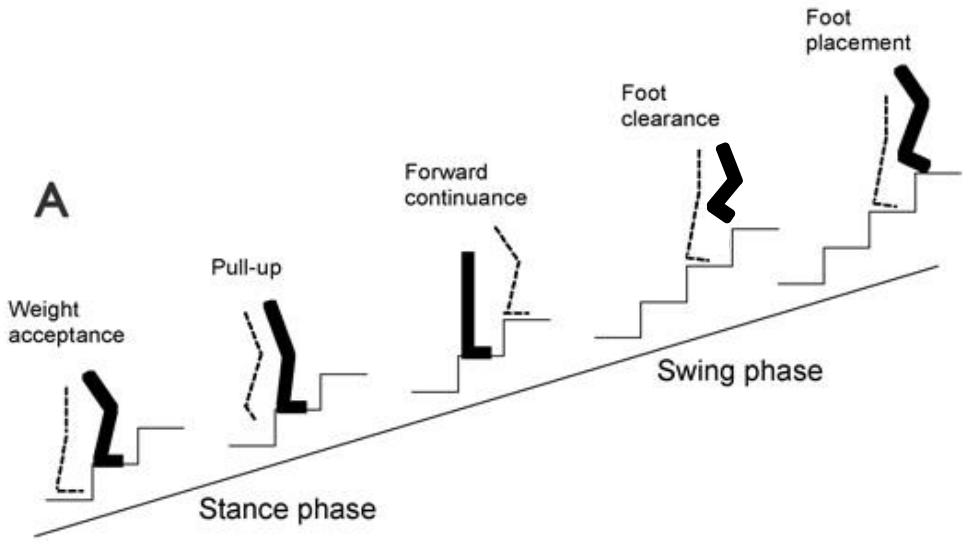


**Figure 2.4.** Phases of stair ascent (bold limb) as defined by McFayden & Winter, (1988) (Image adapted from Spanjaard *et al.* (2007)).

Example joint angle, moment and power curves are depicted in Figure 1, appendix A1. In order to elevate the body vertically from one step to the next, concentric contractions are required from the lower limbs. The knee extensors are primarily utilised during the pull-up phase, lifting the body vertically. This single limb support phase is challenging as the individual must maintain dynamic postural stability whilst all lower limb joints are all flexed. Therefore muscle action is necessary in all three lower-limb joints to provide enough muscle power to prevent the lower limbs from buckling. The ankle plantarflexors are dominant during forward continuance, providing the necessary propulsive forces to elevate the body vertically. Both knee flexion and ankle dorsiflexion are then required during the foot clearance phase to ensure adequate clearance of the nosing of the staircase to avoid tripping (McFadyen & Winter, 1988).

There are indications that older adults walk slower than the young (Novak & Brouwer, 2011) with further declines in speed with advancing older age (Oh-Park et al., 2011). However this has not been observed in all studies (Stacoff et al., 2005, Reeves et al., 2009b) and the significant difference in cadence observed by Novak & Brouwer (2011) was small. Given the well-reported age-related declines in strength and functional ability (Grimby, 1995, Clark & Fielding, 2011), and the relationships between strength and falls (Moreland et al., 2004), the lack of notable differences in stair walking speed with ageing suggests a much greater demand is being placed on weaker muscles.

This is evident in those studies quantifying joint moments experienced during stair ascent relative to the maximum capabilities of the individual (assessed through isokinetic dynamometry) (Reeves et al., 2009b, Samuel et al., 2011). A large demand is placed on the extensors of the hip and knee with less relative demand on the flexors. At both the hip and knee, the elderly work much closer to their maximum strength capacity compared to the young (Reeves et al., 2009b, Samuel et al., 2011) and in some cases, exceed maximum measured strength during stair ascent (111% in knee extensor demand and 103% in hip extensor demand elderly females) (Samuel et al., 2011). At the ankle, both the elderly and young operate closer to maximum capacity (93% and 85% of elderly and young, respectively). However the comparable functional demands existed because the elderly adopted strategies to maintain ankle joint moments within those safe limits (Reeves et al., 2009b). The elderly kept the ground reaction force vector close to the ankle joint reducing the external moment arm and therefore reducing internal plantarflexor moment. Furthermore, a transfer of energy from the knee extensors to the ankle plantarflexors via the bi-articular gastrocnemius appears to have been utilised during forward continuance (Reeves et al.,

2009b). The fascicles in the medial gastrocnemius remain relatively constant in length, working almost isometric even during the concentric power generation burst in forward continuance with both the soleus muscle (McFadyen & Winter, 1988) and the gastrocnemii (Spanjaard et al., 2007) playing important roles in raising the body to the next step. This energy transfer mechanism seems to be a useful strategy to compensate for age-related muscle weakness, particularly if the soleus muscle becomes impaired.

### *2.3.2 Stair descent*

The task of stair descent can be characterised by five phases depicted in Figure 2.5: weight acceptance, forward continuance, controlled lowering, leg pull-through and foot placement (McFadyen & Winter, 1988).

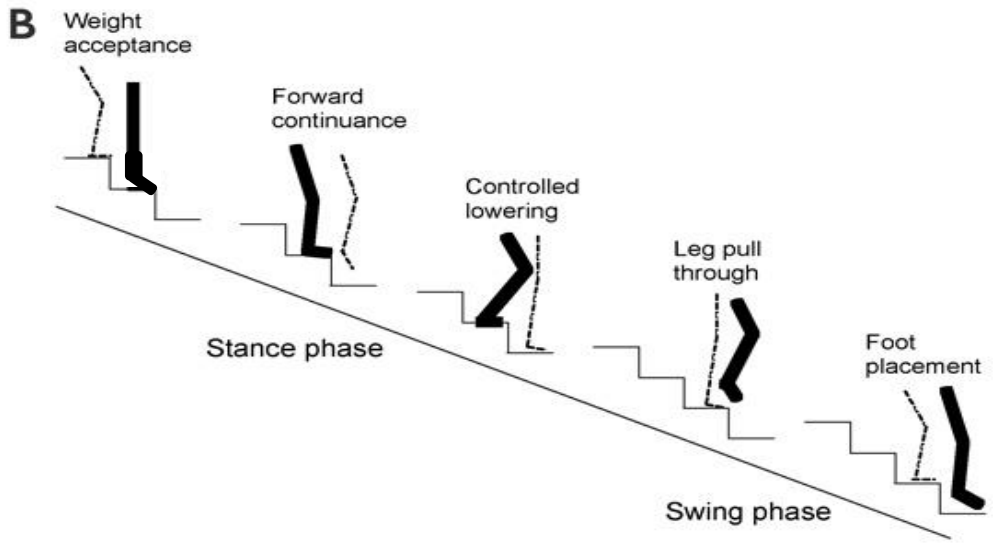


**Figure 2.5.** Phases of stair descent (bold limb) as defined by McFayden & Winter, (1988) (Image adapted from Spanjaard *et al.* (2007)).

Example joint angle, moment and power curves are depicted in Figure 2 appendix A1. In order to control the downwards momentum of the centre of mass, eccentric muscle action of the lower limbs is required. Weight acceptance is characterised by large power absorption seen in both the knee and ankle joints. Controlled lowering is primarily achieved by substantial eccentric knee extensor activity with a small burst of ankle power generation as a means to control increased dorsiflexion just prior to toe-off. The hip flexors are largely responsible for the leg pull-through phase with small bursts of power generation followed by extension of all lower limb joints in foot placement in preparation for foot contact (McFadyen & Winter, 1988).

There is clearer evidence of reduced speed during stair descent in the elderly compared to the young (Mian et al., 2007, Novak & Brouwer, 2011) with further reductions (Oh-Park et al., 2011), and correlations (Tiedemann et al., 2007), seen with advancing older age. Peak moments are reduced at the ankle during weight acceptance (Reeves et al., 2008a), and at the hip and knee during controlled lowering, with reduced peak support moments observed in both phases (Novak and Brouwer, 2011) in the elderly compared to the young. The demands on the hip extensors are less than those observed during stair ascent (Samuel et al., 2011) indicating that the musculature surrounding the knees and ankles provides the majority of strength and control required to accomplish this task safely.

Previous work, however, is contradictory regarding the functional demands placed on the knees with maximal strength capacity values ~120% (Samuel et al., 2011) and ~42% (Reeves et al., 2008a) both been reported. This discrepancy is likely related to methodological

variations used to assess and normalise joint moments. Reeves *et al,* (2008) normalised to peak eccentric joint moment at the velocity that best matched the velocity experienced during gait; whereas Samuel *et al,* (2011) normalised to peak isometric moment, estimated through linear interpolation at the angle of peak moment during gait. Given the superiority of eccentric over isometric contractions for force generation (Winter, 1979, Lindstedt et al., 2001), it is not surprising that the functional demand far exceeded 'maximum' capabilities reported by Samuel *et al,* (2011). The knee extensor demand is much less in stair descent compared to stair ascent (42% vs 75%) but remains increased compared to younger counterparts (Reeves et al., 2008a). It is clear that the plantarflexors in particular play a substantial role in absorbing power during stair descent (Riener et al., 2002, Protopapadaki et al., 2007, Cluff & Robertson, 2011). Therefore, as a means to maintain ankle joint moments within safe limits, the elderly re-distribute the demands of the task towards the knee musculature, where there is a greater reserve that can be utilised (Reeves et al., 2008a).

The muscle-tendon unit of the medial gastrocnemius undergoes substantial length changes during stair descent; however, during weight acceptance, it is the Achilles tendon that lengthens and the muscle fascicles actually shorten (Spanjaard et al., 2007). This concentric muscle contraction acts to regulate the rapid length changes of the tendon to provide adequate stiffness around the ankle during the transition to single-limb support and produce energy that can be stored, and subsequently reused, in the tendon (Spanjaard et al., 2007). Older individuals also appear to redistribute the control of the downwards acceleration of the centre of mass during weight acceptance to the trailing limb (acting in the controlled lowering phase), as a means to avoid rapid eccentric ankle action of the leading/landing limb (Buckley et al., 2013). In young individuals, there is a great demand on the plantarflexor muscle

fascicles to shorten rapidly in order to control length changes in the tendon and arrest the downwards acceleration of the centre of mass. In an elderly individual, the same demand exists, however the stiffness of the Achilles tendon is reduced (Kubo et al., 2003, Onambele et al., 2006, Stenroth et al., 2012), neuromuscular function is impaired (Clark and Fielding, 2011) and muscle power is diminished (Thom et al., 2007). As such, the redistribution of joint moments depicted by Reeves *et al,* (2008a) serves to compensate for more distal deteriorations in functional capabilities.

Given the presence of intermittent claudication pain, primarily in the calf (Norgren et al., 2007), potential multi-level muscle weakness in claudicants (Scott-Okafor et al., 2001, McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012) and impaired balance (Gardner and Montgomery, 2001, Mockford et al., 2011, Gohil et al., 2013b), greater biomechanical adaptations might be expected in those with PAD-IC. Indeed a greater prevalence of falls has been reported in claudicants (Gardner & Montgomery, 2001), therefore it is imperative to investigate stair gait biomechanics in this population in order to make evidence-based recommendations for targeted exercise interventions.

## 2.4 Thesis aims

Whilst the strength of lower limb muscles in claudicants have been previously assessed (Scott-Okafor et al., 2001, McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012), the disparity between studies and the variation in effectiveness of strength-based rehabilitation interventions likely stems from the current lack of understanding of how factors that contribute to muscle strength are affected by PAD-IC and disease severity. Furthermore, the impact of these potential adaptations on whole body function reflected by walking endurance and during demanding daily tasks, i.e. stair negotiation, is also unknown. The overarching aim of this doctoral thesis was to investigate the structural and functional in the gastrocnemii muscle and Achilles tendon in claudicants with PAD-IC and to determine the effects on functional capabilities as assessed by walking endurance and stair negotiation biomechanics. This was achieved by exploring relationships with disease severity and making comparisons to otherwise healthy adults. In order to achieve this aim, the following specific objectives were set:

1) To determine how the structure and dimensions of the gastrocnemii muscle-tendon unit and mechanical properties of the Achilles tendon are altered in claudicants and to establish relationships with disease severity and walking endurance. It was hypothesised that claudicants would exhibit longer muscle fascicles with shallower pennation angles, reduced tendon Young's modulus and tendon stiffness as well as increased tendon hysteresis compared to healthy controls. It was also hypothesised that these musculoskeletal parameters would be associated with increased disease severity and reduced walking endurance. This is explored in Chapter 4.

2) To determine whether the muscle strength and intrinsic muscle quality of the gastrocnemii muscle is altered in claudicants and to deduce relationships with disease severity and walking endurance. It was hypothesised that claudicants would generate less voluntary isometric plantarflexor moment and concentric plantarflexor power, possess smaller gastrocnemii muscles and reduced intrinsic muscle quality. It was hypothesised that these musculoskeletal parameters would be associated with increased disease severity and reduced walking endurance. This is explored in Chapter 5.

3) To determine whether gait biomechanics during stair ascent and descent is altered in claudicants and healthy controls and explore relationships with disease severity. It was hypothesised that claudicants would demonstrate modified ankle kinematics, reduced ankle kinetics and compensatory increases in knee and hip kinetics. It was hypothesised that these variables would be associated with increased disease severity and reflect the hypothesised deleterious adaptations in gastrocnemii muscle strength and quality and Achilles tendon properties. This work is described in Chapters 6 and 7.

# Chapter 3. General methods

The aims of the thesis were to determine the relationships between functional properties of the Achilles tendon, the size, architecture and function of the gastrocnemii muscles and stair gait parameters in claudicants with peripheral arterial disease. To achieve this, musculoskeletal ultrasound was used at rest, and synchronously with an isokinetic dynamometer, to determine the functional properties of the Achilles tendon and gastrocnemii muscles. 3-D motion capture was employed to quantify gait parameters during stair negotiation.

This Chapter includes specific details of the participants recruited for the thesis; gives an overview of the general testing procedures for musculoskeletal imaging and gait analysis employed throughout the experimental Chapters; and explores key technical aspects of relevant equipment and data processing. Any specific methodological descriptions, along with statistical analyses that relate specifically to one Chapter only, are described in greater detail in that Chapter.

## 3.1. Ethical approval and participant recruitment

Ethical approval was granted by the Yorkshire and Humber Local Research Ethics Committee (REC reference: 11/YH/0335). Males and females aged 55-80 years and diagnosed with Grade 1 Chronic Limb Ischemia (Rutherford et al., 1997) with a narrowing of the superficial femoral artery were recruited via consultant referral from the outpatient

vascular clinic based at Hull Royal Infirmary. Those with extensive disease were also included, however the primary stenosis identified using vascular imaging was located in the superficial femoral artery for all participants. Healthy older adults were recruited from the local community as a control group. Exclusion criteria are presented in Table 3.1.

**Table 3.1**. Exclusion criteria for both claudicants and healthy controls.

| **Exclusion criteria** | |
|---|---|
| Overall health status | Functional ability |
| Severe or acute cardiovascular or pulmonary illness | Observable gait abnormalities |
| Severe or acute musculoskeletal or neurological disorders | Previous lower limb joint replacement |
| History of stroke of myocardial infarction (<10years) | Requires the use of a walking aid(s) |
| | Unable to negotiate stairs or walk >20m unassisted |

## 3.2. Clinical measures

### *3.2.1 Ankle brachial pressure index (ABPI)*

ABPI is a simple, non-invasive procedure that quantifies the ratio of upper and lower limb blood pressure. Values <0.9 are 95% sensitive and 99% specific for the presence of peripheral arterial disease (Fowkes, 1988). An ABPI between 0.5 and 0.8 is typical in those with intermittent claudication and between 0.9 and 1.2 is typical for healthy individuals (Caruana et al., 2005); therefore low ABPI indicates high disease severity. In the current study, the ABPI measurements of claudicants were taken at Hull Royal Infirmary Vascular Unit as part

of the patient's standard medical assessment and by a member of their medical care team prior to recruitment into the study. For healthy controls, ABPI measures were taken during the first testing session and the Human Performance laboratory at the University of Hull. Systolic blood pressure was measured in the posterior tibial and dorsalis pedis arteries of each leg and the brachial pressure of both arms, separately, using a sphygmomanometer cuff and a hand held Doppler instrument (Parks Medical Electronics Inc., Oregon, USA). ABPI measures for both lower limbs were taken pre- and post- a standardised exercise protocol performed on a motorised treadmill (5minutes, 2.5km/h, 10% incline).

Post-exercise ABPI was used to determine the presence of disease and assess disease severity. A 'better' (higher ABPI) and 'worse' (lower ABPI) limb were identified in bilateral claudicants; and a 'symptomatic' and 'asymptomatic' limb in unilateral claudicants. Previous research has indicated that asymptomatic PAD can present, i.e. those with low ABPI values but no exertional leg pain, and this still results in substantial functional deteriorations (McDermott et al., 2008a). However, it is unclear whether unilateral claudicants demonstrate the same deteriorations as those with no diagnosis in either leg and no PAD symptoms. Furthermore, the ABPI is still the recommended assessment to classify disease severity in general clinical practice (Hirsch et al., 2006, Norgren et al., 2007), therefore the asymptomatic limb in unilateral claudicants was defined as the limb with an absence of prior lower-extremity vascular events or claudication symptoms alongside an ABPI >0.9 (Diehm et al., 2009). Control participants also undertook the exercise protocol to determine ABPI values and confirm the absence of disease at the Human Performance laboratory at the University of Hull. In accordance with standard protocol, the ABPI for both legs was then

calculated as the higher of the two leg artery pressures normalised to the higher brachial pressure of the two arms (Norgren et al., 2007).

### *3.2.2 Walking endurance*

The six-minute walk test is a useful tool to assess functional capacity in claudicants (Guyatt et al., 1985), is a reliable and responsive test reflecting the requirements of daily living (Solway, 2001) and is a reliable alternative to treadmill walk tests in those with PAD-IC (Zwierska et al., 2004). A modified six-minute walk test on level ground was performed, and combined with the ACSM claudication pain rating scale (Durstine & Moore, 2003) to allow those that are able to walk longer than 6-minutes to do so (King et al., 2012). Patients walked continuously along a 10m walkway at a self-selected pace and reported the level and position of any pain every 20m. Initial claudication distance (ICD) was classed as level 1 on the pain scale and signifies the onset of pain. Absolute claudication distance (ACD) was classed as level 4 on the pain scale and signifies maximal pain.

### *3.2.3 Limb classification*

Following ABPI assessment, a 'better' and 'worse' limb were identified in bilateral claudicants and a 'symptomatic' and 'asymptomatic' limb in unilateral claudicants. These were then classified into two groups; the claudicating-limb group and the asymptomatic-limb group (Figure 3.1). The limbs of healthy controls were classified using a ball-kicking exercise to determine the 'dominant limb'; being the limb chosen to kick the ball, and the 'non-dominant limb' as the standing leg.

### 3.3. Participant details

A total of 23 participants were recruited over a 14-month period (April 2012 – June 2013) consisting of 13 claudicants (seven unilateral and six bilateral) and ten healthy controls (Table 3.2 and see Table 1, Appendix A2 for individual participant characteristics). Participants were then classified into three groups; claudicating-limb, asymptomatic-limb and healthy control limb groups as depicted in Figure 3.1. Only the dominant limb from the healthy controls was selected for further analysis to avoid the violating the assumption of independent sample. This approach was not taken with the bilateral claudicants (i.e both the better and worse limbs were taken forward into the claudicating-limb group) to allow us to assess potential between-limb differences caused by different levels of disease severity. Whilst this categorisation creates a statistical imbalance between groups (i.e. the dominant limb only is taken forward from the healthy control group, whereas both limbs are taken forward for further analysis from the claudicant group), this method is common practice in PAD-IC research (Scott-Pandorf et al, 2007, Celis et al, 2009, Huisinga et al 2010, Wurdeman et al, 2012). Participants were required to attend the Human Performance Laboratory at the University of Hull on two occasions, separated by no longer than one week, and were instructed to bring comfortable flat shoes and shorts to both sessions. The participants' height and mass were determined whilst barefoot using a stadiometer (Seca, Leicester Height Measure, Birmingham, UK) and electronic weighing scales (Salter, Kent, UK) and BMI was computed as mass/height$^2$ (kg/m$^2$).

**Table 3.2**. Participant characteristics. Data are presented as group mean (SD) unless otherwise stated. BMI – Body mass index, ABPI – Ankle brachial pressure index, ICD – Initial claudication distance, ACD – Absolute claudication distance

| | Uni-lateral | | Bi-lateral | | Control | |
|---|---|---|---|---|---|---|
| **#** | 7 | | 6 | | 10 | |
| **% Males** | 57.1 | | 100 | | 40 | |
| **Age (years)** | 66.1 (7.5) | | 62.2 (6.0) | | 61.6 (3.6) | |
| **Height (m)** | 1.69 (0.10) | | 1.74 (0.02) | | 1.66 (0.09) | |
| **Mass (Kg)** | 82.3 (21.1) | | 82.6 (6.4) | | 72.3 (10.9) | |
| **BMI (Kg/m$^2$)** | 28.5 (4.8) | | 27.3 (5.6) | | 26.1 (3.7) | |
| **ABPI pre-exercise** | Asymptomatic | 1.01 (0.16) | Better | 0.85 (0.19) | Dominant | 1.01 (0.09) |
| | Symptomatic | 0.84 (0.28) | Worse | 0.81 (0.24) | Non-Dominant | 0.97 (0.11) |
| **ABPI post-exercise** | Asymptomatic | 0.90 (0.06) | Better | 0.68 (0.27) | Dominant | 1.01 (0.16) |
| | Symptomatic | 0.62 (0.22) | Worse | 0.52 (0.20) | Non-Dominant | 0.98 (0.10) |
| **Walking distances** | ICD | 80.0 (16.7) | ICD | 125.0 (53.9) | N/A | |
| | ACD | 195.0 (82.6) | ACD | 318.3 (151.8) | | |
| **Time since diagnosis (months (range))** | 31.9 (3 - 108) | | 47.5 (3 - 108) | | N/A | |
| **% Hypertension** | 42.9 | | 66.6 | | 10 | |
| **% Hypercholesterolemia** | 71.4 | | 50 | | 20 | |
| **% past smokers** | 57.1 | | 50 | | 30 | |
| **% present smokers** | 42.9 | | 50 | | 0 | |

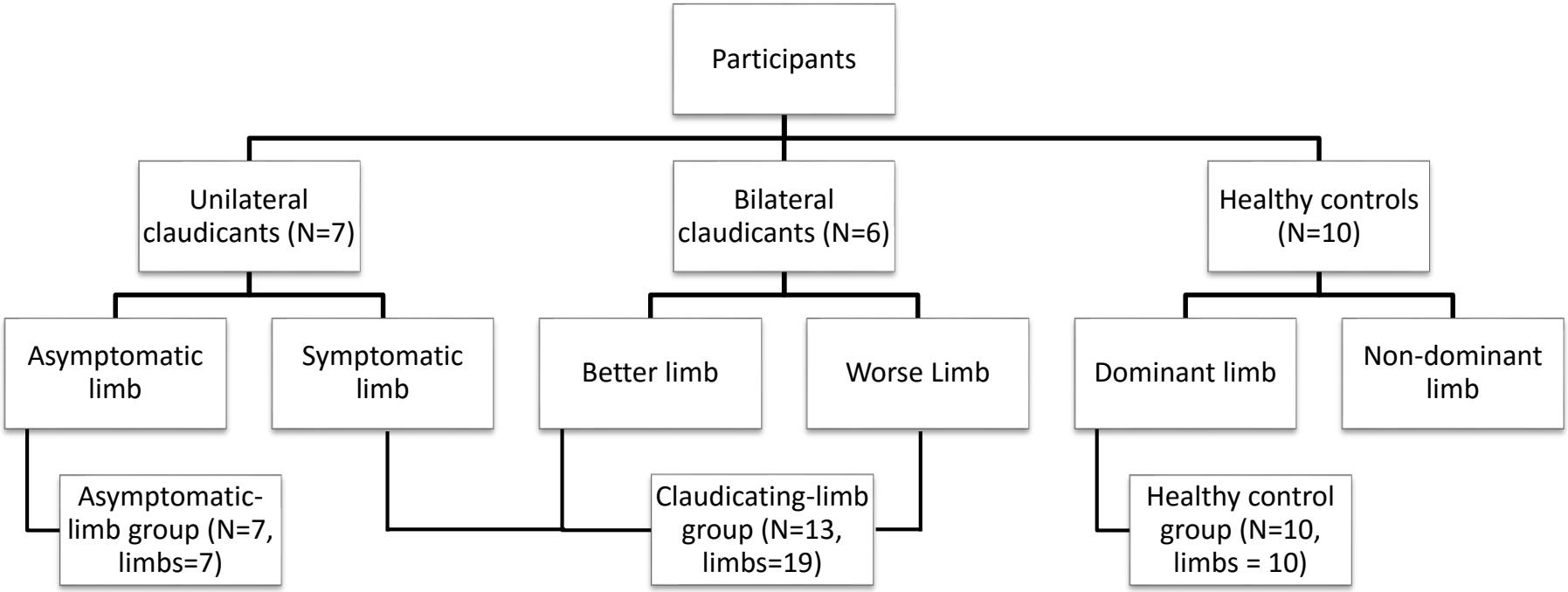


**Figure 3.1**. Limb classification of unilateral and bilateral claudicants, and healthy controls, into asymptomatic-limb, claudicating-limb and healthy control groups.

## 3.4 Functional properties of the Achilles tendon and gastrocnemii muscles

In this section the muscle-tendon parameters of interest will be defined and the principles of assessment outlined. A brief overview of the musculoskeletal model used to assess joint mechanics is introduced. This is followed by details of how each parameter contributing to maximum voluntary contraction, for the calculation of static muscle quality (specific tension), and isokinetic strength for the calculation of dynamic muscle quality, was quantified.

### *3.4.1 Joint mechanics*

Factors contributing to the measured joint maximum voluntary contraction (MVC) are based on the musculoskeletal model depicted in Chapter 2 (Figure 2.1) and duplicated below for clarity (Figure 3.2). The methodology employed in the thesis is based upon the below principles with specific adjustments made to these steps detailed further in this section and in the relevant Chapters.

Net plantarflexor joint moment was calculated using equation 3.1 and Achilles tendon force calculated using equation 3.2:

3.1 $$Net\ plantarflexor\ moment = joint\ moment - antagonist\ moment \mp passive\ joint\ moment$$

3.2 $$Tendon\ force = \frac{Net\ plantarflexor\ moment}{moment\ arm\ length}$$

Achilles tendon force consists of soleus and gastrocnemii contributions. Each muscle's contribution is equal to the component of fascicle force acting along the line of action of the muscle, calculated from its pennation angle (θ) and determined using equation 3.3.

3.3 $$Fascicle\ force = \frac{Tendon\ force}{cos\theta}$$

For maximal muscle, or tendon, force to be calculated, electrical stimulation of the muscle is required during maximal plantarflexor contraction. Finally, muscle quality (specific tension) is calculated using equation 3.4:

3.4 $$Muscle\ quality = \frac{Fascicle\ force}{PCSA}$$

where *PCSA* is the physiological cross-sectional area of the relevant muscle.

The following section describes how each of these components were measured and/or calculated.

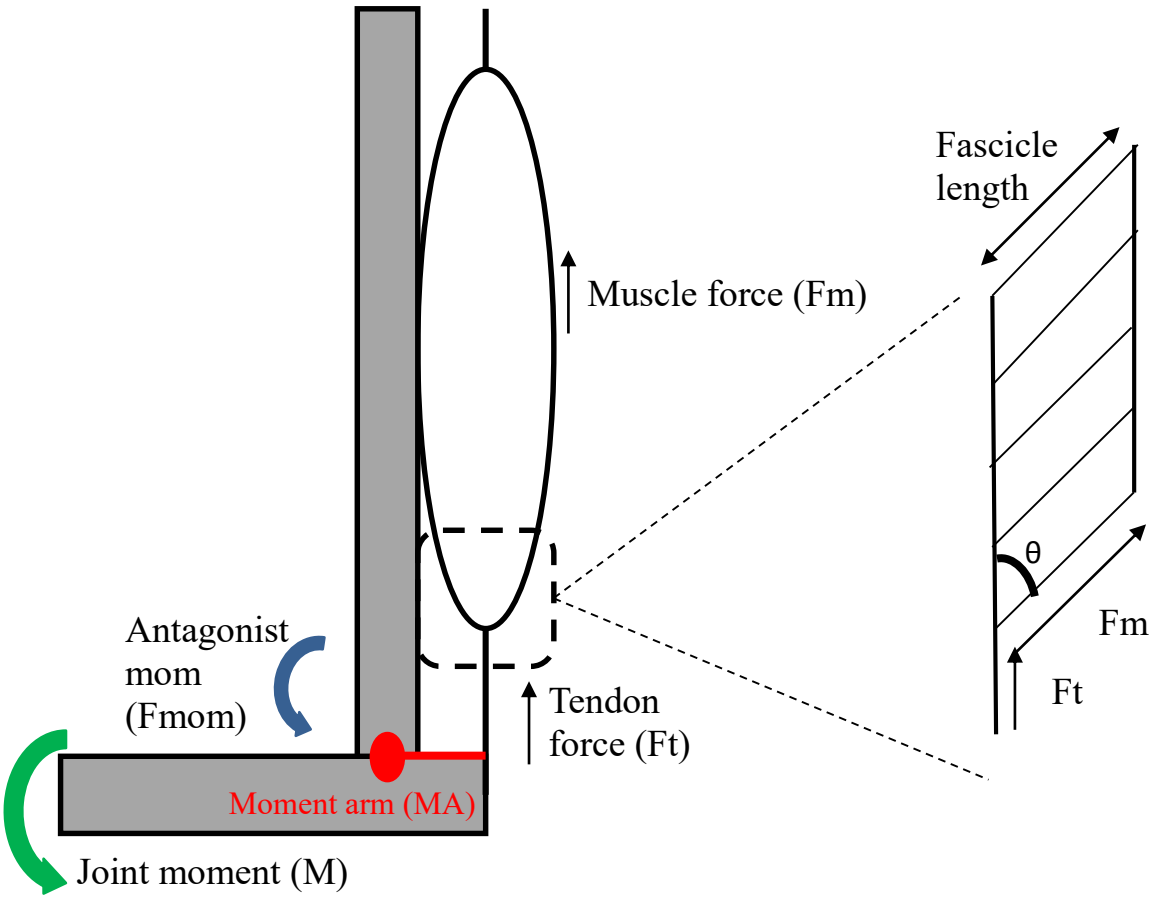


**Figure 3.2.** Musculoskeletal model schematic depicting the factors contributing to plantarflexion MVC

*3.4.2 Isometric and isokinetic plantarflexor strength*

Plantarflexor strength was assessed using an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems Inc., New York, USA) in both isometric and concentric conditions. Participants were secured into the chair, sat in an upright position with their hip flexed (85°), knee extended (0°) and the lateral malleolus aligned with the centre of rotation of the dynamometer arm during muscle contraction. Isometric maximum voluntary contractions were performed at 10° intervals across the full range of motion and concentric plantarflexor contractions were performed across the full range of motion at angular velocities of 60, 90, 120 and 180°/s. Previous research has demonstrated that erroneous ankle rotation during an 'isometric' plantarflexion contraction resulted in an overestimation of plantarflexion moment (Arampatzis *et al,*. 2005) with comparable values observed during isokinetic contractions (Arampatzis *et al.*, 2007). This rotation was minimised using Velcro straps to fasten the foot to the foot-plate as securely as possible. In trials where erroneous ankle rotation was large, the Velcro straps were subsequently tightened and the trial repeated. Whilst absolute peak values may be overestimated and some error introduced into the force-elongation relationship (and subsequent calculations of tendon stiffness and strain), there is no reason to assume that the presence of claudication would influence additional joint rotation and therefore this overestimation should have a minimal effect on between-group comparisons, Practice trials were performed prior to testing and visual feedback provided to ensure consistent rise in plantarflexor moment during each test. Adequate rest was provided between trials and verbal encouragement was given throughout all trials. Joint moment data were recorded synchronously with surface electromyography via Noraxon MyoResearch V1.08.38 (Noraxon, Arizona, USA) sampling at 3000 Hz.

Peak passive moment-corrected plantarflexor moment generated during the isometric plantarflexor trials were selected for further analysis. Furthermore, the following parameters were measured in the previously described joint configuration unless otherwise stated.

### *3.4.3 Antagonist co-activation*

The contribution of antagonist co-activation to isometric joint MVC (as described above) was estimated from the surface electromyography (EMG) (Telemyo 2400T, Noraxon, Arizona, USA) of the tibialis anterior (TA), to represent the ankle dorsiflexors. The skin was prepared by shaving the relevant areas and cleaning with an antiseptic wipe. Two Ag-AgCL electrodes were placed at 1/3 of the distance between the head of the fibular and the medial malleolus with the third earth electrode attached to the lateral malleolus in accordance with SENIAM guidelines (Hermens et al., 2000). All data were collected using Noraxon MyoResearch V1.08.38 (Noraxon, Arizona, USA), sampled at 3000 Hz then band-pass filtered between 10 and 500 Hz, and smoothed using the root mean square over 50 ms prior to further analysis. The EMG of the TA was recorded synchronously with the isometric plantarflexor MVC's (TA working as an antagonist) and then combined with the EMG-moment relationship quantified during dorsiflexion contractions (TA working as an agonist) (Kellis & Baltzopoulos, 1997).

### *3.4.4 Soleus contribution*

The contribution of soleus to plantarflexor moment was quantified with additional plantarflexor contractions with the knee flexed at 90° where the gastrocnemii contribute negligibly to the measured joint moment (Maganaris, 2003). To detect any changes in muscle activation due to change in joint configuration, surface EMG (Telemyo 2400T,

Noraxon, Arizona, USA) electrodes were placed on the soleus muscle belly at 2/3 of the line between the medial femoral condyle and medial malleolus (Hermens et al., 2000). All data were collected using Noraxon MyoResearch V1.08.38 (Noraxon, Arizona, USA), sampled at 3000 Hz then band-pass filtered between 10 and 500 Hz, and smoothed using the root mean square over 50 ms prior to further analysis. Activation changes between the two positions were corrected using the EMG-moment relationship in the two joint configurations using equation 3.5:

$$\text{3.5} \qquad \textit{Soleus moment Knee } 0° = \frac{\textit{Soleus moment Knee } 90° * \textit{ Soleus EMG Knee } 0°}{\textit{Soleus EMG Knee } 90°}$$

Where soleus moment was taken as the average moment over 50 ms at peak MVC and soleus EMG taken as the average EMG across the same 50 ms window. It must be acknowledged that previous research demonstrated soleus and GM activation differ disproportionally compared to the change in plantarflexion moment (i.e. there is a greater reduction in GM EMG than soleus EMG for the same reduction in plantarflexion moment as knee flexion increases) (Arampatzis et al., 2006). Arampatzis et al. (2006) reported ~60% reduction in plantarflexion moment from a position of knee extension and ankle dorsiflexion to a position of knee flexion and ankle plantarflexion, with ~10% reduction in soleus activation and ~30% reduction in GL and GM activation. Within the present cohort, plantarflexion moment reduced by ~40% with comparable joint configurations, therefore the relative between-muscle activation differences will likely be smaller than that reported by Arampatzis et al. (2006) and the subsequent activation imbalance errors associated with this correction will be minimised.

*3.4.5 Voluntary activation capacity*

The level of muscle activation achieved during voluntary contraction was calculated using the interpolated twitch technique (Rutherford et al., 1986). Joint moment data were recorded via Noraxon MyoResearch V1.08.38 (Noraxon, Arizona, USA). Percutaneous neuromuscular electrical stimulation (200 μs pulse duration, 400 V; Digitimer model DS7AH, Welwyn Garden City, UK) was used to evoke involuntary twitches of the plantarflexor muscles via two 8x10 cm carbon rubber neurostimulation electrodes (Axelgaard, California, USA) placed over the proximal and distal ends of the muscle. Maximal current intensity was determined by progressively stimulating the calf with electrical twitches of increasing current steps of 50 mA until further increments in current did not increase joint moment. Once this level was established, a superimposed twitch was evoked at the point of isometric MVC and a resting twitch was applied approximately 3 s afterwards. This was repeated during three trials at peak joint angle. The percentage of voluntary activation was calculated using equation 3.6 (Behm et al., 2001):

3.6 $$Voluntary\ activation = \left(1 - \frac{Superimposed\ twitch}{Resting\ twitch}\right) x\ 100$$

Previous research has demonstrated that the contractile properties of the gastrocnemius and soleus differ by assessing action potentials during submaximal stimulation to the respective muscle bellies (Vandervoort & McComas., 1983). The experimental protocol employed in the thesis did not permit the investigation of each triceps surae muscle in order to estimate voluntary activation of each component. As such some error may be introduced in our assumption that activation capacity is similar between muscles, however, it is likely that this error will be small.

*3.4.6 Moment arm*

Achilles tendon moment arm (MA) length was measured using B-mode ultrasound video recordings sampling at 25 Hz (50-mm probe length, MyLab50 x-vision, Esaote Biomedica, Genoa, Italy) of the muscle-tendon junction of medial gastrocnemius and calculated using the tendon excursion method (Ito et al., 2000, Maganaris et al., 2000, Maganaris and Paul, 2002, Fath et al., 2010) (equation 3.7) during passive joint rotations of 10° from maximal dorsiflexion on the isokinetic dynamometer. Still images were exported from the video recordings and analysed in ImageJ (version 1.44, NIH, USA).

3.7 $$MA = \frac{\Delta L}{\Delta \theta}$$

where $MA$ is moment arm length, $\Delta L$ is linear tendon displacement and $\theta$ is ankle angle in radians.

This method has been shown to be a reliable alternative to the more costly magnetic resonance imaging technique (Fath et al., 2010), but relies on the assumption that during rotation there is a) no change in tendon length due to a passive stretch or muscle contraction b) no medial-lateral or proximal-distal movement of the ultrasound probe and c) no non-linear tendon displacement, with respect to joint rotation (Maganaris et al., 2000). To minimise these errors; real-time joint moments were observed to ensure moments did not exceed those recorded for passive joint moments (see section 3.4.2), and the ultrasound probe was secured in place with an adhesive tape and an echo-absorptive marker placed onto the skin to assess whether the probe moved over the skin. Such a rigid attachment of the probe means that any out of plane displacement of the tendon will be missed and therefore be underestimated. However, the out of plane rotation over a small

change in ankle angle will likely be small and have a negligible effect on moment arm calculation.

Using the steps described above, maximal Achilles tendon force was calculated using the following equation (3.8);

3.8 $$Maximal\ Achilles\ tendon\ force = \frac{(Joint\ MVC + Antagonist\ moment - Soleus\ moment)*100}{(Moment\ arm * Voluntary\ activation)}$$

*3.4.7 Muscle volume*

B-mode ultrasound imaging of the lateral and medial gastrocnemii (GL and GM, respectively) were taken at rest and volume for each head was quantified using methodology previously described (Esformes et al., 2002, Reeves et al., 2004a, Matschke et al., 2010). Serial transverse plane images were taken across each muscle at 25, 50 and 75% of measured muscle length, determined through ultrasound imaging of the proximal and distal muscle-tendon junctions. Images were overlaid using ImageJ to reconstruct a full anatomical cross-sectional area (ACSA) for each level (Figure 3.3). Volume for the GL and GM, respectively, were calculated using the ACSA's and muscle length by considering each head as two cones (equation 3.9) either side of two truncated cones (equation 3.10):

3.9 $$V = \left(\frac{1}{3} * \pi\right) * \left(\frac{a}{\pi}\right) * d$$

3.10 $$V = \left(\frac{1}{3} * d\right) * \left[a + \sqrt{a * b} + b\right]$$

where *d* is the distance between the two ACSA's (*a* and *b*). For equation 3.9, *a* represents the ACSA at either 25 of 75% of muscle length.

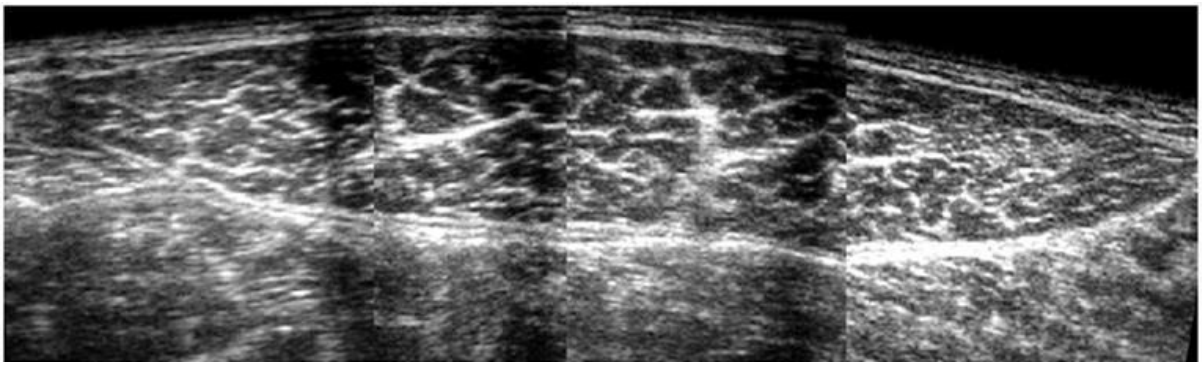

**Figure 3.3**. Example image of the overlaid images of the medial gastrocnemius at 25% of muscle length. The ACSA was quantified by tracing the aponeurosis of the muscle

*3.4.8 Muscle architecture at rest*

Participants were asked to lie prone on a plinth with their ankle plantarflexed and supported on the bed with the musculature relaxed. B-mode ultrasound imaging was used to visualise resting muscle architecture of the GL and GM in the sagittal plane at 50% of muscle length. Ample aquasonic gel was used to ensure a good contact with minimal pressure applied to the skin, and care was taken throughout to avoid compression of the soft tissue and deformation of images and subsequent measurements. Fascicle length, pennation angle and muscle thickness were measured from three separate images using ImageJ, with the average taken forward for further analysis. For each image, the length of one fascicle with its insertion angle onto the deep aponeurosis and muscle thickness measured at the mid-point of the image were measured. In cases where the fascicle length exceeded the ultrasound viewing window, the aponeurosis was extrapolated to allow for fascicle length measurements to be estimated (Reeves & Narici, 2003). Prior to patient recruitment, intra-assessor reliability was performed on a cohort of young, healthy individuals (N=20). Muscle thickness, pennation angle and fascicle length in both GL and GM were measured during two testing sessions separated by ~one week. The Bland-Altman 95% limits of agreement for GL and GM were -1.4 - 2.2 mm and -1.0 - 1.1 mm

for muscle thickness, -2.0 - 2.3° and -3.4 - 4.5° for pennation angle and -5.1 - 4.8 mm and -3.9 - 4.2 mm for fascicle length. No systematic bias between measurements was apparent. Data are presented in Figure 1 in Appendix A3.

### *3.4.9 Muscle architecture at MVC*

Optimum fascicle length and pennation angle were measured from synchronised sagittal-plane B-mode ultrasound video-recordings of the muscle belly of GL and GM, sampling at 25 Hz, during MVC. A custom made trigger unit was used to apply a synchronous 300 mV pulse in a separate channel of the Noraxon MyoResearch unit, which was acquiring the dynamometer and EMG data, and into the ECG channel of the ultrasound video. The frame corresponding to peak tendon force was extracted for each muscle during three separate MVC trials and analysed in ImageJ.

### *3.4.10 Calculation of static muscle quality*

Static muscle quality was calculated as maximal Achilles tendon force (equation 3.8) normalised to the reduced PCSA of the gastrocnemii (equation 3.11):

$$3.11 \quad Reduced\ PCSA = \left(\frac{GL\ V}{GL\ FL_{MVC}}\right) * cos \cdot GL\theta_{MVC} + \left(\frac{GM\ V}{GM\ FL_{MVC}}\right) * cos \cdot GM\theta_{MVC}$$

where *PCSA* is physiological cross-sectional area, *GL* is lateral gastrocnemius and *GM* is medial gastrocnemius, *V* is muscle volume, *FL* is fascicle length and $\theta$ is pennation, both quantified during maximum voluntary contraction (*MVC*).

A previous investigation into *in vivo* measures of muscle quality reported an approximate error of 10% in calculated muscle quality when an error of ±10% was introduced into a number of variables (Maganaris et al., 2001), with the authors deeming this error too

small to alter the meaning of results. Whilst this gives confidence to calculations of muscle quality when only one variable is modified; an accumulation or propagation of error across multiple variables has not been investigated. Exploration of data presented in the thesis indicates that a summation of +10% or -10% error in measures of MVC, soleus contribution, moment arm length and PCSA yielded errors of < ±16% in calculated muscle quality, which is less than the between-group difference (~21%) reported in Chapter 5. The true error associated with our methodology will likely be lower than this estimate given the unlikelihood of a consistent error of ±10% in all variables. Nonetheless, the impact of error propagation in such a study must be taken into consideration.

### *3.4.11 Calculation of dynamic muscle quality*

Joint power across the participants' full range of motion at angular velocities of 60, 90, 120 and 180 °/s using an isokinetic dynamometer. Peak power from each trial was recorded and the power-velocity profile constructed. The volume-normalised power-velocity relationship was established by normalising power at each velocity to gastrocnemii muscle volume. Dynamic muscle quality was defined as peak power normalised to gastrocnemii muscle volume. Verbal encouragement was given during trials and adequate rest (>1 min) was provided between trials.

### *3.4.12 Achilles tendon dimensions*

At rest, free tendon cross-sectional area (CSA) was measured at 1, 2 and 3 cm proximal to the insertion onto the calcaneus using axial-plane ultrasound imaging (Maganaris & Paul, 2002) and analysed using ImageJ. The average of all three sites was used for further calculations. Achilles tendon resting length was measured from the proximal origin at the

myotendinous junction (MTJ) of GM to the distal insertion at the calcaneus whilst the ankle was in maximum dorsiflexion prior to plantarflexor contractions (participant positioning described above). These locations were identified using ultrasound imaging and the length measured using a tape.

*3.4.13 Achilles tendon elongation and functional properties*

Maximal Achilles tendon force was calculated as detailed above The ultrasound probe was aligned with the distal MTJ of the GM and the Achilles tendon in the sagittal plane and securely fixed to the skin with an echo-absorptive marker within the viewing window to allow for correction of any artefacts caused by probe movement (Maganaris & Paul, 2000) (Figure 3.4). Ultrasound videos recorded were synchronously with plantarflexor moments during MVCs (described above) to associate joint moments and tendon force with MTJ displacement. Images were digitised to measure tendon elongation at each 10% of peak tendon force using ImageJ.

Force-elongation curves were constructed for the loading (increasing contraction) and unloading (relaxation) phases for all participants and each fitted with a 2nd order polynomial equation between 10-100% of tendon force (for all $R^2$<.95). The following parameters were calculated for each participant at their individual MVC: tendon stiffness, strain, stress and Young's modulus. Stiffness was calculated by differentiating the polynomial equation of the force-elongation curve at each individual's MVC. Tendon strain was calculated by normalising elongation to resting length. Tendon stress was calculated by normalising tendon force to CSA. Tendon Young's modulus was calculated as tendon stiffness multiplied by the ratio of tendon length to CSA (Maganaris & Paul, 1999, Maganaris & Paul, 2002, Reeves et al., 2003b). Energy stored in the tendon was

calculated as the area beneath the whole of the loading curve, and energy released as the area beneath the unloading curve, by integrating a second $2^{nd}$ order polynomial equation describing the respective force-elongation curves between 0-100% of tendon force. Hysteresis was calculated as the difference between the energy stored and energy released, normalised as a percentage of the energy stored.

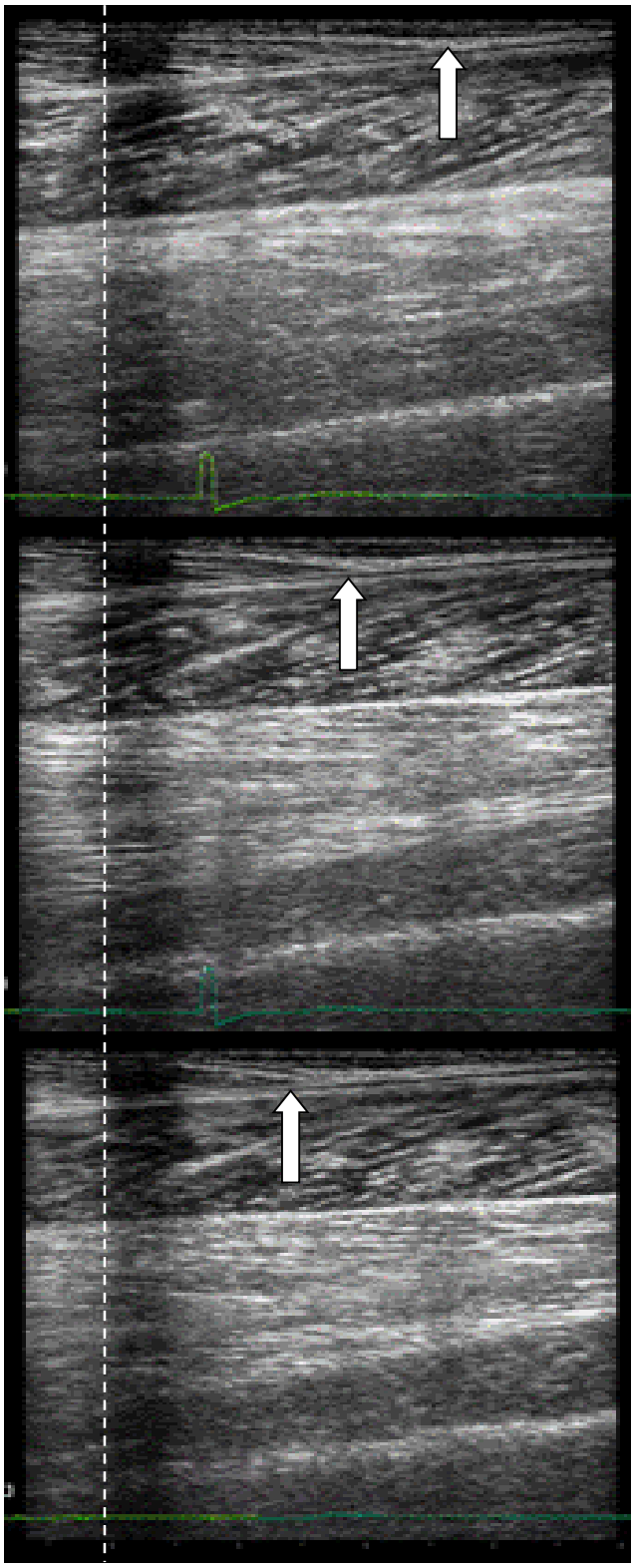

**Figure 3.4.** Example stills of Achilles tendon myotendinous junction (MTJ) during ramped isometric plantarflexor contractions. Dashed white line represents the echo-absorptive marker placed on the skin to ensure accurate positioning of the ultrasound probe and to assess whether the probe moved during the plantarflexor contraction. White arrow identifies the displacement of the MTJ from the transition from rest (top) to MVC (bottom)

## 3.5 Gait biomechanics

The specific procedures relating to stair ascent are detailed in Chapter 6 with stair descent detailed in Chapter 7. Below is a general overview of the equipment set-up and key technical details related to data processing that are applicable for both tasks.

### *3.5.1 Equipment set-up*

Ten Qualisys Oqus 400 cameras (Qualisys, Gothenburg, Sweden) and two Kistler force plates (model 9286AA, Kistler, Winterthur, Switzerland), sampling at 100 Hz and 1000 Hz respectively, were used to collect kinematic and kinetic data synchronously using Qualisys Track Manager (version 2.8) via a 64-channel analogue-to-digital board (Qualisys, Gothenburg, Sweden). Within our current laboratory set-up, force-plates are imbedded into the floor and required moving into the staircase prior to data collection. Previous work has investigated the errors associated with moving force-platforms from level-ground to a wooden staircase design and established spectral power was only lost at high frequencies that are not typically associated with gait kinetics (Chesters et al., 2013). Therefore the integrity of our kinetic data was maintained in our experimental set up. The measurement area was calibrated for 100 seconds using a 750x550 mm L-frame and 749.9 mm length wand covering a volume of ~33.75 $m^3$. Marker residuals were all below 2 mm prior to data collection. The tracking parameters employed were: prediction error of 30 mm, maximum residual of 10 mm and minimum trajectory length of 2 frames.

*3.5.2 Staircase dimensions*

The 5-step custom built wooden staircase used in the present thesis conformed to buildings regulation guidelines (H.M. Government, 2010b) for private staircase design (step height; 200 mmm, step tread; 300 mm, step width; 800 mm, Figure 3.5) and was equipped with a safety handrail. The staircase was instrumented with force-plates, which were imbedded into steps two and three, to facilitate the collection of kinetic data during steady state stair ascent and descent.

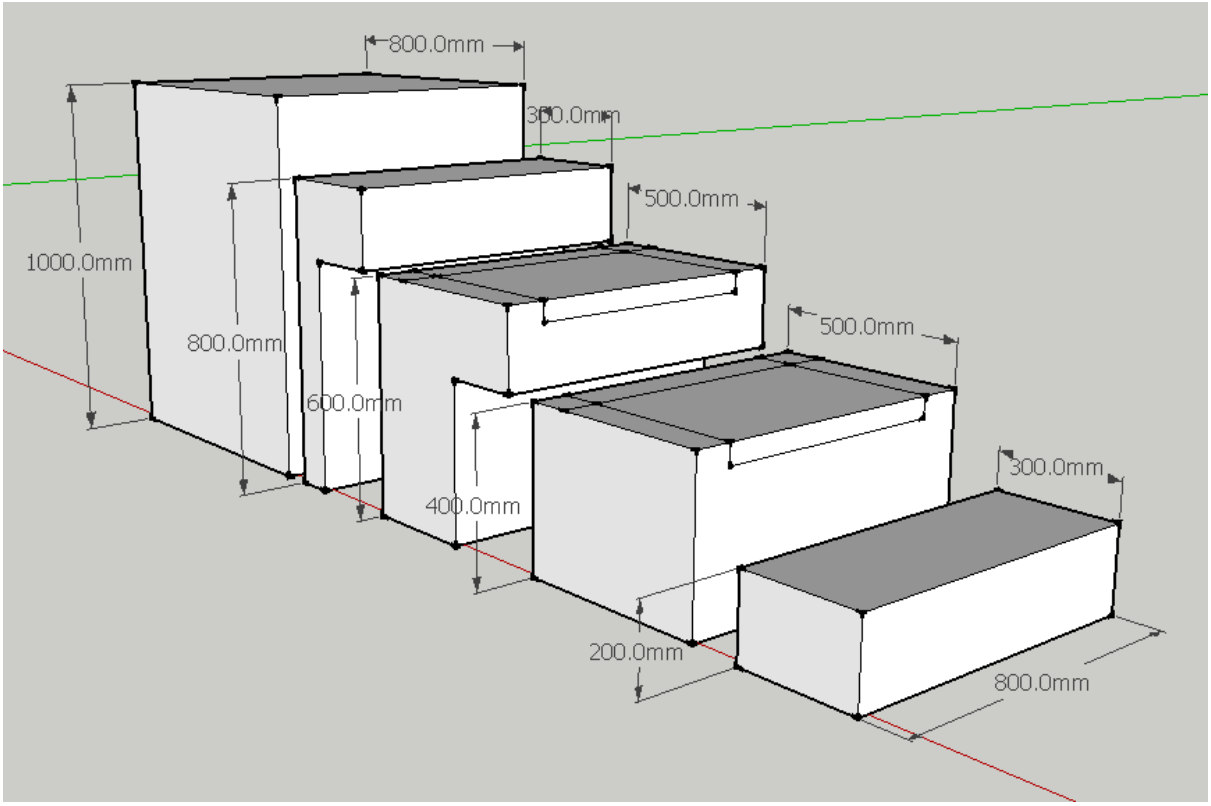


**Figure 3.5.** Staircase dimensions (excluding the handrail)

### *3.5.3 Marker placement*

A total of 47 retro-reflective passive markers (14 mm diameter) were positioned according to the six Degrees-of-Freedom (6DoF) marker set (Cappozzo et al., 1995). This model is a frequently used alternative to the traditional Helen Hayes (or Conventional Gait Model, Davis Model) (Kadaba et al., 1990, Davis et al., 1991) model which contains three rotational DoF and is associated with kinematic error propagation distally due to the limitations of segment definition (Collins et al., 2009, Buczek et al., 2010). The 6DoF model allows for each segment to be tracked independently and minimises the error cascade from proximal to distal segments. For this independent segment tracking to occur, the relationship between the anatomical marker set (placed on specific bony landmarks (blue in Figure 3.6)) and technical marker set (rigid clusters attached to segments (green in Figure 3.6) needs to be defined in a standing pose (static trial). Following this, functional calibration trials were performed (details below) and markers defining the hip, knee and ankle centres (Table 3.3) were removed before participants performed the dynamic walking trials.

### *3.5.4 Technical aspects of Visual 3D modelling*

Visual 3D (C-motion, Rockville, MD, USA) is a musculoskeletal modelling software used to generate the 6DoF model, define the segments used in the model, animate the model and derive joint angles from the relative positioning of said joint segments. The local coordinate system of each joint and the calculation of joint angles utilised the Cardan sequence of rotations (X-Y-Z) according to the right hand rule. The markers used to define each segment are detailed in Table 3.3. The definition of the pelvis segment, the hip joint centre and foot segment require special consideration and are described in more detail below. The knee axis was defined as the plane between the medial and lateral femoral epicondyles markers and the ankle axis was defined as the plane between the

medial and lateral malleoli markers. Unlike the Helen Hayes model, the 6DoF model does not create ‘joint centres’, instead the joint coordinate system is defined as the intersection between the proximal and distal segments (i.e. the intersection between the thigh and shank segments) and is located at the proximal end of the distal segment (i.e. the proximal end of the shank). This allows for segments to be ‘linked’ but not constrained about a central axis (C-motion, 2009).

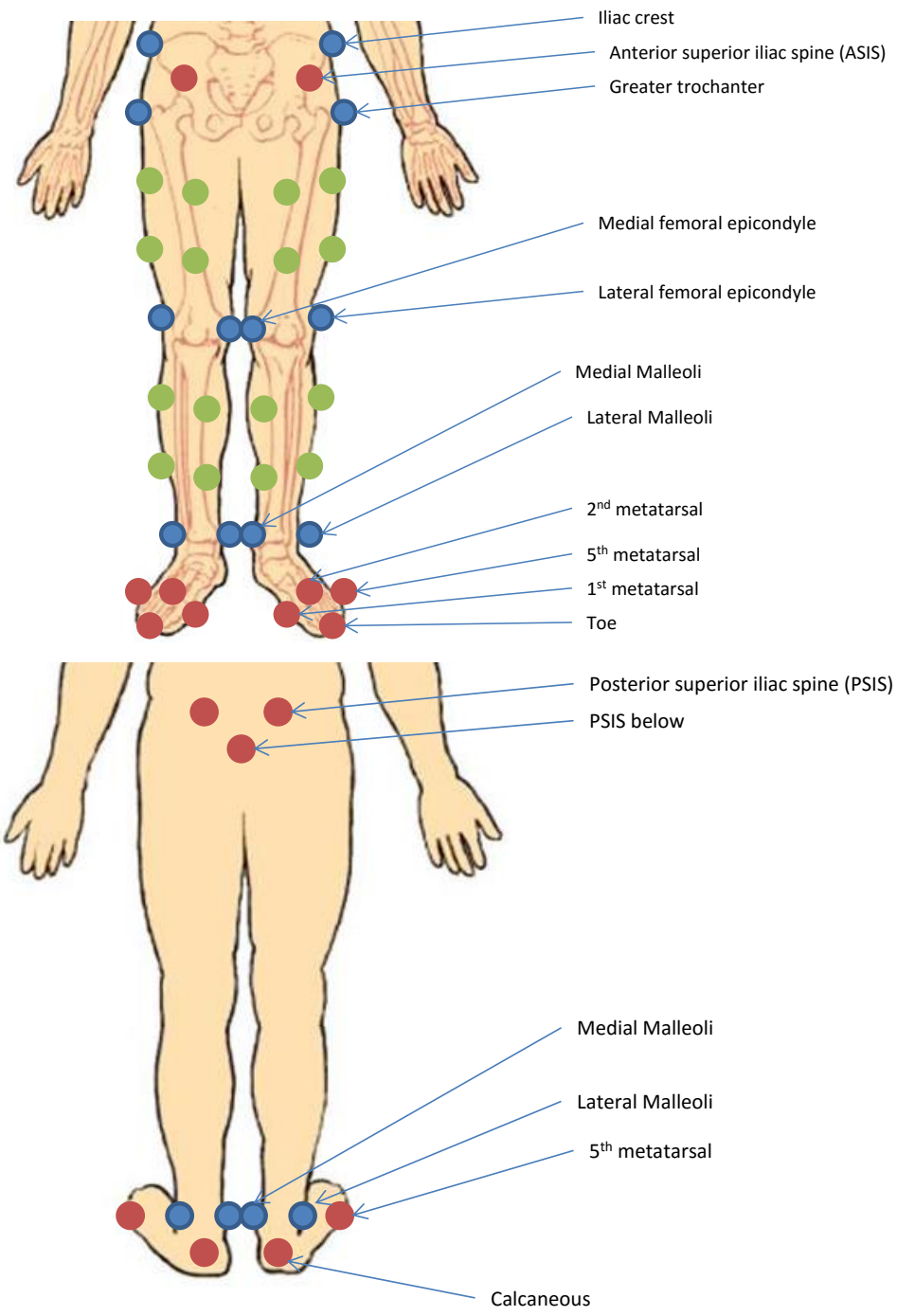


**Figure 3.6.** Marker placement according to the 6 DOF marker set. Blue markers defined joint centres and were only used during static trails. Red markers were affixed to the skin/tight clothing/shoes. Green markers represented the cluster markers around the thigh and shank that served to track limb movement (tracking markers).

**Table 3.3** Markers used to determine each segment.

| Segment | Markers |
|---|---|
| Pelvis | Anterior superior iliac spine (ASIS)<br>Posterior superior iliac spine (PSIS)<br>PSIS below<br>Iliac crest<br>Greater trochanter |
| Thigh | Thigh cluster<br>Medial and lateral femoral epicondyles |
| Shank | Shank cluster<br>Medial and lateral femoral epicondyles |
| Foot | Medial and lateral malleoli<br>Posterior aspect of the calcaneus<br>Head of the 1$^{st}$ metatarsal<br>Head of the 5$^{th}$ metatarsal<br>Dorsum of the 2$^{nd}$ metatarsal<br>Toe |

The musculoskeletal hybrid model in Visual3D was adjusted for each participant's height (m) and mass (kg) and the length of each segment was estimated from anatomical marker coordinates. The mass of each segment were estimated as a percentage of participant mass using regression equations from cadaver data (Dempster, 1955). The geometry of each segment were also estimated from participant height and regression equations from previous anthropometric reports (Hanavan, 1964). The combination of this data allowed for the local coordinate system to be located at the centre of mass of each segment which is required for the calculation of joint angles. For the computation of joint kinetics in the swing phase, segmental mass and geometry were used to calculate the inertial properties of each segment.

*Pelvis*

A CODA pelvis (Charnwood Dynamics, Codamotion, Leicester, UK) was used to construct the pelvis segment using the ASIS and PSIS markers. The local segment coordinate system was located at the mid-point between the ASIS markers (Figure 3.7). The x-y plane was defined as the plane passing through the ASIS markers and the mid-point between the PSIS markers. The x-axis was defined from the local coordinate system towards the right ASIS; the z-axis was defined as perpendicular to the x-y plane; and the y-axis was defined as the cross product of the x- and z-axis. The hip joint centre in this model was created using the regression equations (Bell et al., 1989, Bell et al., 1990), however given the difficulty in palpating these landmarks, functional joint centres were utilised in the present study.

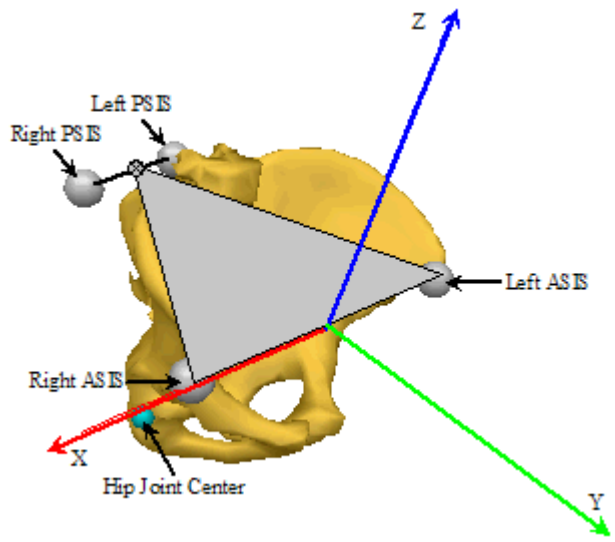


**Figure 3.7.** Schematic of the CODA pelvis (C-motion, 2009).

*Functional hip joint centre calculation*

The hip joint centre was defined using the functional joint centre method (FJC) within Visual3D, which was adapted from Schwartz & Rozumalski (2005). For the FJC to be calculated, Visual3D requires the movement of one segment relative to another (C-motion, 2009), i.e., for the hip joint centre, the thigh was tracked relative to the pelvis.

This method assumes the hip joint moves as a ball and socket joint about the fixed centre of rotation in the pelvis. Participants were instructed to stand upright and circumduct their leg. A chair was placed next to the participant to hold on to for support. It has previously been reported that this approach requires multiple repetitions to ensure greatest accuracy (Begon et al., 2007). Therefore participants performed 6-10 circumduction movements of the thigh bilaterally. During these movements, markers on the femur follow a spherical path which was centred on the joint centre. A least squares fit of the data within Visual3D allows the location of the hip joint centre to be calculated (Leardini et al., 1999, Piazza et al., 2001, Baker, 2006). Inputting this functional movement data into the Visual3D model then allowed for the functionally-derived hip joint centre to be selected as the proximal joint for the thigh segment.

*Virtual foot segment*

Within the Visual3D model, two foot segments were utilised, the traditional foot segment (using markers defined in Table 3.3) used for kinetic calculations and a virtual foot (using projected landmarks relative to the lab origin based on anatomical marker locations) used for kinematic calculations. This virtual foot segment accounts for the plantarflexion offset present in the traditional foot segment due to the non-parallel positon of the proximal joint (malleoli) and distal joint ($1^{st}$ and $5^{th}$ metatarsals), which creates a more clinically relevant ankle angle (C-motion, 2009).

### *3.5.5 Determination of internal joint moments and powers*

As per convention for gait biomechanics, internal joint moments and powers were reported and represent the combined action of the muscles and ligaments acting about a particular joint. Inverse dynamic analysis was used to calculate joint moments and

normalised to body mass (Nm/kg). The ankle moment and associated forces were solved first and then utilised for the following calculations for the proximal segment. The shank was then used to calculate the knee moment and finally the thigh segment was used to solve the hip moment. The following equations were used (within Visual3D) to calculate joint moments about the ankle, knee and hip;

Ankle Moment:

$$M_{ankle} = F_y(COP - x_{foot}) + F_x(y_{CoM} - y_{foot}) - R_y(x_{CoM} - x_{ankle}) - R_x(y_{ankle} - y_{CoM}) + I_{foot}\alpha_{foot}$$

Knee Moment:

$$M_{knee} = F_y(x_{ankle} - x_{shank}) + F_x(y_{shank} - x_{ankle}) - R_y(x_{shank} - x_{knee}) - R_x(y_{knee} - y_{shank}) + I_{shank}\alpha_{shank} - (-M_{ankle})$$

Hip Moment:

$$M_{hip} = F_y(x_{knee} - x_{thigh}) + F_x(y_{thigh} - x_{knee}) - R_y(x_{thigh} - x_{hip}) - R_x(y_{hip} - y_{thigh}) + I_{thigh}\alpha_{thigh} - (-M_{knee})$$

where $M$ is joint moment, $F$ is force, $x$ is the horizontal distance calculated from marker coordinates, $y$ is the vertical distance calculated from marker coordinates, $R$ is joint reaction force, $I$ is moment of inertia and $\alpha$ is angular acceleration of the segment.

Joint powers were normalised to body mass (W/kg) using the following equation for each joint;

Joint Power: $(M_x + M_y + M_z) * (\omega_x + \omega_y + \omega_z)$

where $M$ is joint moment and $\omega$ is angular velocity.

### *3.5.6 Variables of interest*

Generic variables of interest for stair ascent and stair descent are presented in Table 3.4 with task-specific variables described in the relevant Chapter.

**Table 3.4**. Definition of temporal-spatial, kinematic and kinetic variables, how they were determined, units and conventional direction of motion. All kinetic variables were normalised to body mass. GRF – ground reaction force

| Variable | Determination | Units | Direction of motion (+ve) |
|---|---|---|---|
| Speed | Rate of motion from foot contact of one limb to the next foot contact of the ipsilateral limb | m/s | |
| Stance and swing duration | Relative contribution of respective stance and swing phases to the full gait cycle | % | |
| Double support duration | Relative duration of time spent with both feet in contact with the floor | % | |
| Sagittal joint kinematics | Peak sagittal hip and knee flexion/ extension and ankle dorsiflexion/ plantarflexion | deg | Flexion and dorsiflexion |
| Hip, knee and ankle ROM | Sagittal range of motion at each respective joint | deg | |
| Sagittal joint angular velocities | Peak sagittal hip, knee and ankle angular velocities | deg/s | |
| Vertical GRF | Initial vertical peak (Fz1), second vertical peak (Fz2) | N/kg | Positive |
| Anterior and posterior GRF | Peak value representing braking (posterior) and propulsive (anterior) force | N/kg | Propulsive |
| Medial and lateral GRF | Peak value representing medial and lateral force | N/kg | Medial |
| Sagittal joint moments | Peak sagittal hip, knee and ankle joint moments | Nm/kg | Extensor and plantarflexor |
| Sagittal joint powers | Peak sagittal hip, knee and ankle joint powers | Nm/kg | Generation |

# Chapter 4. Gastrocnemii muscle architecture and Achilles tendon properties influence walking distance in claudicants with peripheral arterial disease

## 4.1 Introduction

Peripheral arterial disease with intermittent claudication (PAD-IC) primarily affects older adults, and prevalence increases with advancing age (Roger et al., 2011). The disease can be physically limiting by impacting adversely on individual quality of life, walking endurance, functional ability and independence (Chetter et al., 1997, McDermott et al., 2001, Spronk et al., 2007). The calf muscle is frequently reported as a site of claudication pain (Norgren et al., 2007) and there is evidence of plantarflexor dysfunction during level walking (Koutakis et al., 2010a, Wurdeman et al., 2012a). However, the contribution of musculoskeletal factors, either individually or in combination with one another, to the functional and quality of life limitations associated with PAD-IC are as yet unclear.

The functional properties of muscle depend on overall size and fascicle arrangement (Ward et al., 2009). Muscles required to generate large forces develop highly pennate architecture (the angle between fascicles and the muscle's line of action) with short fascicles, whilst those requiring large excursions/high velocity develop long fascicles (Lieber & Friden, 2000). Long fascicles, relative to tendon length, also have the advantage of reducing relative fascicle velocity for any given movement (Lieber & Friden, 2000), and decreasing energy cost for the same mechanical work (Beltman et al., 2004). Architectural characteristics adapt to chronic loading, unloading and ageing (Narici & Maganaris, 2007). Those with PAD-IC are typically older individuals (Roger et al., 2011) that are less physically active than healthy counterparts (McDermott et al., 2004b) and have the added burden of reduced blood supply to working muscles. Consequently, it is

expected that the architecture of claudicant muscles may be different from healthy controls, impacting on muscle function and energy requirements.

Muscle work is transmitted to the skeleton by the tendon, which deforms, stretching and recoiling, during movement. Consequently, tendon properties can modulate the outcome of muscle contraction, impacting muscle length and thus maximum muscle force production, and the rate of force development (Maganaris & Paul, 1999). Tendons store elastic energy when stretched, some of which is lost as heat (defined as hysteresis), but the remainder is recovered during recoil to contribute to the next shortening task. This reduces the metabolic energy required from the muscle during shortening (e.g., propulsion in walking), improving movement efficiency (Peltonen et al., 2013).

Tendon properties have been shown to deteriorate with increasing age (Kubo et al., 2003) and these adverse changes may be linked to reduced blood supply (Del Buono et al., 2013). Given the increasing prevalence of PAD-IC with advancing age (Roger et al., 2011) combined with disease-induced reductions in blood supply, it is possible that the tendons of claudicants undergo significant deterioration compared to healthy counterparts. The reduced levels of physical activity associated with PAD-IC (McDermott et al., 2001) mean that claudicants' tendons may experience further deterioration associated with disuse (Reeves et al., 2005a). In combination, it seems likely that the tendons of claudicants would be smaller, weaker and have greater hysteresis (lost elastic energy) than those of healthy individuals.

The purpose of this study was to determine (i) whether PAD-IC causes *in vivo* alterations in gastrocnemii muscle architecture and the material and mechanical properties of the Achilles tendon and (ii) whether these parameters influence walking endurance. This was achieved by (i) exploring relationships between muscle-tendon characteristics and disease severity (ankle brachial pressure index (ABPI)) and drawing comparisons to a healthy control group of older adults, and (ii) multiple regression modelling of muscle-tendon characteristics to explain initial and absolute claudication walking distances. It was hypothesised that PAD-IC would induce changes comparable to disuse and ageing: shorter relative fascicle lengths (fascicle: tendon length ratio), reduced pennation angles, tendon stiffness and Young's modulus, and greater hysteresis and peak strain. Our second hypothesis was that these muscle-tendon parameters would be able to explain a large portion of walking endurance with the aforementioned changes having detrimental effects.

## 4.2 Methods

### *4.2.1 Participants*

A total of 22 participants were recruited consisting of 12 claudicants (seven unilateral and five bilateral) and ten healthy controls (Table 4.1). Details pertaining to the assessment of disease severity and walking endurance are depicted in Chapter 3. Briefly, the post-exercise ankle brachial pressure index classified the severity of disease in claudicants and was used to determine the sub-groups. One individual (bilateral) was deemed an outlier and was consequently removed from all analysis. The tendon force of this individual was 47% larger than the largest tendon force measured in the full cohort. Due to errors during data collection, one limb from a unilateral claudicant (symptomatic) was excluded from further analysis. Symptomatic limbs (ABPI <0.9) for all the claudicants were then

categorised into those with low disease severity (high ABPI, N=7 providing 8 limbs for analysis) and high disease severity (low ABPI, N=7 providing 8 limbs for analysis) groups, by splitting them at the median ABPI (0.59). For clarity, these groups will be referred to as 'low ABPI' and 'high ABPI' throughout. This threshold does not necessarily reflect a clinically important marker of vascular function, but allows an exploration of whether disease severity-induced changes in muscle and tendon properties were detectable between participants within the ABPI range of our sample. The non-claudicating limb of the unilateral patients was subsequently identified to represent the 'asymptomatic-limb' group. Control participants also undertook the exercise protocol to determine ABPI values and confirm the absence of disease.

### *4.2.2 Muscle architecture measures*

Full details are described in Chapter 3. Briefly, resting muscle architecture of both lateral and medial gastrocnemius (GL and GM, respectively) were imaged using B-model ultrasound imaging (50 mm probe length, MyLab50 x-vision, Esaote Biomedica, Genoa, Italy). Fascicle length, pennation angle and muscle thickness were measured from three separately exported images using ImageJ, with the average taken forward for further analysis. Ultrasound imaging was also used to identify the proximal and distal ends of the muscle, and the calcaneal insertion of the Achilles tendon. A tape measure was then used to measure muscle-tendon unit (MTU) and muscle lengths. Data were analysed in absolute terms and after scaling to individual anthropometric dimensions.

### *4.2.3 Calculating Achilles tendon force*

The gastrocnemii contribution to Achilles tendon force during isometric plantarflexor maximal voluntary contractions (MVCs) was calculated using equations 3.2 and 4.1:

4.1 $$GS\ moment = joint\ moment + antagonist\ moment - soleus\ moment$$

where each component is detailed in Chapter 3 and summarised below.

Joint moment was recorded while participants performed three ramped plantarflexor MVCs lasting approximately five seconds and then returned to rest across the same time period on an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems Inc., New York, USA). Adequate rest was proved between trials (~1 min) and the trial with the highest MVC was selected for further analysis. The moment-angle relationship was explored (Figure 1, Appendix A4) and for all participants, MVC was achieved at maximum dorsiflexion which is consistent with previous research (Maganaris, 2003).

Antagonist co-activation during the plantarflexor MVC was assessed using the surface EMG of the tibialis anterior (Telemyo 2400T, Noraxon, Arizona, USA). The dorsiflexion EMG-moment relationship was constructed from four dorsiflexion contractions of increasing intensity. The tibialis anterior EMG at each stage of the ramped plantarflexor trials was then substituted into this relationship to predict antagonist dorsiflexion moment (Kellis & Baltzopoulos, 1997). The soleus contribution to plantarflexion moment was quantified during additional plantarflexor contractions with the knee flexed to 90° where the gastrocnemius muscles were slack and did not contribute to the joint moment (Maganaris & Paul, 2002). The soleus EMG-moment relationship across the two joint configurations (knee extended (0°) and knee flexed (90°)) was used to correct activation differences (see equation 3.5).

Achilles tendon moment arm (MA) was calculated using the tendon excursion method (Maganaris and Paul, 2002, Fath et al., 2010), and ultrasound imaging to quantify linear GM myotendinous junction (MTJ) displacement.

### *4.2.4 Achilles tendon dimensions and elongation*

For the purposes of calculating tendon properties, Achilles tendon resting length was measured from the proximal origin of the GM MTJ to the distal insertion at the calcaneus whilst the ankle was in maximum dorsiflexion prior to plantarflexor contractions. Free tendon cross-sectional area (CSA) was measured at 1, 2 and 3 cm proximal to the insertion onto the calcaneus using axial-plane ultrasound imaging (Maganaris & Paul, 2002) and analysed using ImageJ. The average of all three sites was used for further calculations.

The ultrasound probe was aligned with the distal GM MTJ and the Achilles tendon in the sagittal plane and securely fixed to the skin with an echo-absorptive marker within the viewing window to allow for correction of any artefacts caused by probe movement (Maganaris & Paul, 2000). Ultrasound videos were recorded synchronously with plantarflexor moments during MVCs to track MTJ displacement. Images were digitised to measure tendon elongation at each 10% of peak tendon force using ImageJ.

### *4.2.5 Tendon stiffness, Young's modulus and tendon hysteresis*

Tendon stiffness was calculated as the gradient of the force-elongation curve by differentiating the polynomial equation at MVC for each participant. Tendon strain was calculated by normalising elongation to resting length. Tendon stress was calculated by normalising tendon force to CSA. Tendon Young's modulus was calculated as tendon

stiffness multiplied by the ratio of tendon length to CSA. Energy stored in the tendon was calculated as the area beneath the whole of the loading curve, and energy released as the area beneath the unloading curve, by integrating the equation describing the respective force-elongation curves. Hysteresis was calculated as the difference between the energy stored and energy released, normalised as a percentage of the energy stored. Due to technical difficulties analysing the unloading curve in four participants (two healthy controls, one unilateral claudicant and two bilateral claudicants), tendon hysteresis was calculated for 6 high ABPI limbs, 6 low ABPI limbs, 6 asymptomatic limbs and 8 healthy control limbs

*4.2.6 Statistical analysis*

A Pearson's partial product-moment correlation was performed to assess relationships between disease severity (as assessed by ABPI and controlled for the influence of age), walking endurance (as assessed by ICD and ACD) and gastrocnemii architecture parameters and all Achilles tendon parameters in the symptomatic limbs only. Data were examined for normality and outliers by visual inspection of histogram and box-plots. A one-way ANOVA was performed to compare differences in muscle-tendon parameters between the healthy controls, asymptomatic-limb group and high and low ABPI groups. Sidak post-hocs were applied when appropriate. Where non-parametric variables were identified, independent samples Kruskal-Wallis tests were performed with subsequent Mann-Whitney *U* tests applied where appropriate.

To assess which architectural parameters and Achilles tendon properties were most important to explain variations in walking endurance (as measured by ICD and ACD), a backwards step-wise regression was performed on the symptomatic limbs (N=16) to

avoid the suppressor effect typically associated with forwards step-wise regression models (Menard et al., 2004). Key variables included in the analysis were GL and GM fascicle: tendon lengths, pennation angle and muscle thickness; tendon force, strain, stiffness and mechanical hysteresis; and ABPI.

For all statistical tests, significance was accepted at $P \leq .05$ and trends were accepted at $P < .10$. For correlation and regression analyses, a moderate relationship was accepted as R=.40 – .59, a strong relationship as R=.60 – .79 and a very strong relationship as R=.80 – 1 (Taylor, 1990). Since low ABPI values indicate high disease severity, a positive relationship signifies a decrease in the respective parameter with increasing disease severity.

### 4.3 Results

No significant differences were found between any groups for age (P=.414), height (P=.345), mass (P=.543) or BMI (P=.796) (Table 4.1). No significant differences existed between low ABPI, high ABPI or unilateral (asymptomatic-limb) groups in ICD (P=.197) and ACD (P=.321). Between-group differences in ABPI were consistent with disease presentation.

**Table 4.1**. Participant characteristics. Data are presented as group mean (SD) unless otherwise stated. BMI – Body mass index, ABPI – Ankle brachial pressure index. ICD – Initial claudication distance. ACD – Absolute claudication distance.

| | **Low ABPI** | **High ABPI** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|---|
| **# limbs** | 8 | 9 | 7 | 10 |
| **% Males** | 77.8 | 87.5 | 57.1 | 40 |
| **Age (years)** | 64.3 (4.7) | 65.5 (8.0) | 66.1 (7.5) | 61.6 (3.6) |
| **Height (m)** | 1.72 (0.07) | 1.73 (0.06) | 1.69 (0.10) | 1.66 (0.09) |
| **Mass (Kg)** | 81.1 (15.9) | 82.5 (21.5) | 82.3 (21.1) | 72.3 (10.9) |
| **BMI ($Kg/m^2$)** | 27.6 (5.3) | 27.3 (5.9) | 28.5 (4.8) | 26.1 (3.7) |
| **ABPI pre-exercise** | 0.71 (0.19) | 0.89 (0.22) | 1.01 (0.16) | 1.01 (0.09) |
| **ABPI post-exercise** | 0.39 (0.17) | 0.63 (0.15) | 0.90 (0.06) | 1.01 (0.16) |
| **ICD (m)** | 106.3 (51.0) | 123.8 (47.2) | N/A | N/A |
| **ACD (m)** | 285.0 (141.7) | 298.8 (147.0) | N/A | N/A |
| **Disease duration (months)** | 42.8 (44.2) | 52.9 (46.7) | N/A | N/A |
| **% Hypertension** | 50 | 50 | 42.9 | 10 |
| **% Hypercholesterolemia** | 50 | 50 | 71.4 | 20 |
| **% past smokers** | 50 | 62.5 | 57.1 | 30 |
| **% present smokers** | 50 | 37.5 | 42.9 | 0 |

*4.3.1 Correlation analysis*

Increasing disease severity was significantly correlated with longer GL and GM fascicle: tendon lengths, shorter tendons and greater tendon hysteresis (Figure 4.1) and greater tendon strain (Table 4.3). Poorer walking endurance, as measured by ICD, was associated with longer GL and GM fascicle: tendon lengths, greater GM pennation angle, and trends towards higher tendon strain and hysteresis. Poorer maximum walking endurance, as measured by ACD, was associated with increased GL and GM pennation angle. Individual R- and P-values are presented in Table 4.2 and 4.3 for all correlations. Disease severity was not associated with ICD (R=.215, P=.441) or ACD (R=.161, P=.566).

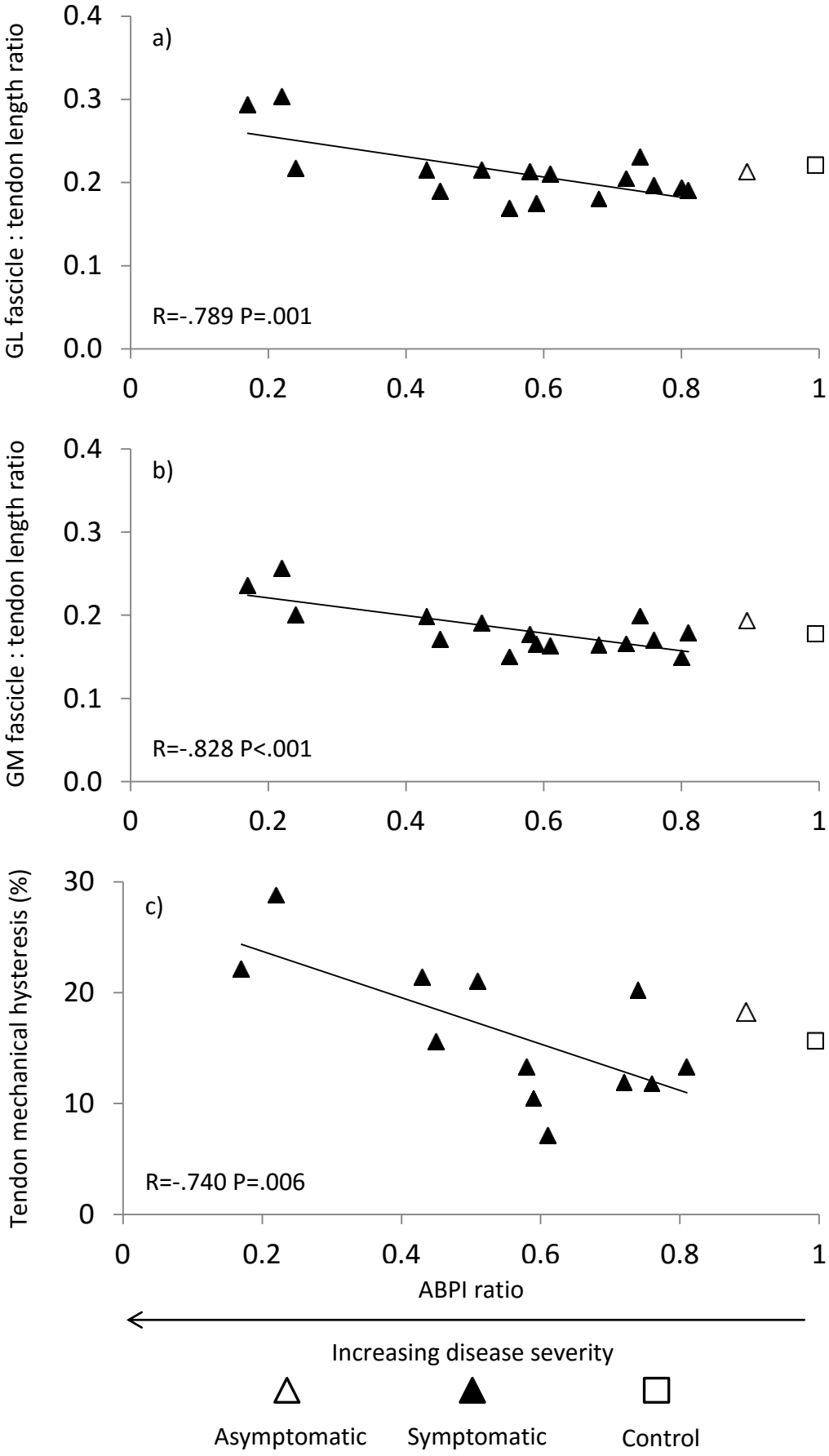


**Figure 4.1.** Correlations between disease severity (ABPI) and GL and GM fascicle: tendon length ratio (a and b respectively) and tendon mechanical hysteresis (c). Average control and asymptomatic-limb groups are shown for comparison and are not included in correlation analysis

**Table 4.2**. Pearson partial correlations (controlled for the influence of age) between disease severity (ABPI), walking endurance (ICD and ACD) and gastrocnemii architectural parameters. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10).

| **Gastrocnemii architecture** | | GL fascicle : tendon length | GM fascicle : tendon length | GL fascicle : muscle length | GM fascicle : muscle length |
|---|---|---|---|---|---|
| ABPI | Correlation | -.789 | -.828 | -.451 | -.267 |
| | Significance | .001 | <.001 | .106 | .357 |
| ICD | Correlation | -.547 | -.487 | -.312 | -.252 |
| | Significance | .043 | .081 | .277 | ..385 |
| ACD | Correlation | -.436 | -.345 | -.290 | -.353 |
| | Significance | .120 | .228 | .315 | .216 |
| **Gastrocnemii architecture** | | GL pennation | GM pennation | | |
| ABPI | Correlation | .188 | -.332 | | |
| | Significance | .503 | .226 | | |
| ICD | Correlation | -.310 | -.807 | | |
| | Significance | .261 | <.001 | | |
| ACD | Correlation | -.566 | -.803 | | |
| | Significance | .028 | <.001 | | |

**Table 4.3**. Pearson partial correlations (controlled for the influence of age) between disease severity (ABPI), walking endurance (ICD and ACD) and Achilles tendon properties. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10).

| **Achilles tendon properties** | | Tendon length | Tendon force | Elongation at maximal tendon force | Stiffness at maximal tendon force |
|---|---|---|---|---|---|
| ABPI | Correlation | .728 | .052 | -.061 | .166 |
| | Significance | .003 | .854 | .836 | .570 |
| ICD | Correlation | .365 | -.205 | -.110 | -.141 |
| | Significance | .199 | .463 | .709 | .630 |
| ACD | Correlation | .262 | .224 | -.124 | .165 |
| | Significance | .366 | .423 | .672 | .573 |
| **Achilles tendon properties** | | Young's modulus at maximal tendon force | Peak strain | Mechanical Hysteresis | |
| ABPI | Correlation | .247 | -.490 | -.740 | |
| | Significance | .395 | .075 | .006 | |
| ICD | Correlation | -.146 | -.261 | -.598 | |
| | Significance | .619 | .367 | .040 | |
| ACD | Correlation | .115 | -.219 | -.277 | |
| | Significance | .696 | .453 | .384 | |

*4.3.2 Between-group comparisons*

Several differences were detected between groups in absolute and relative muscle-tendon dimensions (Table 4.4). In the GL, relative fascicle: tendon length was smaller in the high ABPI group compared to the control group (P=.027, *ES*=.37, power=.40). In the GM, the low ABPI (high disease severity) group had longer fascicle lengths compared to controls (P=.014, *ES*=.55, power=.78) and longer fascicle: tendon lengths compared to the high ABPI group (P=.050, *ES*=.56, power .29).

At individual maximum tendon force, both claudicant groups and the asymptomatic-limb group demonstrated reduced Young's modulus compared to the control group (P=.029-.100, *ES*=.41-.47, power=.50-.65; Table 4.5). Compared to controls, tendon stiffness was lower in the asymptomatic-limb group (P=.053, *ES*=.57, power=.85; Table 4.5). The low ABPI (high disease severity) had significantly greater mechanical hysteresis compared to the high ABPI group (P=.004, *ES*=.62, power=.88) and showed a trend towards increased hysteresis compared to the control group (42%, P=.065, *ES*=.49, power=.65) (Table 4.5).

No significant differences existed between all groups for MVC (P=.631), GS moment (P=.738), moment arm (P=.414) or peak tendon force (P=.825) (Table 4.5).

**Table 4.4**. Group mean (SD) musculotendinous length and size parameters. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P=≤.10). [L] = vs low ABPI group (High disease severity), [H] = vs high ABPI group (low disease severity), [A] = vs asymptomatic-limb group [Con] = vs control group

| | **Low ABPI** | **High ABPI** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|---|
| Tibia length (cm) | 40.5 (2.4) | 41.6 (1.3)[A] | 39.5 (2.5) | 38.9 (3.2) |
| MTU length (cm) | 45.5 (3.7)[C] | 45.8 (1.1)[Con] | 43.0 (3.7) | 41.6 (4.3) |
| GM Achilles tendon length (cm) | 22.3 (3.0) | 24.2 (1.1)[Con, ,A] | 21.5 (2.7) | 20.6 (2.5) |
| Achilles tendon CSA ($cm^2$) | 89.6 (13.1) | 98.5 (23.9) | 82.5 (19.5) | 85.1 (12.4) |
| ***Lateral Gastrocnemius*** | | | | |
| Muscle length (cm) | 22.4 (1.2) | 21.3 (0.8) | 21.6 (1.8) | 20.4 (2.5) |
| Fascicle length (cm) | 4.98 (0.78) | 4.77 (0.38) | 4.54 (0.50) | 4.60 (0.64) |
| Fascicle length : Muscle length | 0.22 (0.03) | 0.22 (0.02) | 0.21 (0.02) | 0.23 (0.04) |
| Fascicle length : Tendon length | 0.23 (0.05) | 0.20 (0.02)[Con] | 0.21 (0.02) | 0.22 (0.03) |
| Thickness (cm) | 1.26 (0.23) | 1.29 (0.20) | 1.24 (0.24) | 1.17 (0.21) |
| Pennation (°) | 15.2 (2.0) | 16.7 (2.8) | 16.9 (2.8) | 14.8 (1.8) |
| ***Medial Gastrocnemius*** | | | | |
| Muscle length (cm) | 23.4 (2.6) | 22.0 (1.9) | 21.3 (2.5) | 21.4 (2.5) |
| Fascicle length (cm) | 4.34 (0.59)[Con] | 4.09 (0.29) | 4.10 (0.34) | 3.65 (0.45) |
| Fascicle length : Muscle length | 0.19 (0.03) | 0.19 (0.02) | 0.19 (0.03) | 0.17 (0.02) |
| Fascicle length : Tendon length | 0.20 (0.03)[H] | 0.17 (0.01) | 0.19 (0.03) | 0.18 (0.03) |
| Thickness (cm) | 1.77 (0.33) | 1.68 (0.31) | 1.73 (0.17) | 1.62 (0.20) |
| Pennation (°) | 27.5 (4.5) | 26.4 (3.8) | 27.9 (4.0) | 29.4 (3.8) |

**Table 4.5**. Group mean (SD) measures of MVC, Achilles tendon tensile properties and measures of elastic energy. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P=≤.10). [L] = vs low ABPI group (High disease severity), [H] = vs high ABPI group (low disease severity), [A] = vs asymptomatic-limb group [Con] = vs control group

| | **Low ABPI** | **High ABPI** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|---|
| MVC (Nm) | 116.4 (29.0) | 100.6 (27.2) | 102.2 (33.5) | 114.4 (28.5) |
| GS moment (Nm) | 73.6 (20.6) | 64.4 (22.6) | 63.6 (20.8) | 65.2 (14.6) |
| Moment arm (cm) | 3.47 (0.73) | 3.40 (0.48) | 3.59 (0.67) | 3.24 (0.58) |
| Tendon force (N) | 2150.3 (591.0) | 1947.4 (827.9) | 1834.6 (744.9) | 2089.6 (630.7) |
| Tendon elongation (mm) | 18.4 (3.2) | 18.7 (2.2) | 18.2 (4.5) | 15.3 (3.0) |
| Stiffness (N/mm) | 139.8 (49.9) | 129.5 (51.0) | 109.4 (37.2)[Con] | 184.3 (65.6) |
| Young's modulus (GPa) | 0.33 (0.09)[Con] | 0.30 (0.09)[Con] | 0.30 (0.12)[Con] | 0.48 (0.22) |
| Tendon strain (%) | 8.6 (1.6) | 7.8 (1.2) | 8.6 (2.2) | 7.5 (1.1) |
| Tendon stress (MPa) | 24.1 (5.8)[H] | 19.6 (5.7) | 23.2 (10.5) | 24.7 (8.3) |
| ***Energy utilisation*** | | | | |
| Energy stored (kJ) | 20.4 (5.6) | 16.8 (9.7) | 16.4 (11.4) | 13.0 (5.7) |
| Energy released (kJ) | 16.2 (4.3) | 14.5 (7.4) | 12.7 (7.6) | 11.3 (5.0) |
| Mechanical hysteresis (%) | 20.1 (5.7)[Con, H] | 12.4 (4.0) | 17.2 (9.7) | 13.2 (4.7) |

*4.3.3 Regression analysis*

Walking distances were not explained by ABPI alone (see correlations above). The inclusion of muscle-tendon parameters with ABPI led to significant predictions of both ICD and ACD (P=.041 and P=.037, respectively for models with the highest adjusted $R^2$). Sixty-five percent of the variance in ICD could be explained using ABPI, GL and GM pennation angle, tendon force, tendon stiffness and mechanical hysteresis (Table 4.6). Similarly, ABPI, GL and GM pennation angle, tendon force and mechanical hysteresis was the strongest combination to predict ACD and could explain 59% of the variance (Table 4.7).

**Table 4.6**. Backward step-wise regression between architectural parameters, tendon properties and disease severity (ABPI) and walking endurance (ICD). Prediction equations are depicted for the model that explains the highest portion of variance (highest adjusted $R^2$) and the most efficient model (fewest parameters).

| ICD | R | $R^2$ | Adjusted $R^2$ | P-value |
|---|---|---|---|---|
| Model 1 | .918 | .843 | .371 | .345 |
| Model 2 | .918 | .843 | .528 | .179 |
| Model 3 | .918 | .842 | .621 | .080 |
| Model 4 | .908 | .825 | .649 | .041 |
| Model 5 | .891 | .795 | .648 | .023 |
| Model 6 | .842 | .710 | .565 | .027 |
| Model 7 | .820 | .672 | .563 | .015 |

**Prediction for Model 4** = 483.5 - (4.489*Hysteresis) + (0.027*Tendon Force) - (0.269*Tendon stiffness) + (4.044*GL pennation) - (11.401*GM pennation) - (136.36*ABPI)

**Prediction for Model 7** = 506.690 – (4.935*Hysteresis) – (9.054*GM pennation) – (126.544*ABPI)

**Model 1:** ABPI, GM pennation, hysteresis, tendon stiffness, tendon force, GL pennation, GM fascicle: tendon length, GL fascicle: tendon length, strain
**Model 2:** ABPI, GM pennation, hysteresis, tendon stiffness, tendon force, GL pennation, GM fascicle: tendon length, GL fascicle: tendon length
**Model 3:** ABPI, GM pennation, hysteresis, tendon stiffness, tendon force, GL pennation, GM fascicle: tendon length
**Model 4:** ABPI, GM pennation, hysteresis, tendon stiffness, tendon force, GL pennation
**Model 5:** ABPI, GM pennation, hysteresis, tendon stiffness, tendon force
**Model 6:** ABPI, GM pennation, hysteresis, tendon stiffness
**Model 7:** ABPI, GM pennation, hysteresis

**Table 4.7**. Backward step-wise regression between architectural parameters, tendon properties and disease severity (ABPI) and walking endurance (ACD). Prediction equations are depicted for the model that explains the highest portion of variance (highest adjusted $R^2$) and the most efficient model (fewest parameters).

| ACD | R | $R^2$ | Adjusted $R^2$ | P-value |
|---|---|---|---|---|
| Model 1 | .892 | .796 | .184 | .460 |
| Model 2 | .892 | .796 | .387 | .271 |
| Model 3 | .890 | .793 | .499 | .145 |
| Model 4 | .887 | .787 | .574 | .069 |
| Model 5 | .873 | .762 | .593 | .037 |
| Model 6 | .839 | .704 | .556 | .029 |
| Model 7 | .798 | .637 | .516 | .023 |
| Model 8 | .765 | .585 | .502 | .012 |
| Model 9 | .699 | .489 | .442 | .008 |
| **Prediction for Model 5** = 1322.244 - (15.515*Hysteresis) + (0.099*Tendon Force) - (14.474*GL pennation) - (22.324*GM pennation) - (294.257*ABPI) | | | | |
| **Prediction for Model 9** = 934.509 – (-23.988*GM pennation) | | | | |

**Model 1:** GM pennation, tendon force, hysteresis, ABPI, GL pennation, tendon stiffness, strain, GM fascicle: tendon length, GL fascicle: tendon length
**Model 2:** GM pennation, tendon force, hysteresis, ABPI, GL pennation, tendon stiffness, strain, GM fascicle: tendon length
**Model 3:** GM pennation, tendon force, hysteresis, ABPI, GL pennation, tendon stiffness, strain
**Model 4:** GM pennation, tendon force, hysteresis, ABPI, GL pennation, tendon stiffness
**Model 5:** GM pennation, tendon force, hysteresis, ABPI, GL pennation
**Model 6:** GM pennation, tendon force, hysteresis, ABPI
**Model 7:** GM pennation, tendon force, and hysteresis
**Model 8:** GM pennation, tendon force
**Model 9:** GM pennation

## 4.4 Discussion

This is the first study to have quantified the fascicle architecture of the gastrocnemii muscles and the mechanical and material properties of the Achilles tendon in patients with PAD-IC. In partial support of our first hypothesis, associations were found between low ABPI values (increased disease severity) and relatively longer GM fascicles and increased tendon mechanical hysteresis. These were supported by significant differences between claudicants, particularly those with more severe forms of disease, and controls in both architectural parameters and tendon properties. Our results indicate that these changes in muscle-tendon properties play an important role in influencing walking endurance in claudicants, and can explain a large portion of the variance in walking distances that ABPI alone cannot.

Correlation analysis revealed that both GL and GM fascicle lengths increased while tendon length decreased significantly, leading to greater fascicle: tendon length ratios with increasing disease severity. Additionally, those with lower ABPI had significantly longer GM fascicle: tendon lengths compared to those with higher ABPI (Table 4.2). These adaptations allow the muscle-tendon unit to lengthen and shorten with less relative fascicle, and therefore sarcomere, displacement. As a result, the GM MTU in those with low ABPI values appear to have adapted in such a way that would facilitate length changes during movement with less energy consumption per unit of muscle force (Beltman et al., 2004). However, the impact of this potential energy saving adaptation may be negated by the concomitant increase in mechanical hysteresis, which was 42% greater in those with low ABPI compared to the control group (Figure 4.1 and Table 4.5). Those individuals with more severe forms of PAD-IC and those with limited walking endurance, are less able to utilise this energy recovery mechanism in the tendon, and so

must provide metabolic energy to the muscles to make up the shortfall, increasing the energy cost of movement. This observation is commensurate with reported reductions in walking economy with greater disease severity (Gardner et al., 2010). Therefore, efforts to improve the recovery and utilisation of the energy stored in the tendon (by reducing hysteresis) through appropriately designed interventions, such as progressive resistance training (Reeves et al., 2003b), may have substantial benefits for walking endurance in this population.

The second aim of this study was to try and elucidate the extent to which gastrocnemii muscle architecture and Achilles tendon properties influence walking endurance. ABPI alone could not explain variations in walking distances, but when combined with the muscle-tendon parameters, significant models that could explain a moderate-large portion of the variance (highest adjusted $R^2$ =.65 and $R^2$=.59 for ICD and ACD, respectively) were found. The construct of both models with the highest adjusted $R^2$ (Table 4.6 and 4.7) has justifiable biomechanical and physiological reasoning, and this provides confidence in their validity.

It was hypothesised that greater hysteresis would have a negative impact with walking endurance, which has been substantiated. Pennation angle, which was included in both models, can be considered as an index of muscle functional "design", with lower angles suited to large excursions rather than force production (Lieber & Friden, 2000). Since pennation angle was predominantly associated with negative coefficients, in both models containing the fewest parameters and those with the highest adjusted $R^2$ (Table 4.6 and 4.7), this suggests that muscles with a "design" favouring length changes are beneficial to walking endurance. Longer fascicle: tendon length ratios would also reflect such a

functional design, thus, the exclusion of fascicle: tendon length ratio from the models suggests that pennation angle was adequate to explain this portion of the variance. Interestingly, GM pennation with negative coefficients was present in models that could explain the most variance and the most efficient models for both ICD and ACD, reinforcing the importance of this muscle "design" in predicting walking capacity. Finally, tendon force had a positive coefficient in both models, indicating that greater muscle strength allowed longer walking distances. This may be because a greater maximum strength would mean the mechanical demands of walking are lower relative to maximum capacity, thus according to the size principle (Henneman et al., 1965), the muscle may rely to a greater extent on the more efficient slow-type muscle fibres. It must be acknowledged that the sample size of the present study was small for typical multiple regression models, which require further exploration and validation. Future work should further explore the role of each parameter in explaining walking endurance, and consider how these variables respond to treatment and the subsequent impact on walking endurance.

Interestingly, the tendon properties in the asymptomatic-limb group were more similar to the claudicating limbs than the controls. This observation was confirmed by additional pairwise t-tests between the symptomatic and asymptomatic limbs of unilateral claudicants that revealed no significant differences between limbs ($p>.110$ for all tendon parameters) and supports previous reports of impairments in those with asymptomatic PAD (McDermott et al., 2008a). It suggests that either systemic adaptations were impacting the asymptomatic limb, in particular the asymptomatic tendon, or disuse resulting from reduced physical activity levels were leading to a deterioration in tendon properties. At this stage it is not possible to determine which of these mechanisms may be responsible.

Architectural characteristics were measured at a single site within the gastrocnemii muscle. However, whilst architecture may be homogenous in young, healthy individuals (Maganaris et al., 1998b), this may not be the case across the entire claudicant muscle. Regional CSA differences have been reported in both the patella (Westh *et al.,* 2007, Seynnes *et al.,* 2009) and Achilles tendons (Westh *et al.,* 2007). Given that the GM Achilles tendon was significantly longer in the high ABPI group, the absolute measurement sites of 1, 2 and 3 cm used in the present study may have introduced relative inconsistency between groups in the calculated average CSA used for further analysis. However, the effect of this is small since actual difference in scanning site equated to <6mm therefore the potential confounding influence of these regional variations will be minimal. In relation to measurement of moment arm length, any force acting through the tendon during joint rotation would result in a greater deformation in the claudicant group than controls, thus confounding comparisons. However, we consider the force acting to be very small and this effect non-significant (see section 3.4.6). Additionally, the calculation of tendon force required the simplification of the forces acting about the joint, but the present approach has been used in numerous previous studies (Maganaris & Paul, 1999, Maganaris & Paul, 2002, Reeves et al., 2003b). Specifically, accounting for antagonistic co-activation using the EMG of the TA during dorsiflexor contractions likely underestimates the true dorsiflexor co-activation moment (Billot et al., 2010). Furthermore, it was assumed that the gastrocnemii did not contribute towards measured plantarflexor moment with the knee flexed at 90°, though we were unable to quantitatively confirm. However, it is certain that, at such a short muscle length, the gastrocnemii force was substantially reduced compared to longer muscle lengths. There were no between group differences in antagonist co-activation (Chapter 5), moment-angle relationships (King et al., 2014) or associations with disease severity, therefore we do not believe these assumptions have a confounding effect on our data.

The present study indicates that improving tendon properties and increasing strength, but without increasing pennation angle, would be beneficial for walking endurance. Finding such an intervention is not simple, since the majority of exercise interventions that improve strength, e.g. resistance training, also increase pennation angle (Reeves et al., 2009a). However, eccentric resistance training may provide a viable solution, since it has been shown to improve tendon properties (Malliaras et al., 2013) and increase muscle strength whilst lengthening fascicles but not increasing pennation (Reeves et al., 2009a). Previous research on resistance training with claudicants is sparse with conflicting reports of effectiveness (Parmenter et al., 2011). This inconsistency could be due to the use of conventional, predominantly concentric resistance training which may not elicit the optimal adaptations for walking endurance. Future exercise studies should evaluate the effectiveness of eccentric resistance training for improving walking endurance of individuals with PAD-IC.

## 4.5 Conclusions

The present study has shown that more severe forms of PAD-IC are associated with muscle remodelling towards longer GM fascicle: tendon length ratios and less effective utilisation of elastic energy stored in the tendon (increased hysteresis). Importantly, when combined with ABPI, tendon hysteresis, architectural parameters of muscle functional design and the muscle's force producing capacity were able to explain large portions (~65%) of walking endurance. The present findings suggest that eccentric resistance training of the plantarflexor muscles may be a valuable intervention to improve tendon properties, muscle function and ultimately walking endurance.

# Chapter 5. Dynamic muscle quality of the plantarflexors is impaired in claudicants with peripheral arterial disease and associated with poorer walking endurance

## 5.1 Introduction

The most frequent site of claudication pain is in the plantarflexor (triceps surae) muscles (Norgren et al., 2007), where there are clear signs of dysfunction, such as reduced ankle power generation during gait (Wurdeman et al., 2012a, Koutakis et al., 2010a). However, the few previous studies directly investigating plantarflexor function are inconsistent about whether strength is diminished in claudicants compared to healthy controls (Scott-Okafor et al., 2001, McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012). Poor muscle strength, notably plantarflexor strength, is a strong predictor of mortality in men with PAD-IC (Singh et al., 2010, McDermott et al., 2012), so it is essential to understand the nature of any strength impairments and the underlying mechanisms, so that exercise interventions may be designed accordingly.

The "strength" of a muscle group, as measured externally by hand-held or isokinetic dynamometer, depends on numerous factors, including: muscle size and quality; voluntary activation level; any resistance to intended effort from co-activation of the antagonist muscle; and length of the moment arm about which the muscle is working (Maganaris et al., 2001). Muscle quality during isometric contractions (often known as specific tension or specific force) is defined as the maximal potential muscle force (calculated using the above factors) normalised to the physiological cross-sectional area (PCSA) (Maganaris et al., 2001). In PAD-IC voluntary joint moments have been measured previously (Scott-Okafor et al., 2001, McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012) but the factors that determine externally-measured

strength have not. Consequently, the underlying mechanisms explaining any disease-induced strength losses have not been identified, and muscle quality has not yet been quantified in claudicants. Thus, it remains unknown if/how any deleterious changes in muscle properties contribute to reduced functional ability. Therefore, it is not apparent exactly how exercise interventions should be optimally designed to improve physical function.

Muscle quality is known to reduce with ageing and disuse (Suetta et al., 2009) and increase in response to resistance training (Reeves et al., 2004b). It is reasonable to assume muscle quality would be altered in claudicants given that the disease primarily affects the elderly (Roger et al., 2011) and is associated with reduced physical activity (Garg et al., 2006). Additional factors associated with PAD-IC that may further affect muscle quality include intra-muscular fat infiltration (Raval et al., 2012), which would reduce the quantity of contractile material within a given muscle, and altered fibre type composition, with contradicting findings of shifts towards more type II (fast-twitch) (McGuigan et al., 2001b, Askew et al., 2005, Gasparini et al., 2012) and conversely to more type I fibres (slow-twitch) (Regensteiner et al., 1993, Steinacker et al., 2000). As specific tension differs between fibre types (Widrick et al., 1996) any changes at the fibre level may affect whole muscle quality, force producing potential and thus functional strength. If isometric muscle quality is altered with PAD-IC then it follows that the ability to utilise this force producing potential during dynamic contraction would also be impaired, especially if the proportion of fast type-II fibres is reduced. Any change in muscle quality might also reduce the responsiveness of muscles to exercise training, a vital component of treatment for PAD-IC (Norgren et al., 2007). This may contribute to the inconsistent effects reported following progressive resistance training in claudicants (Parmenter et al., 2011).

The purpose of the study was to determine whether PAD-IC causes changes in the strength characteristics of the plantarflexors and quality of the gastrocnemii muscles. This was achieved by exploring relationships between static and dynamic measures of muscle quality and disease severity (as assessed through the ankle brachial pressure index; ABPI), and comparing asymptomatic and symptomatic limbs of claudicants to those of healthy controls. To explore the effects of muscle quality on function, correlations were performed between the factors affecting muscle strength and walking endurance (quantified through initial and absolute claudication distances). Our first hypothesis was that increased disease severity would be associated with lower voluntary isometric plantarflexor moments and concentric plantarflexor powers, and that this would be explained by smaller muscle size and reduced static and dynamic muscle quality. Our second hypothesis was that walking endurance would be associated with reduced maximum isometric plantarflexor moment, concentric plantarflexor power, and static and dynamic muscle quality.

## 5.2 Methods

### *5.2.1 Participants*

A total of 22 participants were recruited consisting of 12 claudicants (seven unilateral, five bilateral) and ten healthy controls (Table 5.1). Details pertaining to the assessment of disease severity and walking endurance are depicted in Chapter 3. Briefly, the post-exercise ankle brachial pressure index classified the severity of disease in claudicants and was used to determine the 'claudicating-limb' group (N=12 providing a total of 17 claudicating limbs; 10 from bilateral claudicants and 7 from unilateral claudicants), the 'asymptomatic-limb' group (N=7 providing a total of 7 limbs from the unilateral claudicants). One individual (bilateral) was deemed an outlier and was consequently

removed from all analysis. The tendon force of this individual was 47% larger than the largest tendon force measured in the full cohort. The dominant limb of the healthy controls was determined using a simple ball-kicking exercise and used for subsequent analysis.

### *5.2.2 Static muscle quality calculation*

The static muscle quality (specific tension) of the combined gastrocnemii muscles was defined as maximal potential Achilles tendon force (equation 3.8) normalised to the reduced gastrocnemii physiological cross-sectional area (equation 3.11) (O'Brien et al., 2010). The methods used to determine each component of these equations are detailed in Chapter 3 and summarised below.

### *5.2.3 Joint moment*

Participants were secured into the chair of an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems Inc., New York, USA), sat in an upright position with their hip flexed (85°), knee extended (0°) and the lateral malleolus aligned with the centre of rotation of the dynamometer arm during muscle contraction. To ensure isometric muscle strength of the gastrocnemii muscles was measured at the optimum joint angle, MVCs were elicited at 10° intervals from maximum plantarflexor to maximum dorsiflexion (see Figure 2 in Appendix A4). Verbal encouragement was given throughout all trials. Three maximal isometric plantarflexor contractions were performed at each joint angle and the peak gravity corrected joint moment was taken forward for further analysis. For all participants, peak joint moment was achieved at maximum dorsiflexion, which was consistent with healthy populations (Maganaris, 2003). It must be noted that MVC presented here differs to that reported in Chapter 4. This is due to small variations in MVC

during synchronous ultrasound recordings of GM MTJ (in Chapter 4) and synchronous ultrasound recordings of muscle architecture (in Chapter 5). All further trials to establish voluntary and antagonist activation, soleus contribution, fascicle length and pennation were performed in this joint position.

Antagonist co-activation during the plantarflexor MVC was assessed using the surface EMG of the tibialis anterior (Telemyo 2400T, Noraxon, Arizona, USA). The dorsiflexion EMG-moment relationship was constructed from four dorsiflexion contractions of increasing intensity. The tibialis anterior EMG at each stage of the ramped plantarflexor trials was then substituted into this relationship to predict antagonist dorsiflexion moment (Kellis & Baltzopoulos, 1997). The soleus contribution to plantarflexion moment was quantified during additional plantarflexor contractions with the knee flexed to 90° where the gastrocnemius muscles were slack and did not contribute to the joint moment (Maganaris & Paul, 2002). The soleus EMG-moment relationship across the two joint configurations (knee extended (0°) and knee flexed (90°)) was used to correct activation differences (see equation 3.5).

### *5.2.4 Activation capacity*

The level of muscle activation achieved during voluntary contraction was calculated using the interpolated twitch technique (Rutherford et al., 1986). Percutaneous neuromuscular electrical stimulation (200 μs pulse duration, 400 V; Digitimer model DS7AH, Welwyn Garden City, UK) was used to evoke involuntary twitches of the plantarflexor muscles. A superimposed twitch was evoked at the point of isometric MVC and a resting twitch was applied approximately 3 s afterwards. This was repeated during

three trials at peak joint angle. The percentage of voluntary activation was calculated using equation 3.6 (Behm et al., 2001).

*5.2.5 Measurement of moment arm length*

Achilles tendon moment arm (MA) was calculated using the tendon travel method (Maganaris and Paul, 2002, Fath et al., 2010), and ultrasound imaging to quantify linear myotendinous junction (MTJ) displacement (see equation 3.7).

*5.2.6 Measures of muscle size at rest and architecture during MVC*

To quantify GL and GM muscle volume, serial transverse ultrasound images of each muscle were overlaid to reconstruct a full anatomical cross-sectional area at 25, 50 and 75 % of muscle length. Muscle volume was then calculated using the anatomical cross-sectional area's and muscle length by considering each muscle as two cones at either end of two truncated cones (see equation 3.9 and 3.10) which is a reliable and valid alternative to MRI imaging (Reeves et al., 2004b). Both GL and GM volume were combined for total gastrocnemii (GS) muscle volume.

Optimum fascicle length and pennation angle during MVC were measured from synchronised sagittal-plane ultrasound video-recordings of the muscle belly of GL and GM, captured at 25Hz. The frame corresponding to peak tendon force was extracted for each muscle during three separate MVC trials and analysed in ImageJ (version 1.44, NIH, USA) (O'Brien et al., 2010).

### *5.2.7 Measures of dynamic muscle quality*

Isokinetic plantarflexor joint power was measured across the participants' full range of motion at angular velocities of 60, 90, 120 and 180 °/s in the same dynamometer set up described above. These velocities were selected to represent the range of joint speeds experienced during gait (Mills & Barrett, 2001). Five concentric contractions were performed at each velocity. Peak power from each trial was recorded and the power-velocity profile constructed. The volume-normalised power-velocity relationship was established by normalising power at each velocity to gastrocnemii muscle volume, since the relative size of the gastrocnemii muscles and the soleus remain constant with ageing (Morse et al., 2005a). Dynamic muscle quality was defined as peak power normalised to gastrocnemii muscle volume. Adequate rest (>1 min) was provided between trials.

### *5.2.8 Statistical analysis*

A linear relationship exists between advancing age and dynamic muscle quality (McNeil et al., 2007), therefore a Pearson's partial product-moment correlation was performed to control for the influence of age and assess relationships between disease severity (as assessed by ABPI), walking endurance (as assessed by initial and absolute claudication distance; ICD and ACD, respectively) and gastrocnemii PCSA, volume and measures pertaining to static and dynamic muscle quality.

A one-way ANOVA was conducted to determine if significant between differences existed between the claudicating-limb and asymptomatic-limb groups and healthy controls. Data were assessed for normality, using Shapiro-Wilk's test for normality, and for outliers through box plot analysis. Sidak post-hoc was applied when appropriate. Mann-Whitney *U* tests were performed for non-parametric measures.

For all statistical tests, significance was accepted at P≤.05 and trends were accepted at P<.10. For correlation and regression analyses, a moderate relationship was accepted as R=.40–.59, a strong relationship was accepted as R=.60–.79 and a very strong relationship was accepted as R=.80–1 (Taylor, 1990). Since low ABPI values indicate high disease severity a positive relationship indicates a decrease in the respective parameter with worsening disease.

### 5.3 Results

No significant differences were found between groups in height (P=.230) or mass (P=.167) (Table 5.1). Whilst age and gender were not exactly matched between groups, the between group age-difference (~5years) was not statistically significant and likely too small to have influenced our results (McNeil et al., 2007) and there is no reason to believe gender differences influenced our measures of muscle quality (O'Brien et al., 2010). Between-group differences in ABPI were consistent with disease presentation. One participant (unilateral claudicant) had type II diabetes that was being managed by diet intervention only. Inspection of this data, in comparison to the full claudicant cohort, revealed adaptations that were in keeping with those with similar ABPI values and of similar ages. We do not believe that, for this individual participant, diabetes was a confounding factor.

**Table 5.1**.Participant characteristics. Data are presented as group mean (SD) unless otherwise stated. BMI – Body mass index, ABPI – Ankle brachial pressure index.

| | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| **#** | 12 | 7 | 10 |
| **% Males** | 75 | 57 | 40 |
| **Age (years)** | 65.0 (6.7) | 66.1 (7.5) | 61.6 (3.6) |
| **Height (m)** | 1.71 (0.08) | 1.69 (0.10) | 1.66 (0.09) |
| **Mass (Kg)** | 81.5 (18.2) | 82.3 (21.1) | 72.3 (10.9) |
| **BMI ($Kg/m^2$)** | 27.7 (5.1) | 28.5 (4.8) | 26.1 (3.7) |
| **ABPI pre-exercise** | 0.81 (0.23) | 1.01 (0.16) | 1.01 (0.09) |
| **ABPI post-exercise** | 0.55 (0.21) | 0.90 (0.06) | 1.01 (0.16) |
| **Initial claudication distance (m)** | 105 (45) | N/A | N/A |
| **Absolute claudication distance (m)** | 265 (136) | N/A | N/A |
| **% Hypertension** | 50 | 43 | 10 |
| **% Hypercholesterolemia** | 58 | 71 | 20 |
| **% past smokers** | 58 | 57 | 30 |
| **% present smokers** | 42 | 43 | 0 |

*5.3.1 Correlations*

Increased disease severity was not associated with any change in isometric MVC joint moment or static muscle quality, but was significantly correlated with reduced power at 120°/s and reduced power/volume at 120°/s and 180°/s, the latter being defined as significantly reduced dynamic muscle quality (all R and p values are presented in Tables 5.2 and 5.3). A trend was observed for smaller gastrocnemii PCSA with higher disease severity (P=.073) (Table 5.2).

Shorter ICD and ACD were associated with larger gastrocnemii muscle volume, lower activation capacity and reduced dynamic muscle quality. Shorter ACD was also correlated with reduced static muscle quality and shorter moment arm lengths (all R and p values are presented in Tables 5.2 and 5.3). Trends towards an association existed between shorter ACD and reduced tendon force (P=.053) (Table 5.2).

**Table 5.2**. Pearson correlations (controlled for the influence of age) between disease severity (ABPI), walking endurance (ICD and ACD) and gastrocnemii size and measures of static muscle quality. PCSA – physiological cross-sectional area. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10).

| | | **MVC** | **Soleus contribution** | **Activation capacity** | **Moment arm** | **Tendon force** |
|---|---|---|---|---|---|---|
| ABPI | Correlation | .055 | -.048 | -.312 | -.377 | .198 |
| | Significance | .847 | .865 | .258 | .165 | .480 |
| ICD | Correlation | -.161 | -.419 | .589 | -.424 | .091 |
| | Significance | .566 | .120 | .021 | .116 | .747 |
| ACD | Correlation | .188 | -.277 | .514 | -.668 | .508 |
| | Significance | .502 | .318 | .050 | .007 | .053 |
| | | **Gastrocnemii volume** | **Gastrocnemii reduced PCSA** | **Static muscle quality** | | |
| ABPI | Correlation | -.368 | .475 | -.009 | | |
| | Significance | .117 | .073 | .976 | | |
| ICD | Correlation | -.858 | -.386 | .353 | | |
| | Significance | .000 | .156 | .257 | | |
| ACD | Correlation | -.851 | -.079 | .632 | | |
| | Significance | .029 | .779 | .011 | | |

**Table 5.3**. Pearson correlations (controlled for the influence of age) between disease severity (ABPI), walking endurance (ICD and ACD) and measures of dynamic muscle quality. Dark shaded values represent those reaching significance (P≤.05).

| **Power** | | **60**°/s | **90**°/s | **120**°/s | **180**°/s |
|---|---|---|---|---|---|
| ABPI | Correlation | .071 | .375 | .674 | .375 |
| | Significance | .803 | .398 | .012 | .168 |
| ICD | Correlation | -.256 | -.277 | -.123 | -.368 |
| | Significance | .357 | .318 | .688 | .177 |
| ACD | Correlation | -.007 | -148 | .064 | -.262 |
| | Significance | .981 | .598 | .836 | .346 |
| **Power/Volume** | | **60**°/s | **90**°/s | **120**°/s | **180**°/s |
| ABPI | Correlation | .174 | .323 | .716 | .541 |
| | Significance | .600 | .240 | .006 | .037 |
| ICD | Correlation | .418 | .364 | .408 | .689 |
| | Significance | .121 | .182 | .166 | .006 |
| ACD | Correlation | .421 | .263 | .372 | .550 |
| | Significance | .118 | .344 | .211 | .042 |

*5.3.2 Between-group comparisons*

There were no differences between groups in isometric joint MVC, however the soleus contribution to this joint moment was significantly greater in both the claudicating-limb and asymptomatic-limb groups than in healthy controls (P=.008 and P=.012, respectively). The claudicating-limb group demonstrated trends towards reduced static muscle quality compared to healthy controls (P=.084) (Table 5.4).

At 120°/s the asymptomatic-limb group demonstrated trends towards reduced power (P=.071) with similar trends observed at 180°/s in the claudicating-limb group compared to healthy controls (P=.100). When normalised to gastrocnemii muscle volume, the asymptomatic-limb group had significantly reduced power/volume at 120°/s (P=.036) compared to healthy controls and both the asymptomatic-limb (P=.023) and claudicating-limb (P=.017) groups had significantly reduced power/volume at 180°/s (dynamic muscle quality) (Figure 5.1).

**Table 5.4**. Group mean (SD) measures of static muscle quality. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). PCSA – physiological cross-sectional area. $^{Con}$ = vs Healthy control group

| | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| MVC (Nm) | 120.6 (32.5) | 121.7 (36.1) | 127.5 (34.3) |
| Antagonist co-activation (%) | 2.74 (2.2) | 2.35 (2.5) | 2.01 (1.85) |
| Plantarflexor moment (Nm) | 123.4 (31.8) | 124.0 (35.4) | 130.0 (36.9) |
| Soleus contribution (%) | 62.7 (6.3)$^{Con}$ | 62.1 (1.4)$^{Con}$ | 55.6 (7.9) |
| Gastrocnemii moment (Nm) | 45.1 (10.3) | 46.9 (13.3) | 58.1 (20.2) |
| Activation capacity (%) | 90.7 (6.5) | 87.9 (7.8) | 90.4 (4.6) |
| Gastrocnemii moment at 100% (Nm) | 49.6 (10.7) | 53.5 (15.5) | 64.7 (24.4) |
| Moment arm (cm) | 3.44 (0.58) | 3.71 (0.76) | 3.24 (0.58) |
| Tendon force (N) | 1500.2 (471.8) | 1506.9 (431.2) | 2001.7 (722.7) |
| ***Muscle size and static quality*** | **Claudicating-limb** | **Asymptomatic-limb** | **Healthy control** |
| Gastrocnemii volume ($cm^3$) | 267.4 (71.5) | 249.8 (51.1) | 243.1 (71.3) |
| Gastrocnemii reduced PCSA ($cm^2$) | 55.4 (9.8) | 54.0 (14.1) | 58.1 (12.0) |
| Static muscle quality ($N/cm^2$) | 27.1 (6.6)$^{Con}$ | 28.8 (8.3) | 34.5 (10.4) |

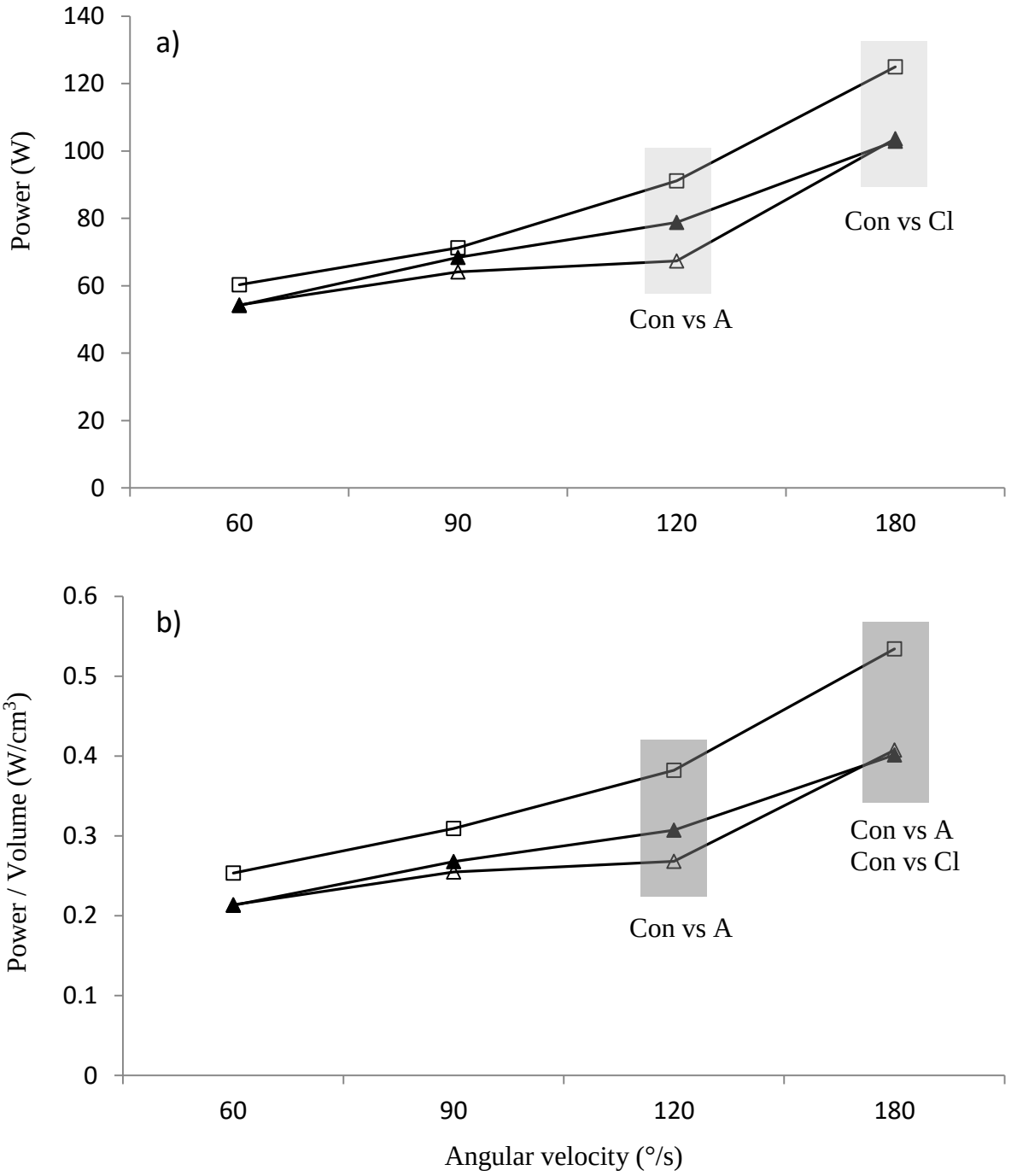


**Figure 5.1**. Group mean power-velocity (a) and normalised power-velocity (b) profiles for claudicating-limb (▲), asymptomatic-limb (Δ) and healthy controls (□). Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). Cl = Claudicating-limb group, A = Asymptomatic-limb group Con = Healthy control group.

## 5.4 Discussion

The aim of the study was to investigate the effects of peripheral arterial disease and intermittent claudication (PAD-IC) on the strength, power, size and *in vivo* whole muscle quality of the plantarflexors. We found no effects of disease on external measures of "strength" during static or low speed contractions, but the claudicants relied on the predominantly type I-fibred soleus to develop overall strength more than healthy controls. Significant strength differences between claudicants and controls were apparent during higher speed (≥120°/s) contractions. These data support our hypotheses that the dynamic muscle quality of claudicants was reduced compared to healthy controls, and this was associated with poorer walking endurance. These novel findings suggest that impaired muscle quality and a greater reliance on the soleus muscle contribute to reduced dynamic strength of claudicants at high speeds, which in turn contributes to the impaired functional ability seen in this population.

Previous studies investigating plantarflexor strength in individuals with PAD-IC are inconsistent (Scott-Okafor et al., 2001, McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012) and comparisons between studies are confounded by differing methods of strength assessment. This study quantified plantarflexor strength across a range of contraction speeds, and observed no between-group differences at low velocities. However, the power generating capacity of the claudicants was 13-26% lower than controls at speeds of 120-180°/s. Given the parabolic nature of the power-velocity relationship (Sargeant, 2007), power would be expected to decrease further at faster speeds. Interestingly, this was the case for both claudicating-limb and asymptomatic-limb groups. This indicates either the presence of systemic effects of

ischemia in the ‘asymptomatic’-limb or that deleterious adaptations were driven by the relative inactivity caused by the symptomatic limb. Alongside poorer lower limb strength, isometric plantarflexor strength has previously been reported as a strong predictor of mortality in men with PAD-IC (Singh et al., 2010, McDermott et al., 2012); however the current data suggest that dynamic contractions at higher velocities may be more sensitive to functional deteriorations, which was not apparent in previous sub-group analyses (King et al., 2014). Future functional assessments and measures of plantarflexor strength should consider the use of dynamic, concentric tests in order to detect strength losses and to identify those with greater strength impairments.

Whilst voluntary joint moments and powers are simple and time-efficient measures, they do not provide information regarding the underlying mechanisms contributing to the externally measured strength. Despite minimal between-group differences in isometric MVC, a substantially lower (25%, but non-significant) tendon force was found in both claudicating-limb and asymptomatic-limb groups compared to controls. Combined with similar physiological cross-sectional areas, this led to a trend towards reduced static muscle quality (21%) in the claudicating-limb group, and a non-significant reduction of 16% in the asymptomatic-limb group, compared to controls. These effects were not mirrored in the correlations with ABPI, suggesting other stimuli must exist, such a physical activity levels, to drive these reductions in static gastrocnemii muscle quality of claudicants.

The reduced tendon force in the claudicating-limb group, despite similar joint moments between groups, can be attributed to a greater (12%) contribution of the

soleus to the overall joint moment, compared to healthy controls. This increased reliance on the soleus during plantarflexor contractions may be linked to the proposed shift in fibre type in claudicants (Regensteiner et al., 1993, Steinacker et al., 2000, McGuigan et al., 2001b, Askew et al., 2005, Gasparini et al., 2012) Therefore, the increased contribution from the slower, type I-dominant soleus muscle (Dahmane et al., 2005) may act as a means to reduce the metabolic cost of the task. However, during dynamic contractions, a greater contribution from soleus would have a detrimental effect on the ability to generate power, particularly at high speeds, which is consistent with the present data.

When muscle power was normalised to volume (dynamic muscle quality) between-group differences became larger and significant associations with walking endurance and disease severity were apparent. This corroborates previous reports of reduced ankle plantarflexor power per kg body mass in gait (Koutakis et al., 2010a , Wurdeman et al., 2012a) and demonstrates the importance of plantarflexor power for functional performance. The reductions in dynamic muscle quality were associated with changes in walking performance that have previously been reported as clinically meaningful (>50 m) (Perera et al., 2006). Long-term efforts to monitor the implications of this appear warranted, and quantification of dynamic muscle quality may provide a useful outcome measure in these efforts. Exercise prescription is a primary treatment option in PAD-IC to improve mobility and to combat muscle weakness (Norgren et al., 2007). It appears that such training interventions should target improvements in plantarflexor power by redressing the relative contribution from the soleus and gastrocnemii muscles through dynamic exercise programmes (high-velocity resistance training). Future work should endeavour to assess how these important musculoskeletal

parameters respond to (exercise-based) interventions and whether they lead to the predicted improvements in walking capacity.

Correlation analysis revealed that variations in activation capacity amongst the claudicating-limb group significantly affected walking endurance. This would increase the perceived effort of walking, possibly leading to altered gait mechanics to redistribute joint kinetics, and consequently alter movement efficiency and endurance. Activation level was not quantified during the isokinetic trials a muscle stimulation during dynamic contractions is technically very challenging, particularly for the plantarflexors where the muscle group works almost exclusively on the ascending limb of the force-length relationship, so stimulation at optimal muscle length is not possible. Future work should endeavour to investigate the activation capacity of the plantarflexor muscles during dynamic contractions, since it may be different to that in isometric conditions and could contribute to the specific power deficits at high velocities. This would provide greater understanding of the neuromuscular adaptations caused by PAD-IC and their influence on functional performance.

Some limitations to the present study must be acknowledged. Static muscle quality should be calculated with measures of truly optimal muscle force and length, i.e., plateau of the force-length relationship. As is typical for the plantarflexors, this plateau was not observed (Maganaris, 2003) and we do not know whether participants reached optimal fascicle length. However, previous work has shown that small changes in joint position do not significantly affect estimates of muscle quality (O'Brien et al., 2010). By calculating the quality of the entire gastrocnemii muscle group, errors associated with distributing tendon force between the GL and GM were avoided. However, it was

necessary to assume that once soleus contribution was removed, the Achilles' tendon force reflected only that produced by the gastrocnemii muscle. Dynamic muscle quality was calculated as plantarflexor joint power normalised to gastrocnemii muscle volume only, assuming the relative size of these muscles remains constant, as is the case in ageing (Morse et al., 2005a). Claudicants relied on the soleus more than healthy controls did, meaning any error associated with this assumption will most likely underestimate the true between-group difference in dynamic muscle quality. Additionally, moment arm length was determined during passive joint rotations at rest (Fath et al., 2010) and it is known to change during contraction (Fath et al., 2013). However, there is no reason to assume the change from rest to contraction would be different between controls and claudicants; consequently, we consider the comparisons presented in this study to remain valid.

## 5.5 Conclusions

The present study quantified the intrinsic quality of *in vivo* claudicant muscle for the first time. Dynamic plantarflexor power, particularly at the highest velocity, was lower in claudicants compared to healthy controls and was significantly associated with disease severity and impaired walking endurance. When plantarflexor power was normalised to muscle size (to calculate muscle quality) between group differences were larger and relationships with walking endurance were stronger. The impaired function at high velocities may be related to a reduction in maximal (static) muscle quality and an increased reliance on the predominantly type-I fibred soleus muscle. Efforts to monitor joint power at high velocities appear the most appropriate way to

detect functional losses early, and improving the dynamic capabilities of the plantarflexors is likely to help maintain walking endurance in claudicants.

# Chapter 6. Stair gait in claudicants with peripheral arterial disease. Part 1: Kinematic and kinetic adaptations during stair ascent

## 6.1 Introduction

In those with peripheral arterial disease and intermittent claudication (PAD-IC) walking endurance declines with disease progression (McDermott et al., 2004a) and alterations in gait biomechanics exist in both the absence and presence of claudication pain (Scott-Pandorf et al., 2007, Koutakis et al., 2010a). Increased daily activity has been shown to slow the rate of functional decline in claudicants (McDermott et al., 2006a, McDermott et al., 2011) and walking therapy is a frequently prescribed and recommended exercise intervention (Norgren et al., 2007, Parmenter et al., 2011).

The ability to ambulate over level ground is functionally important and as such the bulk of current research into claudicant gait biomechanics has investigated adaptations over level ground (Gardner et al., 2001, Scott-Pandorf et al., 2007, Celis et al., 2009, Koutakis et al., 2010a). However the ability to negotiate stairs is also vital to maintaining functional independence (Ariza-Vega et al., 2014). It is well established that there is a high incidence of falls among the elderly during stair walking (Hemenway et al., 1994, Startzell et al., 2000). Balance and strength are vital pre-requisites to perform this task and both of these factors have been associated with self-reported difficulty during stair ascent in older adults without disability (Verghese et al., 2008). Given the previously reported impairments in balance (Mockford et al., 2011, Gohil et al., 2013), and reduced lower limb strength reported elsewhere (McDermott et al., 2004b, Camara et al., 2012) as well as in the present thesis (Chapter

5), stair negotiation likely poses a more physically challenging and potentially hazardous task for claudicants.

Stair ascent in particular is a common daily task but the functional demands placed on the lower limbs are higher than in level gait (Nadeau et al., 2003, Tiedemann et al., 2007). The requirement to develop muscular force during stair ascent compared to the muscular capabilities is much greater for the elderly than the young. The knee extensors in the elderly work at 75% of their maximum capacity compared to 53% in younger adults (Reeves et al., 2009b) and, in some cases, operate in excess of their maximum measured strength at the knee (Samuel et al., 2011). A similar effect is evident at the ankle (elderly 93% vs young 85%) (Reeves et al., 2009b) with both the soleus muscle (McFadyen & Winter, 1988) and the gastrocnemii (Spanjaard et al., 2007) playing important roles in raising the body to the next step in forward continuance.

It is evident that the gastrocnemii, in particular, are impaired in claudicants as there are signs of fibre type adaptations (Steinacker et al., 2000, McGuigan et al., 2001b), infiltration of intra-muscular fat (Raval et al., 2012), neuromuscular impairments (Garg et al., 2011) and, more recently, adaptations in the structure and gait function of the gastrocnemii muscle and Achilles tendon (Chapter 4 and 5). Moreover, there is clear dysfunction in level gait with reduced plantarflexor moments and subsequently smaller power generation at push-off, which worsens in the presence of claudication pain (Chen et al., 2008, Koutakis et al., 2010b, Wurdeman et al., 2012a). However it

remains unknown how those with PAD-IC actually cope with the increased demands of stair ascent.

The purpose of the study was to determine whether PAD-IC results in biomechanical adaptations during stair ascent. This was achieved by drawing comparisons to a control group consisting of healthy older adults and exploring relationships between gait parameters and disease severity. It was hypothesised that claudicants would have modified ankle kinematics, reduced peak plantarflexor moment and ankle power generation compared to controls. Our second hypothesis was that alterations in ankle kinematics and reduced plantarflexor function would be associated with a reduced ankle brachial pressure index (ABPI), an indicator of disease severity.

## 6.2 Methods

### *6.2.1 Participants*

A total of 22 participants were recruited consisting of 12 claudicants (six unilateral, six bilateral) and ten healthy controls (Table 6.1). Due to personal complications with one unilateral claudicant, they were unable to attend a second testing session to assess gait biomechanics. Details pertaining to the assessment of disease severity are depicted in Chapter 3. Briefly, the post-exercise ankle brachial pressure index classified the severity of disease in claudicants and was used to determine the 'claudicating-limb' group (N=12 providing a total of 18 claudicating limbs; 12 from bilateral claudicants and 6 from unilateral claudicants), the 'asymptomatic-limb' group (N=6 providing a total of 6 limbs from the unilateral claudicants). The dominant limb of the healthy

controls was determined using a ball-kicking exercise and used for drawing comparisons with the claudicant groups.

### *6.2.2 Gait analysis*

Details pertaining to 3D motion capture are depicted in Chapter 3. Briefly, retro-reflective passive markers were position according to the six Degrees of Freedom marker set (Cappozzo et al., 1995) utilising the functional method to determine hip joint centres (Leardini et al., 1999, Piazza et al., 2001, Baker, 2006). 3D marker coordinate data were tracked using Qualysis Track Manager (Qualysis, Gothenburg, Sweden) then exported for further processing in Visual 3D (C-motion, Rockville, MD, USA).

Participants were instructed to ascend a custom-made five-step wooden staircase at their self-selected pace. The staircase contained force-plates (Kistler, Winterthur, Switzerland) imbedded into steps two and three (step five being the final step onto the 80 cm landing at the top of the staircase; see Figure 3.5, Chapter 3). The mechanisms employed to negotiate the transition from level ground to stair ascent differ from continuous stair ascent (Alcock et al., 2014) and as such these strategies need to be approached separately. The focus of the present study was continuous, steady-state stair ascent defined as a gait cycle initiated and terminated on the staircase. In the current study, one gait cycle was defined from foot contact on step 2 to the subsequent foot contact of the ipsilateral limb on step 4; and from foot contact on step 3 to the subsequent foot contact of the ipsilateral limb on step 5 for the contralateral limb (see Figure 3.5, Chapter 3). Limb preference for ascending the stairs was explored; no

preferential strategy was evident for all participants and therefore not assessed further. Relevant gait events were identified (foot strike and foot off) using vertical ground reaction force (≥20 N threshold), and were normalised to 100% gait cycle for kinematic and joint kinetic data and 100% stance phase for ground reaction forces.

Throughout, phases will be described according to the descriptions proposed by McFayden & Winter (1988): weight acceptance, pull-up, forward continuance, foot clearance and foot placement. Variables of interest included temporal-spatial parameters, sagittal plane kinematics (peak angles, angular velocities and ranges of motion), 3-dimensional ground reaction forces (GRF), sagittal plane kinetics (peak joint moments and powers), and angles and angular velocities at the instant of peak moment for the hip, knee and ankle joints. Angular velocities at the instant of peak moment occurred during weight acceptance for the hip and knee, and during forward continuance for the ankle. Positive angular velocities indicate changes in joint angle towards ankle dorsiflexion, knee flexion and hip flexion. Data are expressed as mean and standard deviation.

### *6.2.3 Statistical analysis*

Data were exported into SPSS v21.1 (SPSS Inc., Chicago, IL, USA), assessed for normality violations using Shapiro-Wilk's test for normality and assessed for outliers through box plot analysis. To avoid violating the assumption of independent samples, only the bilateral claudicants were included in the claudicating-limb group and unilateral claudicants in the asymptomatic-limb group for between-group analysis of walking speed and time spent in double support. As groups differed in walking speed

(Table 6.2) a univariate analysis of variance was performed for joint kinematics, kinetics and GRF with walking speed as a covariate. Where a significant interaction effect was observed, a Sidak post-hoc comparison was performed. A Pearson partial correlation controlling for the influence of age and walking speed was performed to assess relationships between disease severity and gait parameters.

For all statistical tests, significance was accepted at P≤.05 and trends were accepted at P<.10. For correlation and regression analyses, a moderate relationship was accepted as R=.40–.59, a strong relationship was accepted as R=.60–.79 and a very strong relationship was accepted as R=.80–1 (Taylor, 1990).

## 6.3 Results

No significant differences were found between groups in age (P=.148), height (P=.230), or mass (P=.167) (Table 6.1).

### *6.3.1 Temporal-spatial parameters*

Due to the bilateral nature of determining walking speed and to avoid violating the assumption of independent samples, walking speed and double support time were compared between bilateral and unilateral claudicants and healthy controls. Compared to the control group, trends towards slower walking speed were evident in both the bilateral claudicant (0.60±0.10m/s vs 0.71±0.09m/s, P=.051) and the unilateral claudicant (0.71±0.09m/s vs 0.60±0.12m/s, P=.066) groups. Furthermore, unilateral claudicants spent longer in double support compared to healthy controls (28.7±4.7%

vs 20.2±6.2%, P=.018) with bilateral claudicants demonstrating similar trends (27.4±4.1 vs 20.2±6.2%, P=.088).

**Table 6.1.** Participant characteristics. Data are presented as group mean (SD) unless otherwise stated. BMI – Body mass index, ABPI – Ankle brachial pressure index.

| | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| **#** | 12 | 6 | 10 |
| **Limbs for analysis** | 18 | 6 | 10 |
| **% Males** | 83 | 67 | 40 |
| **Age (years)** | 64.7 (7.1) | 67.3 (7.5) | 61.6 (3.6) |
| **Height (m)** | 1.72 (0.08) | 1.70 (0.11) | 1.66 (0.09) |
| **Mass (Kg)** | 83.3 (18.8) | 83.9 (22.6) | 72.3 (10.9) |
| **BMI (Kg/m$^2$)** | 28.0 (5.2) | 28.8 (5.2) | 26.1 (3.7) |
| **ABPI pre-exercise** | 0.80 (0.21) | 1.00 (0.12) | 1.01 (0.09) |
| **ABPI post-exercise** | 0.56 (0.20) | 0.91 (0.08) | 1.00 (0.16) |
| **Initial claudication distance (m)** | 125 (54) | N/A | N/A |
| **Absolute claudication distance (m)** | 286 (142) | N/A | N/A |
| **% Hypertension** | 50 | 50 | 10 |
| **% Hypercholesterolemia** | 58 | 67 | 20 |
| **% past smokers** | 50 | 50 | 30 |
| **% present smokers** | 50 | 50 | 0 |

*6.3.2 Joint kinematics*

The asymptomatic-limb group spent significantly longer in the stance phase (P=.018) with the claudicating-limb group demonstrating similar trends (P=.085) compared to healthy controls (Table 6.2). No significant between-group differences existed in peak angles and ranges of motion at the hip, knee and ankle (Table 6.2). The claudicating-limb group demonstrated trends towards reduced peak knee flexion in swing (P=.090) and reduced peak knee angular velocity (P=.098) with the asymptomatic-limb group demonstrating similar trends (P=.068) (Table 6.2).

**Table 6.2.** Group mean (SD) temporal-spatial parameters and peak sagittal plane gait kinematics. All values are degrees unless otherwise stated. Superscript text and dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). $^{Con}$ = vs healthy control group

| | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| Stance phase (%) | 61.4 (2.1)$^{Con}$ | 63.7 (2.8)$^{Con}$ | 58.3 (3.5) |
| Hip Flexion Stance | 61.5 (10.6) | 60.5 (13.3) | 69.1 (5.1) |
| Hip Extension Stance | 7.8 (10.3) | 5.3 (11.1) | 15.9 (9.3) |
| Hip Flexion Swing | 66.8 (11.8) | 65.6 (14.8) | 78.5 (5.8) |
| Hip RoM | 58.9 (5.3) | 60.3 (5.6) | 62.6 (6.9) |
| Peak angular velocity (°/s) | 245.1 (57.8) | 237.8 (51.1) | 257.2 (23.7) |
| Knee Flexion Stance | 71.3 (7.9) | 76.8 (4.7) | 76.6 (7.3) |
| Knee Extension Stance | 12.0 (5.2) | 14.2 (3.5) | 17.3 (7.6) |
| Knee Flexion Swing | 102.6 (8.8)$^{Con}$ | 107.0 (7.2) | 114.5 (9.4) |
| Knee RoM | 90.6 (7.1) | 92.8 (9.8) | 97.1 (11.8) |
| Peak angular velocity (°/s) | 213.0 (41.4)$^{Con}$ | 199.5 (32.3)$^{Con}$ | 281.2 (68.1) |
| Dorsiflexion Stance | 19.5 (5.9) | 23.0 (4.2) | 22.4 (4.3) |
| Plantarflexion Swing | -14.0 (4.5) | -17.6 (6.8) | -14.7 (6.2) |
| Dorsiflexion Swing | 22.0 (6.3) | 23.3 (3.6) | 22.1 (4.9) |
| Ankle RoM | 36.4 (6.8) | 43.1 (7.0) | 36.7 (9.2) |
| Peak angular velocity (°/s) | 198.4 (35.5) | 231.1 (60.2) | 229.5 (54.9) |

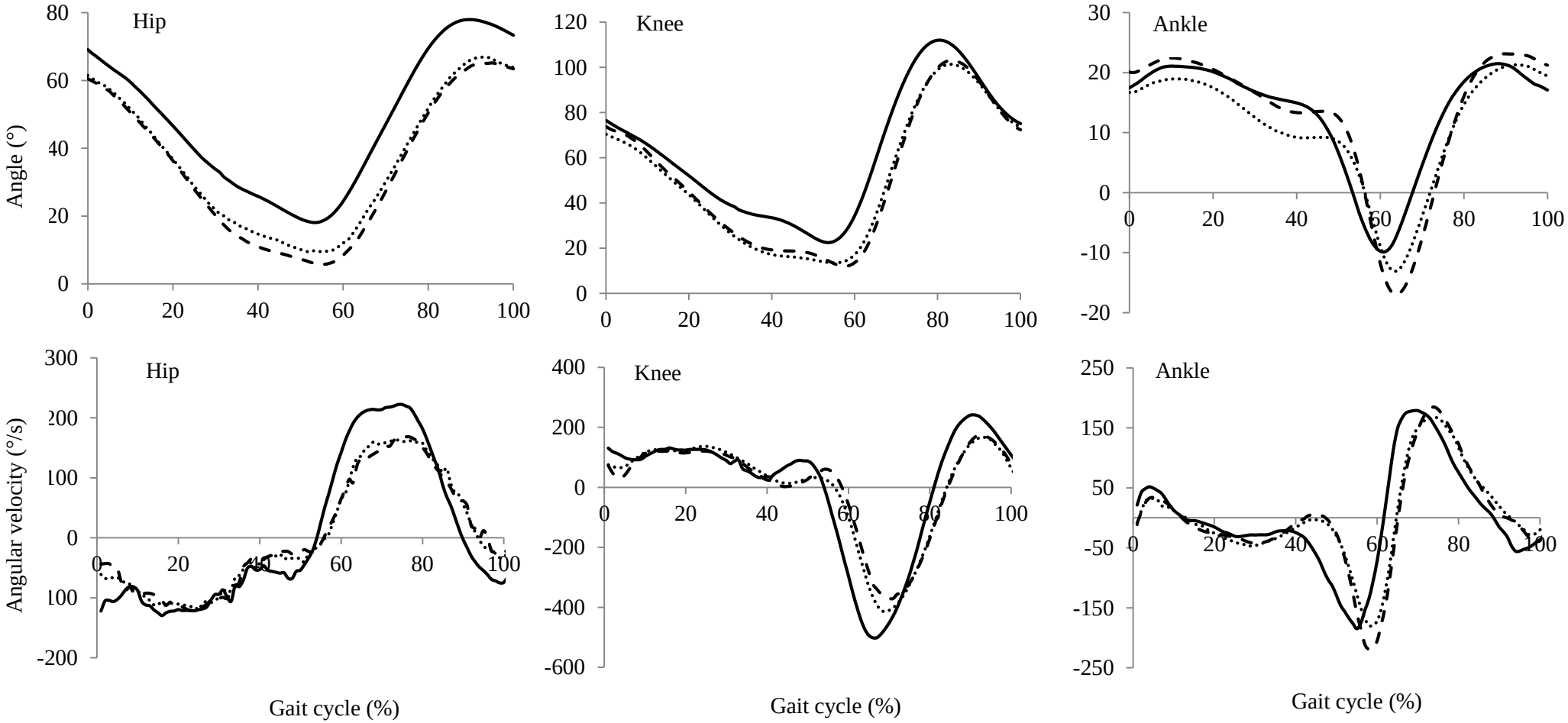


**Figure 6.1**. Group mean angle (top row) and angular velocity (bottom row) for the hip, knee and ankle across 100% gait cycle for claudicating-limb (dotted), asymptomatic-limb (dashed) and healthy controls (solid). For joint angles, positive values indicate dorsiflexion, knee flexion and hip flexion. For angular velocities, positive values indicate changes in joint angles towards hip flexion, knee flexion and ankle dorsiflexion.

*6.3.3 Ground reaction forces and joint kinetics*

Both the claudicating-limb and asymptomatic-limb groups had significantly reduced propulsive (P=..025 and P=.002, respectively) and vertical GRF (P=.005 and P=.001, respectively) in late stance compared to healthy controls (Table 6.3 and Figure 6.2). Furthermore, the claudicating-limb group demonstrated trends towards increased braking force in early stance (P=.087), reduced knee extensor moment in late stance (P=.060) and ankle power generation in late stance (P=.055) compared to healthy controls. The claudicating-limb group had significantly reduced ankle angular velocity at the instant of peak plantarflexor moment (P=.039) compared to healthy controls (Table 6.4).

**Table 6.3.** Peak group mean (SD) ground reaction forces. Superscript text and dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). $^{C}$ = vs healthy control group

| GRF (N/kg) | Claudicating-limb | Asymptomatic-limb | Control |
|---|---|---|---|
| Medial during weight acceptance | 0.60 (0.14) | 0.49 (0.14) | 0.54 (0.03) |
| Medial during forward continuance | 0.55 (0.15) | 0.47 (0.12) | 0.60 (0.23) |
| Posterior during weight acceptance | -0.97 (0.33)$^{Con}$ | -0.76 (0.26) | -0.71 (0.18) |
| Anterior during forward continuance | 0.57 (0.14)$^{Con}$ | 0.44 (0.12)$^{Con}$ | 0.76 (0.10) |
| Vertical during weight acceptance | 1.06 (0.13) | 1.05 (0.11) | 1.11 (0.13) |
| Vertical during forward continuance | 1.15 (0.10)$^{Con}$ | 1.14 (0.22)$^{Con}$ | 1.53 (0.28) |

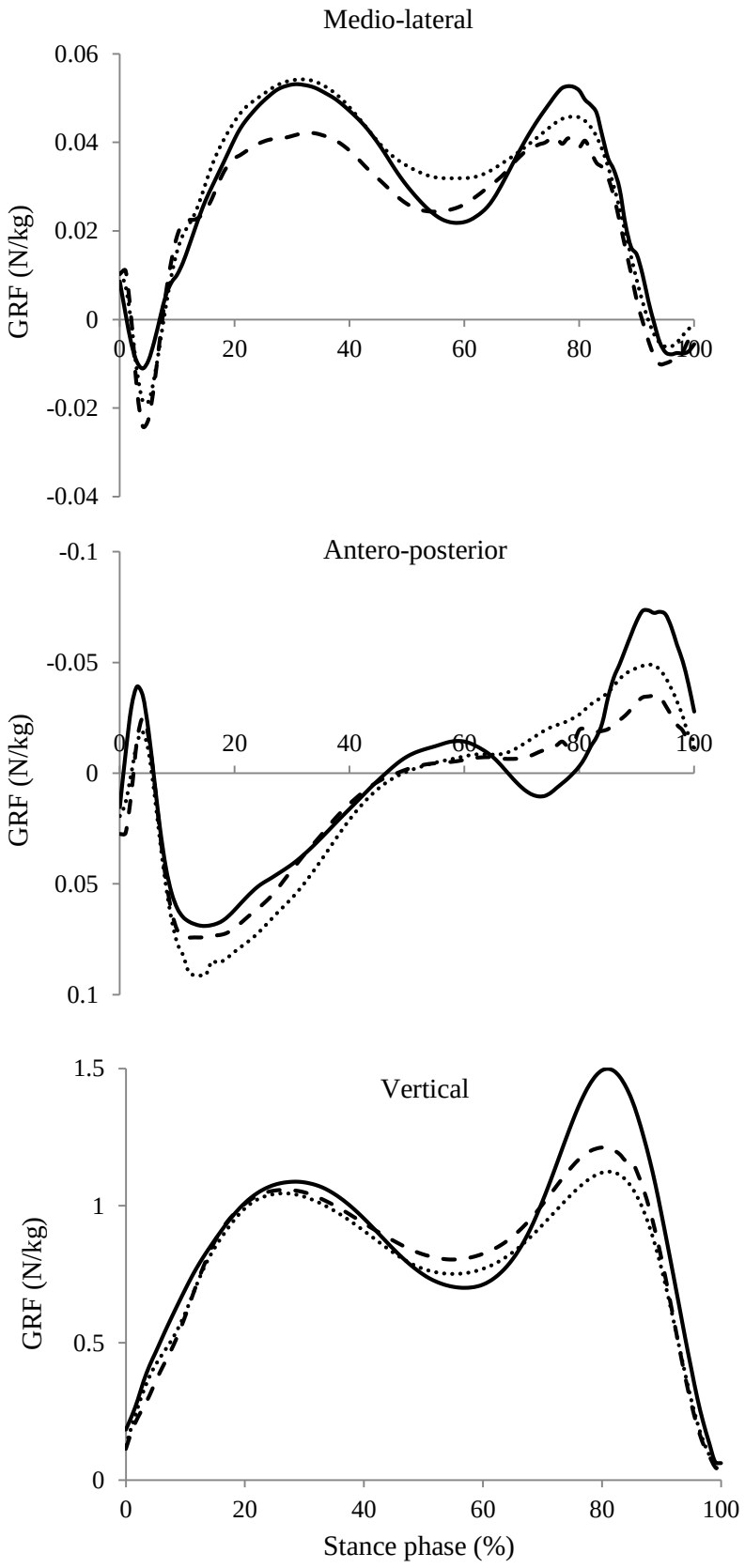


**Figure 6.2.** Group mean ground reaction forces per kg body mass (N/kg) for the claudicating group (dotted line), asymptomatic limbs (dashed line) and control group (solid line) normalised to 100% stance phase. Positive direction indicates medial, anterior (propulsive) and vertical force.

**Table 6.4**. Peak group mean (SD) sagittal plane joint kinetics. Peak moments occurred during weight acceptance for the hip and knee, and during forward acceptance for the ankle. Superscript text and dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). $^{C}$ = vs healthy control group

| **Joint moments** | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| Hip moment weight acceptance (Nm/kg) | 0.91 (0.53) | 0.84 (0.44) | 1.16 (0.43) |
| Angle at peak moment (°) | 54.2 (12.5) | 45.7 (13.4)$^{Con}$ | 59.2 (8.9) |
| Angular velocity at peak moment (°/s) | -103.5 (25.0) | -101.8 (19.2) | -137.2 (61.4) |
| Knee moment weight acceptance (Nm/kg) | 1.05 (0.28) | 1.07 (0.32) | 1.03 (0.23) |
| Knee moment forward continuance (Nm/kg) | -0.14 (0.15)$^{Con}$ | -0.07 (0.20) | 0.51 (0.20) |
| Angle at peak moment (°) | 55.5 (9.3) | 54.7 (8.3) | 55.6 (12.7) |
| Angular velocity at peak moment (°/s) | 122.7 (34.0) | 127.6 (14.0) | 139.6 (33.9) |
| Ankle moment weight acceptance (Nm/kg) | 0.93 (0.48) | 0.88 (0.23) | 0.96 (0.40) |
| Ankle moment forward continuance (Nm/kg) | 1.44 (0.31) | 1.69 (0.39) | 1.66 (0.43) |
| Angle at peak moment (°) | 9.6 (4.6) | 13.1 (2.1) | 13.8 (5.5) |
| Angular velocity at peak moment (°/s) | -61.0 (22.4)$^{Con}$ | -82.4 (25.2) | -93.3 (28.1) |
| **Joint powers (W/kg)** | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
| Ankle power forward continuance | 3.36 (1.19)$^{Con}$ | 4.43 (1.13) | 5.28 (1.93) |
| Knee power weight acceptance | 2.48 (1.05) | 2.50 (0.69) | 2.55 (0.40) |
| Hip power weight acceptance | 2.11 (1.36) | 1.97 (1.45) | 2.90 (1.03) |

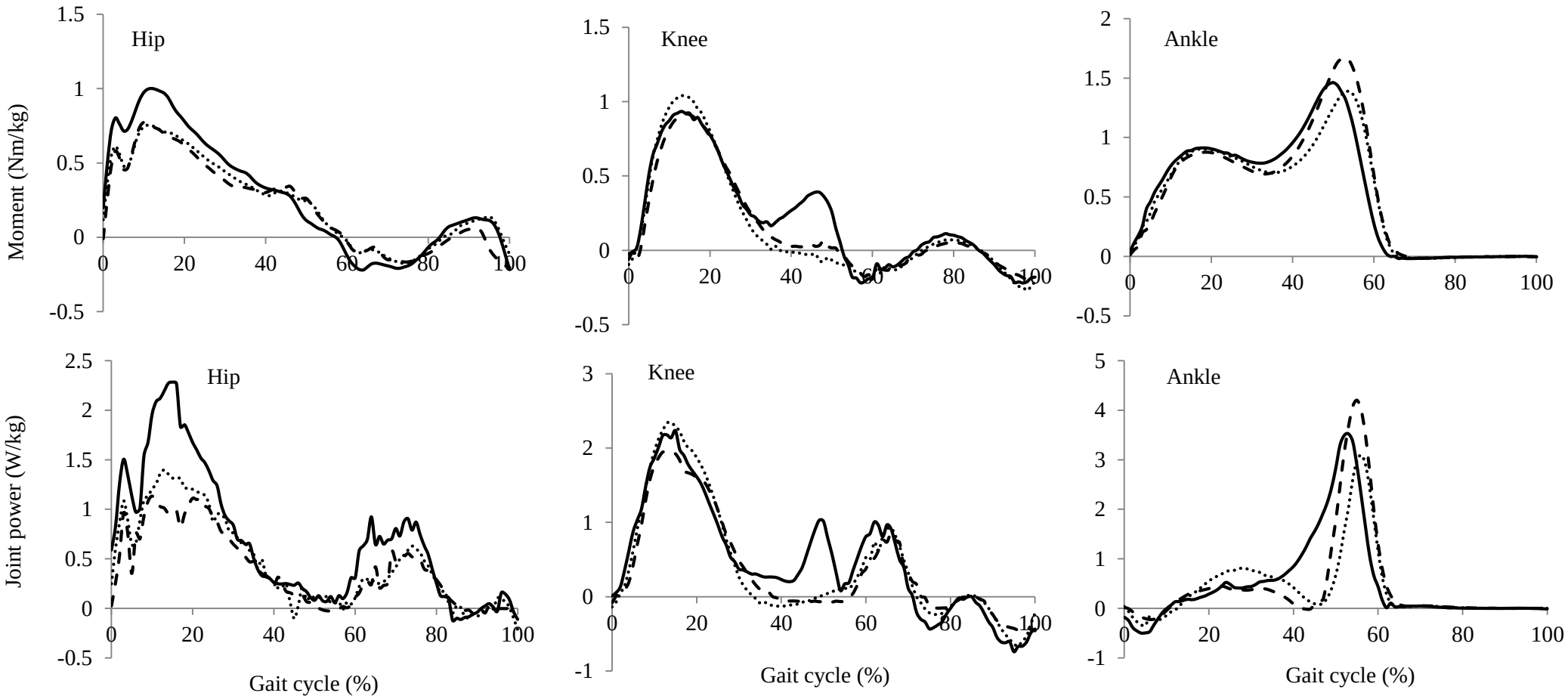


**Figure 6.3**. Group mean internal joint moment (top row) and joint power (bottom row) for the ankle, knee and hip across 100% gait cycle for claudicating-limb (dotted), asymptomatic-limb (dashed) and healthy controls (solid). Positive values indicate hip and knee extensor and ankle plantarflexor internal joint moments and power generation.

*6.3.4 Disease severity correlations*

Increased disease severity was associated with increased peak medial GRF (R=-.630, P=.038) and trends towards reduced peak propulsive GRF (R=.601, P=.051) during forward continuance, reduced knee extension moment during weight acceptance (R=.540, P=.086), reduced peak knee angular velocity (R=-.554, P=.077) and increased plantarflexion angle in swing (R=.442, P=.086).

## 6.4 Discussion

This study has, to the best of the author's knowledge, investigated stair ascent biomechanics in PAD-IC for the first time. The findings suggest that claudicants walk more slowly than healthy controls, irrespective of whether the arterial stenosis and claudication symptoms are present in a single limb or both. In partial support of our first hypothesis, plantarflexor power generation in late stance, alongside propulsive and vertical forces, were smaller in the claudicating-limb group compared to healthy controls. The reduced power generation in the claudicating-limb group appears to result from a slower ankle joint velocity to allow adequate peak plantarflexor moment in late stance to be produced. This highlights the functional importance of the velocity-dependent limitations in claudicant plantarflexors reported in Chapter 5.

The observed trends towards reduced ankle power generation in the forward continuance phase in the claudicating-limb group coincides with reduced angular velocity at peak moment, and reduced propulsive and vertical forces. This could be explained by the previous observation of reduced plantarflexor strength at high velocities (Chapter 5). Previous investigations into level gait mechanics have reported

reduced plantarflexor moments in claudicant compared to healthy controls (Koutakis et al., 2010a, Koutakis et al., 2010b, Chen et al., 2008). However, those studies also observed slower walking speeds in those with PAD-IC, therefore those previous findings may also reflect the variance in walking speed and not solely reduced plantarflexor strength. A previous study on level gait mechanics compared claudicants to speed matched controls (Wurdeman et al., 2012a) and the present study statistically controlled for variance in walking speed; both of which observed reduced joint powers in claudicants. Therefore, velocity-dependent limitations in claudicant plantarflexors appear a genuine adaptation. It seems that claudicants possess adequate levels of strength when moving more slowly but are unable to remain strong when moving more quickly, therefore it could be suggested that the slower walking speed is a means to allow claudicants to operate within safer limits compared relative to their maximal strength capacity. Further investigation following a similar experimental protocol to Reeves *et al.* (2009b) would be required to confirm these inferences. Nonetheless, these findings highlight the importance of maintaining plantarflexor strength in those with PAD-IC. Reductions in maximum strength capacity, without the adoption of adequate compensatory strategies, would place excessive demands on the limited plantarflexors, thus jeopardising the ability to accomplish this task safely.

Previous research into the strategies healthy elderly adopt to negotiate stairs has revealed an increase in knee extensor moment in late stance just prior to peak ankle moment (Reeves et al., 2009b). Those authors suggested that was a mechanism to transfer energy from the proximal knee to distal ankle joint via the bi-articular gastrocnemii muscles, enabling a greater peak ankle moment to be generated. A similar profile was exhibited here by the healthy elderly group (Figure 6.3) but not by

the claudicants, indicating a functionally useful mechanism was not being utilised. An alternative compensation could be an increase in contralateral hip extensor activity during the 'pull-up' phase. No such increase in hip moments or powers were observed for either the claudicating-limb or asymptomatic-limb groups (Figure 6.3). The reasons for this are unclear, however reduced hip extensor strength has previously been associated with increased disease severity and reduced functional mobility in claudicants (Parmenter et al., 2013b) and it may be that they lack adequate capacity to utilise such a compensation irrespective of the disease presence uni- or bi-laterally. Alternatively, it may simply be that the claudicants evade increased muscular effort in any lower-limb muscle group as an attempt to avoid earlier onset of claudication pain and increased metabolic cost (Mockford et al., 2010). The lack of any observable compensatory strategy may also contribute to the aforementioned slower walking speed in claudicants as they are relying on the smaller, weaker and frequently symptomatic plantarflexor group to perform this task.

Given the identified functional decline of the ankle in the claudicating limbs, it may have been expected that in uni-lateral claudicants the asymptomatic limb would demonstrate hip and/or knee strategies to compensate. Interestingly however, the asymptomatic limb demonstrated similar adaptations to the claudicating limb with reduced propulsive and vertical forces, reduced peak knee angular velocity and a (non-significant) 16% reduction in ankle power generation compared to healthy controls. These findings are analogous to those investigations of unilateral claudicants during level gait (Koutakis et al., 2010b, Wurdeman et al., 2012b) and suggest that unilateral claudicants are limited by the functionality of the claudicating limb. This further

highlights the importance of improving the strength and function of the claudicating limb, regardless of whether the disease is present in a single limb or both.

The present study investigated pain-free stair ascent only. Plantarflexor function during level gait deteriorates further in the presence of claudication pain (Scott-Pandorf et al., 2007, Koutakis et al., 2010a). It would be reasonable to assume that adaptations highlighted in the present study may be extrapolated further during painful locomotion, however further investigation is needed to confirm this speculation. Whilst we statistically controlled the influence of walking speed in between-group analyses, a more vigorous investigation comparing claudicants to speed-matched controls is required to fully explore the velocity-dependent limitations in the gastrocnemii. Previous research has also demonstrated light handrail use influences gait biomechanics (Reeves et al., 2008b) and the present study excluded trials in which participants used the handrail as the extent of handrail use could not be quantified. However, given the reported balance deficits in the population (Mockford et al., 2011, Gohil et al., 2013a), handrail use, particularly in the presence of claudication pain for example, may play a larger compensatory role and requires further investigation.

## 6.5 Conclusions

This study provides evidence for specific limitations of the plantarflexor muscles during stair ascent in claudicants with peripheral arterial disease. There was a lack of notable hip or knee strategies in the claudicating limb as a compensatory mechanism for the clear, velocity-dependent limitations of the plantarflexors. Similarly, in unilateral claudicants, there were no observable compensations from the

asymptomatic limb. Thus, the stair climbing function of those with PAD-IC seems to be determined by the limitations of the claudicating limb, highlighting the importance of maintaining or improving strength and power in the plantarflexor muscle group.

# Chapter 7. Stair gait in claudicants with peripheral arterial disease. Part 2: Kinematic and kinetic adaptations during stair descent

## 7.1 Introduction

The calf is a frequently reported site of claudication pain in those with PAD-IC (Norgren et al., 2007). The strength of the plantarflexors has been associated with mortality (McDermott et al., 2012) and there is evidence for functional impairments of the musculature during level walking (Koutakis et al., 2010b, Wurdeman et al., 2012b). There are indications of reduced strength in other lower limb muscle groups (McDermott et al., 2004b, Camara et al., 2012) with further associations between knee extensor strength and all-cause mortality (Singh et al., 2010, McDermott et al., 2012). Yet the functional effects of these more proximal strength deteriorations are not apparent during level gait. This may be because the ground reaction forces are much less in level walking (Hamel et al., 2005, Stacoff et al., 2005) therefore the muscular demand is also likely reduced. Other daily tasks vital for active and independent living, such as negotiating stairs, place a much greater demand on the knee and hip musculature (Nadeau et al., 2003), and in these activities functional impairment may become apparent.

Stair climbing can be a hazardous activity; falls on stairs have been identified as a common cause of hip fractures (Abolhassani et al., 2006) with stair descent being particularly high risk for the elderly (Tinetti et al., 1988, Startzell et al., 2000). Hip fractures lead to a substantial impact on quality of life, long-term care requirements (Carey and Laffoy, 2005), and place a substantial socioeconomic burden on health

services and society in general. The aetiology of falls is multifactorial and includes environmental factors, such as staircase design or lighting (World Health Organisation, 2007), and the biomechanical and physiological capacities of the individual (Nadeau et al., 2003). It has been established that, during stair descent, the moments acting about the knee and ankle joints of healthy elderly are close to, or exceed (Samuel et al., 2011), the maximum capabilities of their muscle strength, and are greater than the relative demands experienced by younger counterparts (Reeves et al., 2008a). We have demonstrated earlier that claudicants have velocity-dependent limitations in plantarflexor strength (Chapter 5); this likely necessitates biomechanical adaptations to elicit compensatory strategies at more proximal muscle groups to meet the requirements for stair negotiation. However, if there are impairments in knee strength of claudicants (McDermott et al., 2004b, Camara et al., 2012) it is likely that these compensations are compromised. Combined with impaired balance (Gardner & Montgomery, 2001, Mockford et al., 2011, Gohil et al., 2013) and a greater prevalence of falls (Gardner & Montgomery, 2001) it is likely that claudicants face significant challenge and risk when negotiating stairs. However, no study has previously examined the stair descent biomechanics of this population, so claudicants' compensation strategies and any implications for risk of falling are not yet known.

The purpose of the study was to determine whether PAD-IC results in gait adaptations during stair descent. This was achieved by drawing comparisons to a control group consisting of healthy older adults and exploring relationships between gait parameters and disease severity. It was hypothesised that PAD-IC would result in a redistribution of knee and ankle joint kinetics towards increased hip kinetics. Our second hypothesis

was that these alterations in joint moments and powers would be associated with increased disease severity.

## 7.2 Methods

### *7.2.1 Participants*

A total of 22 participants were recruited consisting of 12 claudicants (six unilateral, six bilateral) and ten healthy controls (see Table 6.1). Due to personal complications with one unilateral claudicant, they were unable to attend a second testing session to assess gait biomechanics. Details pertaining to the assessment of disease severity are depicted in Chapter 3. Briefly, the post-exercise ankle brachial pressure index classified the severity of disease in claudicants and was used to determine the 'claudicating-limb' group (N=12 providing a total of 18 claudicating limbs; 12 from bilateral claudicants and 6 from unilateral claudicants), the 'asymptomatic-limb' group (N=6 providing a total of 6 limbs from the unilateral claudicants). The dominant limb of the healthy controls was determined using a simple ball-kicking exercise and used for subsequent analysis.

### *7.2.2 Gait analysis*

Details pertaining to 3D motion capture are depicted in Chapter 3. Briefly, retro-reflective passive markers were position according to the six Degrees of Freedom marker set (Cappozzo et al., 1995) utilising the functional method to determine hip joint centres (Leardini et al., 1999, Piazza et al., 2001, Baker, 2006). 3D marker coordinate data were tracked using Qualysis Track Manager (Qualysis, Gothenburg,

Sweden) then exported for further processing in Visual 3D (C-motion, Rockville, MD, USA).

Participants were instructed descend a custom-made five-step wooden staircase at their self-selected pace. The staircase contained force-plates (Kistler, Winterthur, Switzerland) imbedded into steps two and three (step five being the final step onto the 80 cm landing at the top of the staircase). The focus of the present study was continuous/steady-state stair descent; therefore one gait cycle was defined from foot contact on step 3 to the subsequent foot contact of the ipsilateral limb onto step 1; and from foot contact on step 2 to the subsequent foot contact of the same limb onto the floor. Relevant gait events were identified (foot strike and foot off) using vertical ground reaction force (≥20 N threshold) and were normalised to 100% gait cycle for kinematic and joint kinetic data and 100% stance phase for ground reaction forces.

Throughout, phases will be described according to the descriptions proposed by McFayden & Winter (1988); weight acceptance, forward continuance, controlled lowering, leg pull-through and foot placement. Variables of interest included temporal-spatial parameters, sagittal plane kinematics (peak angles, angular velocities and range of motion), sagittal plane kinetics (peak joint moments and powers). Angular velocities at the instant of peak moment were quantified in both the weight acceptance and controlled lowering phases both the hip, knee and ankle. Positive angular velocities indicate changes in joint angle towards ankle dorsiflexion, knee flexion and hip flexion. Support moment was calculated as the summed moments of the hip, knee and ankle (Winter et al., 1990, McFadyen & Winter, 1988) with peak

support moment quantified in both the weight acceptance and controlled lowering phases and the relative contribution from these joints expressed as a percentage of peak support moment. Data are expressed as mean and standard deviation.

### *7.2.3 Statistical analysis*

Data were exported into SPSS v21.1 (SPSS Inc., Chicago, IL, USA), assessed for normality violations using Shapiro-Wilk's test for normality and assessed for outliers through box plot analysis. Due to the non-parametric nature of the data, a Mann-Whitney *U* test was performed to determine if significant between group differences existed between the claudicating and control groups and asymptomatic limbs for temporal-spatial parameters. To avoid violating the assumption of independent samples, the bilateral claudicants and unilateral claudicants were analysed for walking speed and time spent in double support. As groups differed in walking speed, a univariate analysis of variance was performed for joint kinematics, kinetics and ground reaction forces with walking speed as a covariate. Where a significant interaction effect was observed, a Sidak post-hoc comparison was performed.

A Pearson's partial product-moment correlation was performed to assess relationships between disease severity (as assessed by ABPI and controlled for the influence of age) and gait parameters for the claudicating group only.

For all statistical tests, significance was accepted at $P \leq .05$ and trends were accepted at $P < .10$. For correlation and regression analyses, a moderate relationship was accepted

as R=.40–.59, a strong relationship was accepted as R=.60–.79 and a very strong relationship was accepted as R=.80–1 (Taylor, 1990). Since low ABPI values indicate high disease severity, a positive relationship indicated a decrease in the respective parameter with worsening disease.

## 7.3 Results

No significant differences were found between groups in age, height, or mass (see Table 6.1). Between-group differences in ABPI were consistent with disease presentation. Due to technical difficulties regarding the collection of kinetic data during some testing sessions, kinetic data are presented for 15 limbs within the claudicating-limb group, 6 limbs within the asymptomatic-limb group, and 9 limbs in the control group.

### *7.3.1 Temporal-spatial parameters and joint kinematics*

Due to the bi-lateral nature of determining walking speed and to avoid violating the assumption of independent samples, walking speed was compared between bilateral and unilateral claudicants and healthy controls. The bilateral claudicants walked significant slower than healthy controls (0.69±0.21m/s vs 0.85±0.20m/s, P=.050) and the unilateral claudicants spent significantly longer in double support (20.4±4.1% vs 14.5±5.6%, P=.050) compared to healthy controls (Table 7.1). The claudicating-limb group demonstrated trends towards spending longer in stance (P=.095), having reduced ankle range of motion compared to the asymptomatic-limb group (P=.067) and reduced peak angular velocity compared to the control group (P=.073) (Table 7.1 and Figure 7.1).

**Table 7.1.** Group mean (SD) temporal-spatial parameters and sagittal plane gait kinematics. All values are degrees unless otherwise stated. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). [A] = vs Asymptomatic group. [Con] = vs Healthy control. All units are degrees unless otherwise stated.

| | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| Stance phase (%) | 59.8 (3.4)[Con] | 59.3 (3.3) | 55.2 (5.2) |
| Peak Hip Flexion Stance | 44.6 (10.3) | 38.9 (14.6) | 52.3 (8.4) |
| Peak Hip Extension | 16.6 (9.0) | 9.2 (11.2) | 21.3 (6.4) |
| Hip RoM | 28.0 (4.8) | 29.7 (4.5) | 31.0 (4.7) |
| Peak Angular Velocity (°/s) | 110.2 (38.2) | 125.7 (37.0) | 152.1 (40.0) |
| Knee Flexion Early Stance | 35.0 (9.6) | 32.4 (7.4) | 44.6 (11.3) |
| Knee Extension Stance | 8.3 (6.8) | 9.3 (2.2) | 11.3 (8.0) |
| Knee Flexion Swing | 91.0 (4.7) | 95.0 (5.1) | 93.5 (9.7) |
| Knee RoM | 98.9 (8.0) | 101.1 (7.2) | 104.5 (4.3) |
| Peak Angular Velocity (°/s) | 386.5 (63.5) | 378.5 (59.9) | 451.1 (76.0) |
| Dorsiflexion Late Stance | 35.6 (7.8) | 40.8 (4.4) | 36.4 (2.6) |
| Plantarflexion Swing | -22.7 (6.3) | -26.9 (3.6) | -24.2 (6.2) |
| Ankle RoM | 57.7 (8.9)[A] | 67.6 (5.3) | 60.6 (7.2) |
| Peak Angular Velocity (°/s) | 308.6 (75.6)[Con] | 348.3 (52.1) | 410.0 (73.8) |

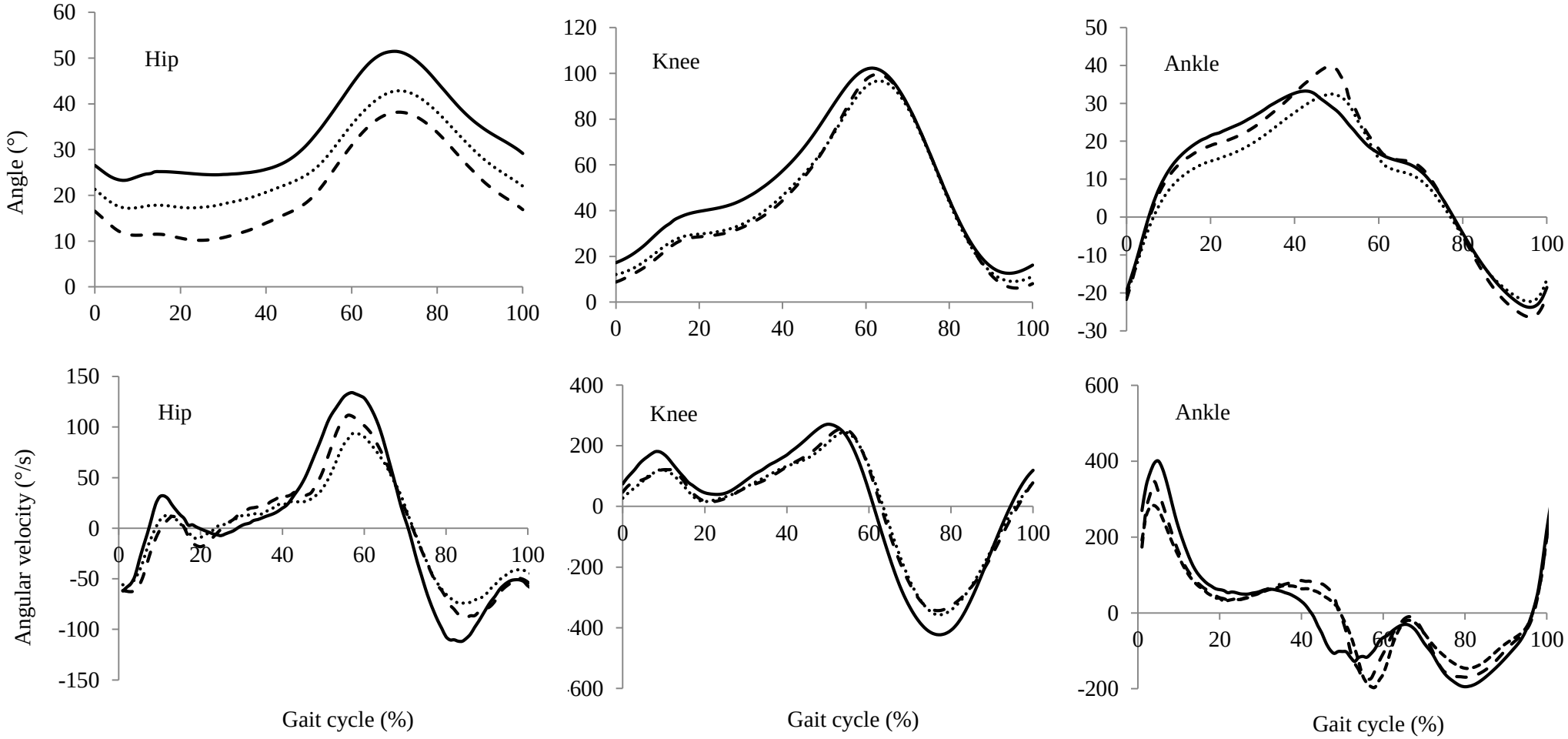


**Figure 7.1**. Group mean angle (top row) and angular velocity (bottom row) for the hip, knee and ankle across 100% gait cycle for claudicating-limb (dotted), asymptomatic-limb (dashed) and healthy controls (solid). For joint angles; positive values indicate hip flexion, knee flexion and dorsiflexion. For angular velocities; positive values indicate changes in joint angles towards hip flexion, knee flexion and ankle dorsiflexion.

*7.3.2 Ground reaction forces*

The claudicating-limb group demonstrated reduced peak braking force (Fy) compared to both the asymptomatic-limb and control groups (P=.004 and P=.016, respectively) and reduced peak vertical landing force (Fz) compared to the control group (P=.021) (Table 7.2 and Figure 7.2).

**Table 7.2**. Group mean (SD) ground reaction force (N/Kg). Dark shaded values represent those reaching significance (P≤.05). [A] = vs Asymptomatic group. [Con] = vs Healthy control

| GRF (N/kg) | Claudicating-limb | Asymptomatic-limb | Control |
|---|---|---|---|
| Medial during weight acceptance | 0.09 (0.02) | 0.08 (0.02) | 0.10 (0.03) |
| Medial during controlled lowering | 0.08 (0.01) | 0.07 (0.02) | 0.09 (0.04) |
| Posterior during weight acceptance | -0.12 (0.03)[A,Con] | -0.16 (0.04) | -0.15 (0.02) |
| Anterior during controlled lowering | 0.14 (0.04) | 0.16 (0.05) | 0.17 (0.03) |
| Vertical during weight acceptance | 1.44 (0.23)[Con] | 1.50 (0.19) | 1.79 (0.24) |
| Vertical during controlled lowering | 0.94 (0.09) | 0.90 (0.06) | 0.96 (0.14) |

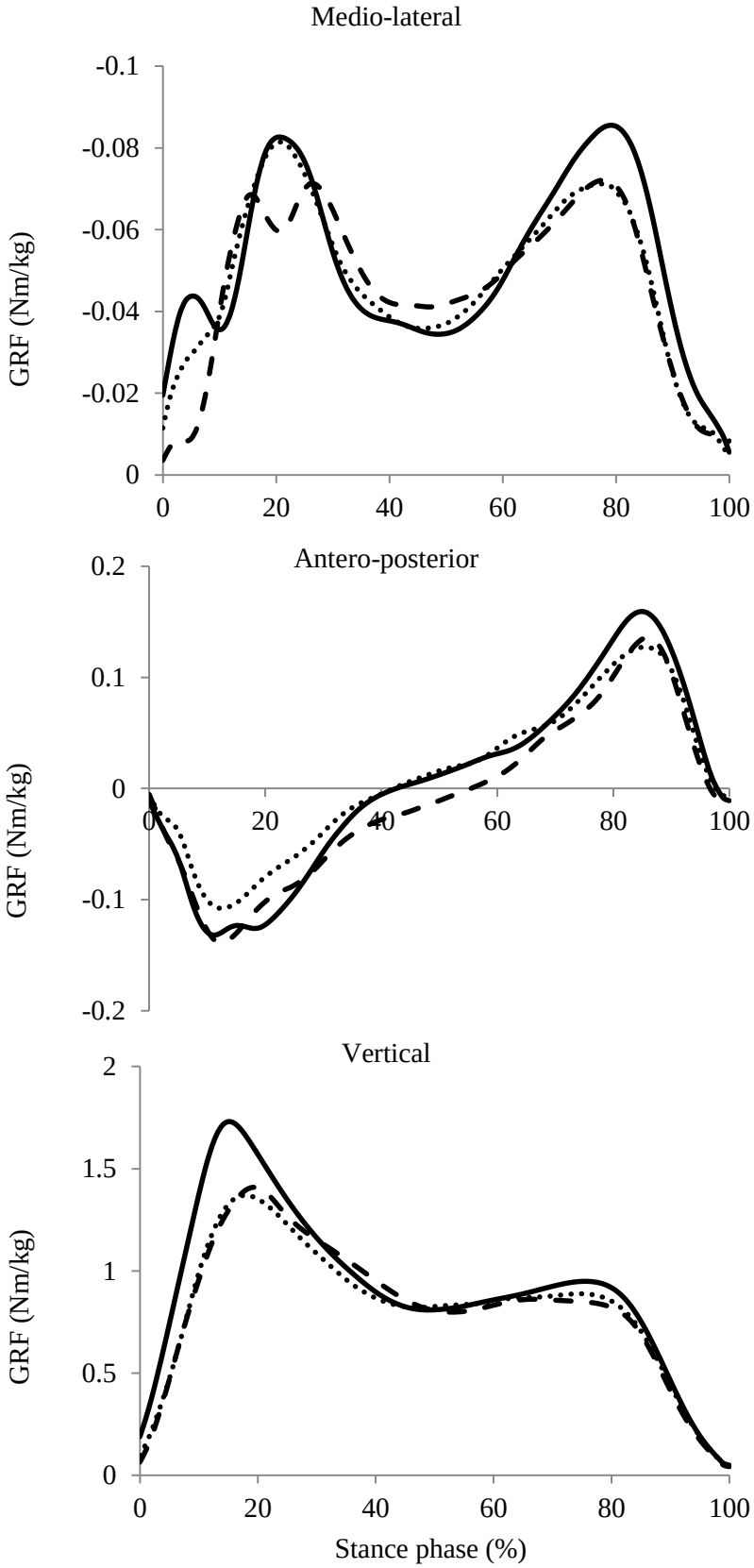


**Figure 7.2.** Group mean ground reaction forces (GRF) for the claudicating group (dotted line), asymptomatic limbs (dashed line) and control group (solid line) normalised to 100% gait cycle. Positive values indicate medial, anterior (propulsive) and vertical force.

*7.3.3 Joint kinetics*

During weight acceptance, the claudicating-limb group demonstrated trends towards reduced ankle angular velocity at the instant of peak ankle moment (P=.073), reduced hip moment (P=.079), increased hip angular velocity at the instant of peak moment (P=.085) and reduced knee power absorption in early stance compared to the control group (P=.073) (Table 7.3 and Figure 7.3). During weight acceptance, the asymptomatic-limb group had reduced hip flexion angle at the instant of peak moment compared to both the claudicating-limb and control groups (P=.014 and P=.016, respectively). Despite a 19% increase in plantarflexor moment and 27% decrease in knee extensor moment between the claudicating-limb group and healthy controls during weight acceptance, neither were significantly reduced (P=.208 and P=.214 respectively) (Table 7.3 and Figure 7.3).

During controlled lowering, the claudicating-limb group demonstrated a trend towards reduced hip flexor moment compared to healthy controls (P=.092) and the asymptomatic-limb group had reduced hip flexion moment compared to both claudicating-limb and control groups (P=.005 and P=.025, respectively).

**Table 7.3**. Group mean (SD) sagittal plane joint kinetics. Positive values indicate ankle plantarflexor, knee extensor and hip extensor moments and power generation. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). [CL] = vs Claudicating-limb group. [Con] = vs Healthy control

| **Weight acceptance** | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| Peak support moment (Nm/kg) | 2.58 (0.57) | 2.80 (0.47) | 2.95 (0.98) |
| Hip moment (Nm/kg) | -0.35 (0.22)[Con] | -0.40 (0.21) | -0.53 (0.22) |
| Hip angle at peak hip moment (°) | 21.3 (9.6) | 5.8 (3.3)[Cl, Con] | 23.3 (6.0) |
| Hip angular velocity at peak hip moment (°/s) | 15.6 (34.8)[Con] | -16.7 (8.6) | -19.4 (51.2) |
| Knee moment (Nm/kg) | 1.11 (0.56) | 1.16 (0.51) | 1.52 (0.57) |
| Knee angle at peak knee moment (°) | 29.9 (8.5) | 24.4 (6.9) | 33.3 (4.8) |
| Knee angular velocity at peak knee moment (°/s) | -72.9 (41.8) | -70.0 (46.3) | -89.7 (47.3) |
| Ankle moment (Nm/kg) | 1.01 (0.28) | 1.14 (0.16) | 0.83 (0.26) |
| Ankle angle at peak ankle moment (°) | 5.7 (4.4) | 8.1 (4.6) | 5.7 (3.5) |
| Ankle angular velocity at peak ankle moment (°/s) | 171.8 (78.4)[Con] | 166.5 (54.0) | 288.6 (96.4) |
| **Controlled lowering** | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
| Peak support moment (Nm/kg) | 2.49 (0.42) | 2.87 (0.23) | 2.76 (0.59) |
| Hip moment (Nm/kg) | -0.35 (0.20)[Con] | -0.52 (0.14) | -0.56 (0.18) |
| Hip angle at peak hip moment (°) | 30.2 (8.6) | 9.2 (4.6)[Cl, Con] | 25.7 (7.3) |
| Hip angular velocity at peak hip moment (°/s) | 85.5 (53.8) | 18.2 (7.2) | 36.9 (557.4) |
| Knee moment (Nm/kg) | 1.22 (0.50) | 1.20 (0.22) | 1.34 (0.39) |
| Knee angle at peak knee moment (°) | 59.6 (10.3) | 60.3 (10.9) | 61.6 (3.7) |
| Knee angular velocity at peak knee moment (°/s) | -176.4 (45.6) | -178.2 (30.2) | -186.2 (43.7) |
| Ankle moment (Nm/kg) | 1.04 (0.18) | 1.15 (0.14) | 0.84 (0.29) |
| Ankle angle at peak ankle moment (°) | 36.5 (5.7) | 36.2 (1.6) | 36.1 (2.4) |
| Ankle angular velocity at peak ankle moment (°/s) | 47.3 (26.3) | 64.2 (49.1) | 34.5 (10.5) |
| **Joint powers** | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
| Hip power controlled lowering (W/kg) | 0.70 (0.39) | 0.59 (0.25) | 0.88 (0.41) |
| Knee power weight acceptance (W/kg) | -2.38 (1.66)[Con] | -2.37 (2.19) | -5.23 (2.96) |
| Knee power controlled lowering (W/kg) | -4.17 (1.42) | -4.14 (0.85) | -4.73 (1.62) |
| Ankle power weight acceptance (W/kg) | -3.78 (1.42) | -4.43 (0.81) | -4.67 (2.03) |
| Ankle power controlled lowering (W/kg) | 2.26 (0.72) | 2.91 (1.13) | 2.04 (1.23) |

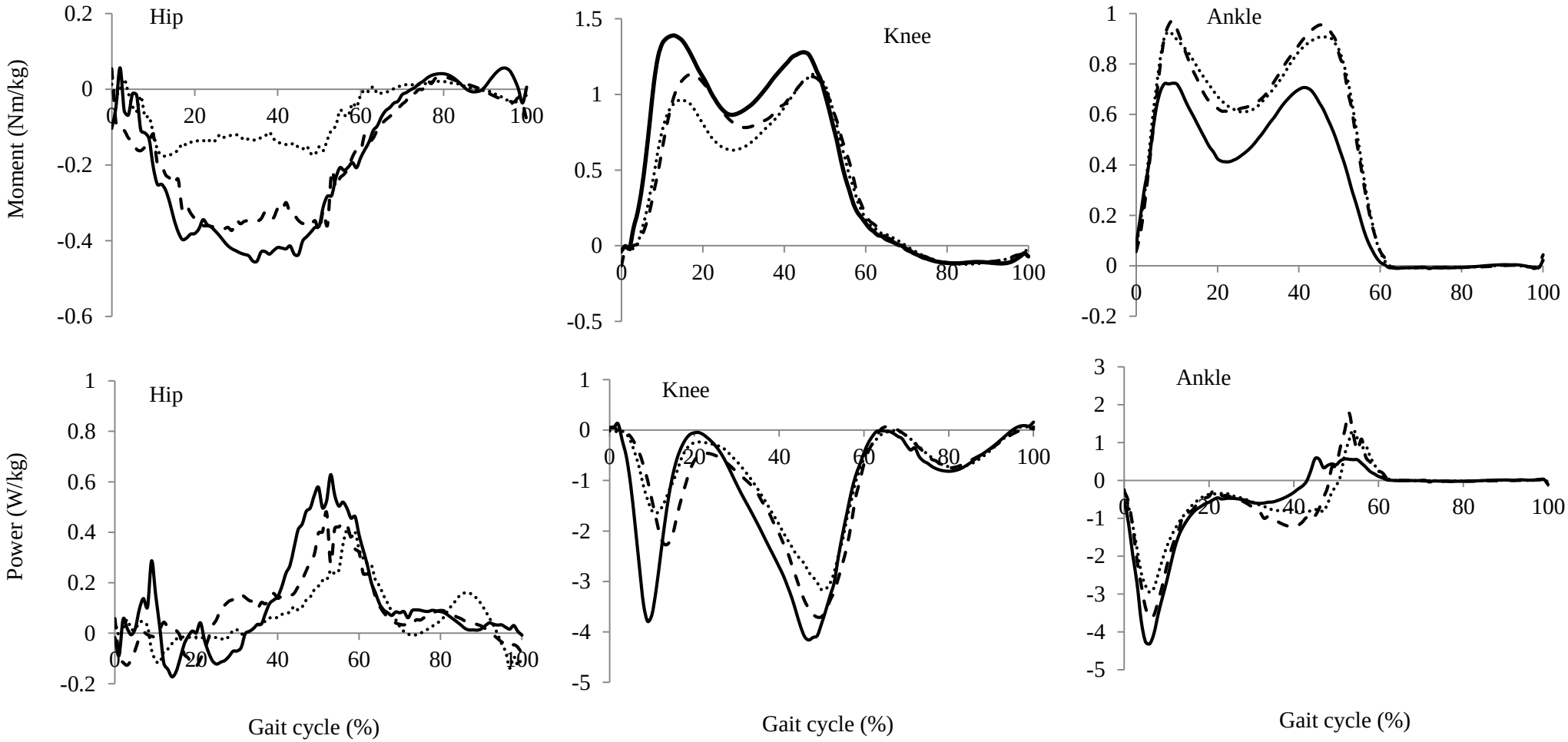


**Figure 7.3**. Group mean internal joint moment (top row) and joint power (bottom row) for the hip, knee and ankle across 100% gait cycle for claudicating-limb (dotted), asymptomatic-limb (dashed) and healthy controls (solid). Positive values indicate hip and knee extensor and ankle plantarflexor internal joint moment and power generation

*7.3.4 Joint contributions to peak support moment*

During weight acceptance, both the claudicating-limb and asymptomatic-limb groups displayed a greater proportion of ankle moment contribution to peak support moment compared to controls (P=.005 and P=.067, respectively). The claudicating-limb group demonstrated trends towards less hip moment contribution to peak support moment (P=.056) (Figure 7.4). During controlled lowering the claudicating-limb group used a greater proportion of ankle moment contributing to peak support moment compared to controls (P=.022) and reduced hip contribution compared to both asymptomatic-limb and control groups (P=.062 and P=.005, respectively).

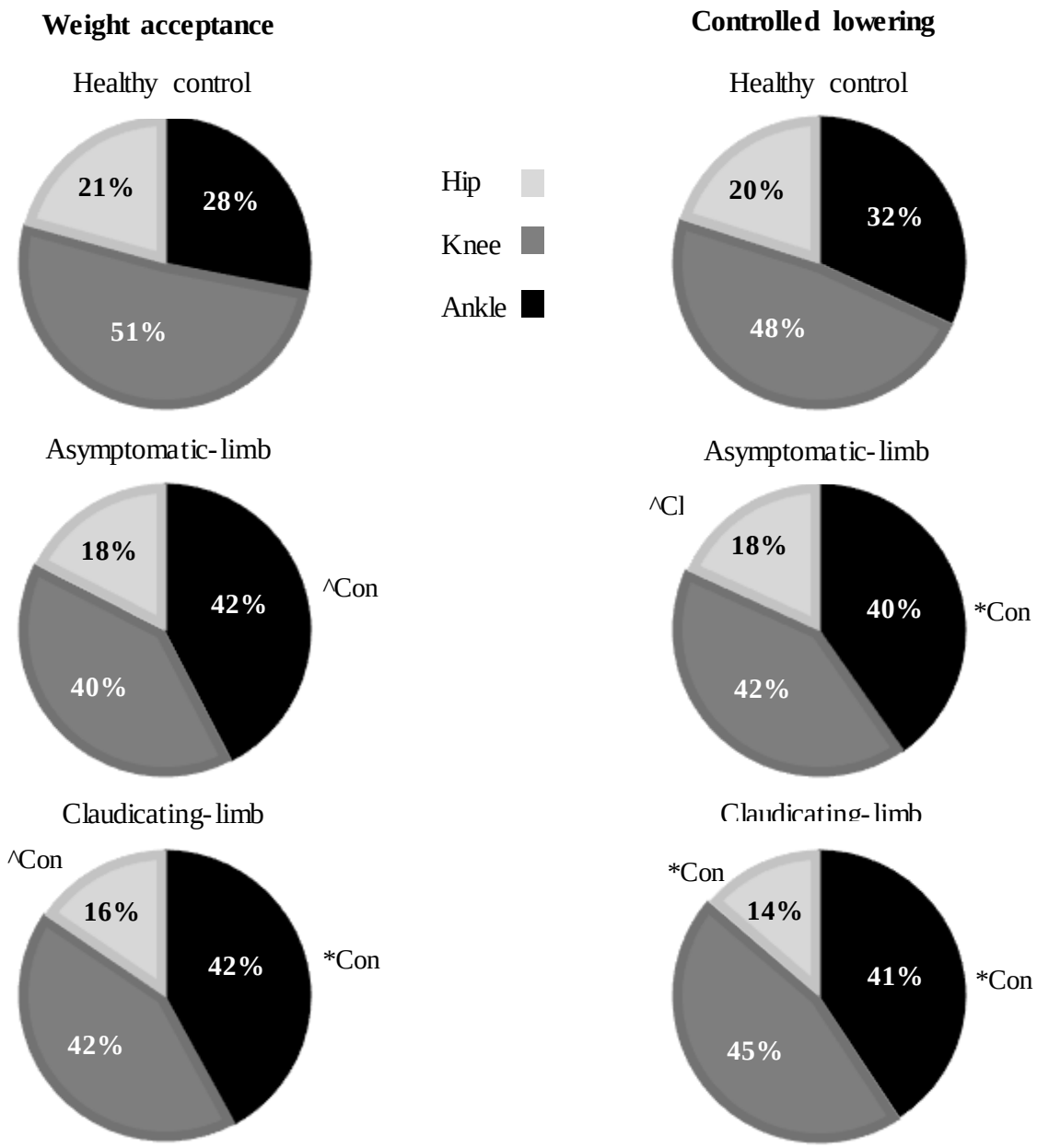


**Figure 7.4**. Percentage contribution to peak support moment during weight acceptance and controlled lowering. Significant between-group differences (P=<0.05) are indicated with (*) and trends towards significance (P=<-.10) indicated with (^). Cl = vs claudicating limb group, Con = vs healthy control group

*7.3.5 Sub-group analysis of claudicating limbs*

Within the claudicating-limb group, an alternate hip moment strategy was observed within the data. As such, a sub-group analysis was performed within the claudicating-limb group, resulting in hip extensor (limbs=11) vs. hip flexor strategy (limbs=4) sub-groups, which were compared to the asymptomatic-limb and control groups (Table 7.4 and Figure 7.5). This strategy was evident during the first 10% of the gait cycle in two healthy control participants; however this was immediately followed by a rapid shift back towards a hip flexion moment. As this was not a clear and sustained hip extensor strategy observed in the claudicating-limb group, this likely reflects the variability of initial foot contact and not an alternative movement strategy. Nonetheless such these participants were removed from the subsequent analysis. During weight acceptance for the claudicating-limb group, the hip extensor sub-group demonstrated a trend towards reduced knee moment compared to the hip flexor sub-group (P=.094) and a hip extensor moment compared to the hip flexor sub-group, asymptomatic-limb and control groups (P=<.000 in all cases). During controlled lowering, the hip extensor sub-group demonstrated a trend towards reduced knee moment (P=.068) and significantly reduced hip joint moment (P=.036) and peak support moment (P=.021) compared to the hip flexor sub-group. The hip extensor sub-group also used a greater proportion of ankle moment towards peak support moment compared to both the hip flexor sub-group and control group (P=.100 and P=.031, respectively).

**Table 7.4.** Sub-group analysis of sagittal plane peak joint kinetics and joint contributions to peak support moment. Positive values indicate ankle plantarflexor, knee extensor and hip extensor moment. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). [CLExt] = vs Claudicating-limb hip extension strategy. [CLFlex] = vs Claudicating-limb hip flexion strategy. [A] = vs Asymptomatic. [Con] = vs Healthy control

| **Weight acceptance** | **Claudicating-limb hip extensor strategy** | **Claudicating-limb hip flexor strategy** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|---|
| Hip moment (Nm/kg) | 0.37 (0.19)[CLFlex, A, Con] | -0.39 (0.22) | -0.51 (0.20) | -0.50 (0.37) |
| Knee moment (Nm/kg) | 0.88 (0.55)[CLFlex] | 1.60 (0.27) | 1.16 (0.51) | 1.48 (0.64) |
| Ankle moment (Nm/kg) | 0.93 (0.27) | 1.08 (0.27) | 1.15 (0.16) | 0.75 (0.26) |
| Support moment (Nm/kg) | 2.13 (0.61) | 3.07 (0.23) | 2.81 (0.49) | 2.73 (0.79) |
| Hip contribution (%) | 17.1 (8.3) | 12.4 (6.0) | 17.5 (5.3) | 20.8 (5.3) |
| Knee contribution (%) | 37.9 (20.7) | 51.9 (5.8) | 40.1 (10.4) | 51.2 (2.6) |
| Ankle contribution (%) | 44.9 (14.6) | 35.7 (10.9) | 42.4 (11.2)[Con] | 28.0 (4.1) |
| **Controlled lowering** | **Claudicating-limb hip extensor strategy** | **Claudicating-limb hip flexor strategy** | **Asymptomatic-limb** | **Control** |
| Hip moment (Nm/kg) | -0.28 (0.09)[CLFlex] | -0.66 (0.30) | -0.46 (0.20) | -0.53 (0.20) |
| Knee moment (Nm/kg) | 1.02 (0.41)[CLFlex] | 1.55 (0.73) | 1.20 (0.22) | 1.30 (0.37) |
| Ankle moment (Nm/kg) | 0.99 (0.20) | 1.01 (0.15) | 1.15 (0.14) | 0.84 (0.14) |
| Support moment (Nm/kg) | 2.32 (0.54)[CLFlex] | 3.22 (0.87) | 2.80 (0.27) | 2.71 (0.51) |
| Hip contribution (%) | 13.5 (3.5) | 20.2 (6.8) | 16.2 (6.6) | 21.4 (6.9) |
| Knee contribution (%) | 42.6 (10.3) | 46.5 (9.4) | 42.5 (4.9) | 47.4 (8.1) |
| Ankle contribution (%) | 43.9 (8.4)[CLFlex, Cn] | 33.3 (10.4) | 41.4 (6.8) | 31.2 (2.7) |

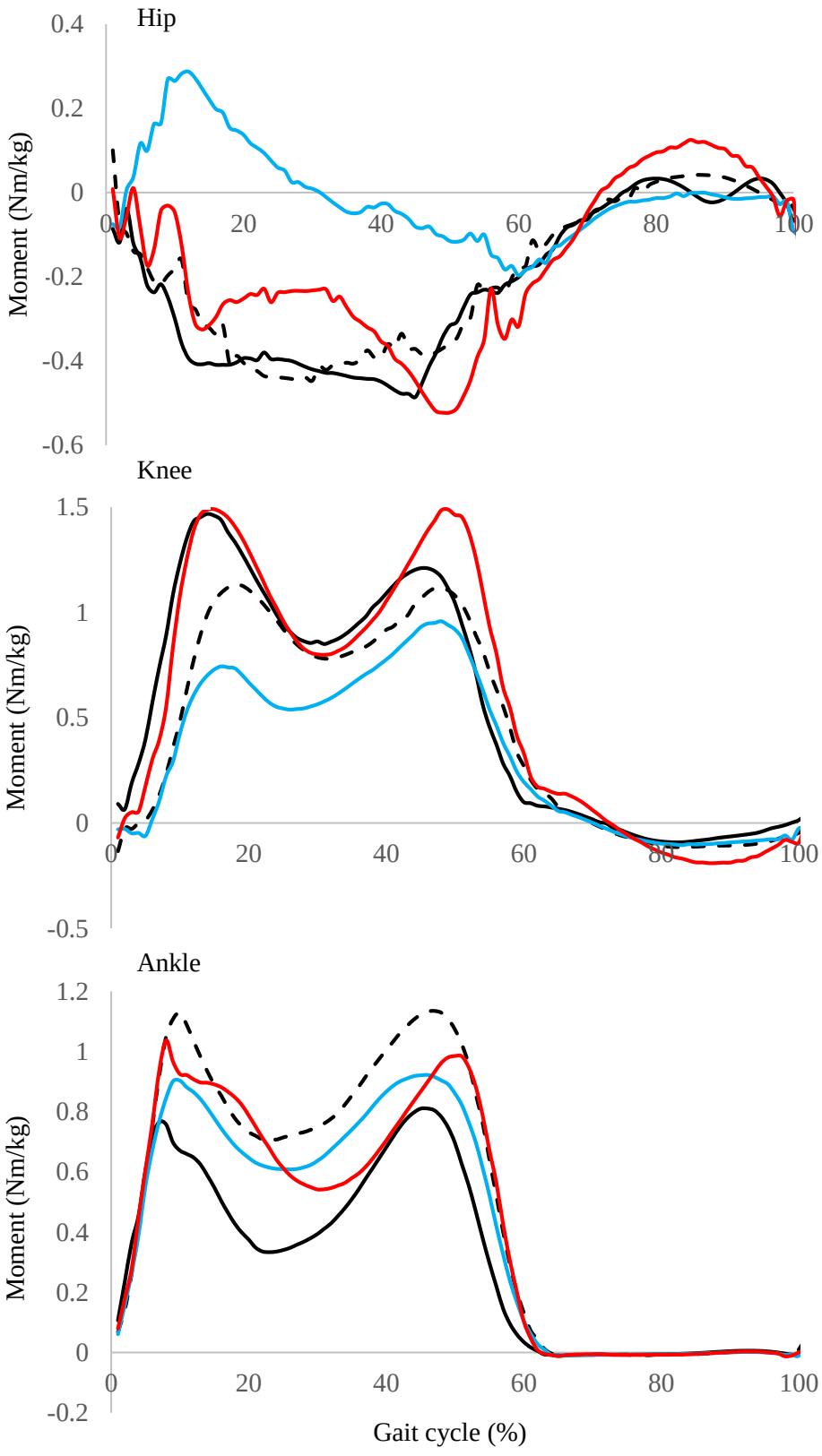


**Figure 7.5.** Group mean internal joint moments for the claudicating-limb group using a hip extensor strategy (blue line), claudicating-limb group using a hip flexor strategy (red) asymptomatic limbs (dashed line) and control group (solid line) normalised to 100% gait cycle. Positive values indicate hip and knee extensor and ankle plantarflexor moment

*7.3.6 Disease severity correlations*

During weight acceptance, increased disease severity was associated with trends towards reduced ankle power absorption (R=-.497, P=.100), reduced knee extensor moment (R=.557, P=.060), reduced hip angular velocity at the instant of peak moment (R=-.624, P=.073), reduced hip flexor moment (R=-.453, P=.100) and increased hip contribution to peak support moment (R=-.760, P=.017) (Table 7.5 and 7.6). During controlled lowering, increased disease severity was associated with reduced knee (R=-.643, P=.024) and hip (R=.579, P=.068) angular velocities at the instant of peak moment.

**Table 7.5**. Pearson partial correlations (controlled for the influence of age) between disease severity (ABPI), support moment and joint contributions. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10).

| | **Weight acceptance** | **Peak support moment** | **Ankle contribution** | **Knee contribution** | **Hip contribution** |
|---|---|---|---|---|---|
| ABPI | Correlation | .393 | .434 | .147 | -.760 |
| | Significance | .296 | .243 | .705 | .017 |
| | **Controlled lowering** | **Peak support moment** | **Ankle contribution** | **Knee contribution** | **Hip contribution** |
| ABPI | Correlation | .336 | .336 | -.440 | .171 |
| | Significance | .377 | .377 | .237 | .660 |

**Table 7.6**. Pearson partial correlations (controlled for the influence of age) between disease severity (ABPI) and angular velocities, joint moments and powers for the ankle, knee and hip. Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P≤.10).

| | **Ankle** | Ankle angular velocity at peak moment (weight acceptance) | Plantarflexor moment (weight acceptance) | Ankle power weight acceptance) | Ankle angular velocity at peak moment (controlled lowering) | Plantarflexor moment (controlled lowering) | Ankle power (controlled lowering) |
|---|---|---|---|---|---|---|---|
| ABPI | Correlation | .090 | .488 | -.497 | -.216 | .221 | -.055 |
| | Significance | .759 | .107 | .100 | .459 | .490 | .865 |
| | **Knee** | Knee angular velocity at peak moment (weight acceptance) | Knee extensor moment (weight acceptance) | Knee Power weight acceptance) | Knee angular velocity at peak moment (controlled lowering | Knee extensor moment (controlled lowering) | Knee power (controlled lowering) |
| ABPI | Correlation | .195 | .557 | -.420 | -.643 | .343 | -.477 |
| | Significance | .543 | .060 | .174 | .024 | .275 | .117 |
| | **Hip** | Hip angular velocity at peak moment (weight acceptance) | Hip moment (weight acceptance) | Hip angular velocity at peak moment (controlled lowering) | Hip moment (controlled lowering) | | |
| ABPI | Correlation | -.624 | -.453 | .597 | .330 | | |
| | Significance | .073 | .100 | .068 | .250 | | |

## 7.4 Discussion

This is the first study to investigate the gait adaptations of those with PAD-IC during stair descent. Contrary to our hypothesis, claudicants did not redistribute joint moments away from the ankle and knee towards the hip. In fact, the plantarflexors contributed a larger percentage to the peak support moment (~40%) with reduced contribution from the hip (~15%) during both weight acceptance and controlled lowering in the claudicating-limb group compared to controls. We also identified a unique shift towards utilisation of hip extensor moments during the weight acceptance phase that was adopted by 73% of the claudicating-limb group. This sub-group however, demonstrated reduced knee moments with no effect on ankle moments suggesting this strategy is not a compensatory mechanism for the functionally limited plantarflexors. Our data suggest claudicants place a much greater reliance on the plantarflexor muscles than the more proximal musculature, which highlights the importance of preserving the strength of this muscle group.

The finding that claudicants do not redistribute joint kinetics *away* from the ankle, but *towards*, in comparison to controls, was surprising. The healthy controls in our study utilised the strength of the knee extensors much more than either the hip or ankle muscles (~50% of peak support moment), which is consistent with previous reports that this strategy allows them to operate within safer limits of maximum strength (Reeves et al., 2008a). In contrast, the claudicants utilised the ankle and knee almost equally to meet the kinetic demands (both ~ 40% of peak support moment). Given that we have previously identified velocity-dependent weakness in the ankle plantarflexors (Chapter 5), the greater reliance on this muscle group seems counter-intuitive. This is

most notable in the weight acceptance phase that is characterised by fast, eccentric muscle action of the plantarflexors in particular, to absorb the falling body mass (McFadyen & Winter, 1988, Cluff & Robertson, 2011) (Figure 2, Appendix A1). Potentially, weakness of the knee extensors may prevent the redistribution away from the plantarflexors that is typically seen in healthy elderly (Reeves et al., 2008a). Knee extensor strength was not assessed in the present programme of research, and previous research is contradictory and sparse. Some reports suggest that knee extensor strength remains largely unaffected by PAD-IC (Scott-Okafor et al., 2001, Camara et al., 2012), but others report reductions (McDermott et al., 2008b) and associations with disease severity (McDermott et al., 2004b). When knee strength is impaired it appears to have important consequences, as weakness is associated with all-cause mortality (Singh et al., 2010) and reduced functional ability (McDermott et al., 2004b, McDermott et al., 2008b). The latter is consistent with the present results. Claudicants demonstrated reduced knee moments (non-significant 27% during weight acceptance), particularly in those adopting an alternate hip strategy, with further associations with disease severity (Tables 7.3, 7.5 and 7.6). This suggests the knee extensors in our cohort may also be functionally impaired and do not possess the necessary strength to sufficiently contribute to this task or provide adequate compensation for the plantarflexors.

We have identified an interesting shift towards utilising the hip extensors, as opposed to the hip flexors, during weight acceptance (Table 7.4 and Figure 7.6) which was present in 73% of our claudicating-limb cohort. However, in those adopting this alternate strategy, plantarflexor moment did not decrease. Instead there were trends towards reduced knee moments which indicates this mechanism serves to compensate for limitations in the knee extensors and not ankle plantarflexors. The trends towards

association between disease severity and hip moment during weight acceptance (i.e. those with low ABPI demonstrate less hip flexor moment and increased hip extension moment) and reduced knee extension moment suggests this compensatory strategy becomes more prevalent in those with severe forms of disease. Hip strength was not assessed in the current programme of research, however previous studies have indicated hip extensor strength is reduced in this population (McDermott et al., 2004b, Parmenter et al., 2013b) and associated with disease severity (Parmenter et al., 2013b), functional decline (Herman et al., 2009), and mortality (Singh et al., 2010). Further research is necessary to fully understand the role of this muscle group in functional tasks, such as stair negotiation. Moreover, given the surprising joint loading distribution patterns away from the knee extensors; exploration of exercise interventions on this functionally important muscle group are required and would likely impact on the relative demand placed on the hip extensors and ankle plantarflexors.

The asymptomatic-limb demonstrated a trend towards increased ankle range of motion compared to the claudicating-limb group (Table 7.1), which is mostly attributable to the increased ankle dorsiflexion angle during controlled lowering (Figure 7.1a). This adaptation may be beneficial for stability and reducing the difficulty of the task. Healthy elderly utilise the trailing limb (in the controlled lowering phase) to control the downwards acceleration of the centre of mass (CoM) rather than relying on the leading limb to decelerate the falling CoM at landing during weight acceptance (Buckley et al., 2013). It appears unilateral claudicants adopted a similar strategy by utilising the unaffected asymptomatic limb for an extended period of controlled lowering to minimise demands on the symptomatic limb during weight acceptance.

This is congruent with the more extended hip during controlled lowering (Figure 7.1) which, given the comparable knee angles between groups, indicates a more upright posture in unilateral claudicants (Table 7.2). It may be inferred that the centre of mass was higher and more posterior, over the asymptomatic limb; another indication of a strategy to avoid increased loading of the symptomatic limb during weight acceptance (Spanjaard et al., 2008).

The greater dorsiflexion angle and extended controlled lowering should also improve stability of unilateral claudicants by (i) maintaining a flat-foot on the step for longer providing a larger base of support (Lark et al., 2004) and (ii) increasing the time spent in double support. Such strategies, coupled with handrail use, appear important in claudicants given previous reports of impaired balance (Gardner & Montgomery, 2001, Mockford et al., 2011, Gohil et al., 2013) and a greater prevalence of falls (Gardner & Montgomery, 2001). Further investigation is necessary to establish if these strategies are adequate to attenuate falls prevalence on stairs and, given that these mechanisms have been identified in unilateral not bilateral claudicants, relationships between falls and the laterality of disease. At this stage it is unclear whether ankle range of motion was limited in bilateral claudicants, preventing the adoption of this strategy, therefore assessments and exercise interventions focusing on ankle joint flexibility are required to elucidate the causes of these differences.

It is important to acknowledge that we have inferred contributions from the lower limb joints based on the ratio of involvement towards the peak support moment. To quantify this further, normalisation of joint moments to maximum strength capacity may

provide further insight in the distribution of joint moments. Furthermore, we have made assumptions regarding control and location of the centre of mass based on lower limb kinematics. This was necessary due to the use of a lower-limb model only, and confirmation is required using a full-body model. Finally, whilst we statistically controlled the influence of walking speed in between-group analyses, a more vigorous investigation comparing claudicants to speed-matched controls is required to fully explore the velocity-dependent limitations in the gastrocnemii.

## 7.5 Conclusions

This study has identified three novel characteristics of stair descent in claudicants that have important implications for function and safety. First, even though the ankle plantarflexors are more functionally-limited in claudicants than healthy controls, the claudicants place greater reliance on them to absorb energy during weight acceptance. Second, a unique hip strategy has been identified that utilises the hip extensor muscles during weight acceptance. This reduces knee moments but not ankle plantarflexor moments; indicating this is not a strategy to reduce demands on the plantarflexors, but rather on the knee extensors. Finally, a foot-flat strategy due to greater ankle dorsiflexion in the asymptomatic limb of unilateral claudicants indicates compensations for better controlled lowering and enhanced dynamic stability thus potentially reducing loading of the claudicating limb. Exercise interventions targeting knee extensor and plantarflexor strength and dorsiflexion range of motion are vital to maintain independent and safe stair descent.

# Chapter 8. Thesis synthesis, limitations and clinical recommendations

Numerous factors contribute to muscle strength including muscle activation, intrinsic quality of the muscle and the properties of the in-series tendon. Whilst external muscle strength has been previously quantified in claudicants with PAD-IC, these key contributing factors have not. As such, the underpinning mechanisms for reduced walking endurance and plantarflexor impairment during level walking are unclear. Furthermore, substantial demands are placed on the lower limb muscles during tasks of daily living, such as stair negotiation; therefore it is imperative to understand potential musculoskeletal adaptations and their influence on functional capabilities. The overarching aim of the doctoral research was to investigate the musculoskeletal adaptations in the gastrocnemii muscle and Achilles tendon in claudicants with PAD and explore relationships with disease severity and functional ability.

## 8.1 Effect of PAD-IC on the functional properties of the Achilles tendon

The Achilles tendon has a notoriously poor blood supply (Chen et al., 2009), with further declines observed with healthy ageing (Halstad *et al*. (1959) citied in Del Buono *et al.,* 2013) that likely contributes to the age-related deteriorations in functional tendon properties (Kubo et al., 2003). Therefore, the additional burden of PAD-IC would likely impact negatively on the Achilles tendon.

The Achilles tendon stores elastic energy during walking and releases that energy during propulsion to reduce the metabolic cost of muscle work (Peltonen et al., 2013),

thereby improving movement efficiency. It was demonstrated that greater disease severity was associated with higher hysteresis values (Chapter 4, Table 4.3). Consequently the tendons of those with more severe forms of PAD are less able to utilise this energy saving mechanism and the energy cost of movement would increase. This observation is commensurate with reported reductions in walking economy with greater disease severity (Gardner et al., 2010). The additional findings that greater disease severity was also associated with relatively longer fascicle lengths, a mechanism that could reduce the energy cost of muscle contraction and benefit functional ability, indicates the negative adaptations in the tendon outweigh potentially positive adaptations in the muscle.

The observed smaller tendon lengths in those with increased disease severity without concomitant increases in stiffness would mean that, for any given force, elongation would remain unchanged but strain would be increased; thus the reported relationships between disease severity and peak strain (Chapter 4 Table 4.3). This would reduce the tendon's safety margin to the failure strain. Indeed, two case studies have reported bilateral Achilles tendon rupture due to ischemia (Shukla, 2002, Jain & Dawson, 2007). Although it was postulated by the respective authors that additional medication and co-morbidities may have contributed to these incidents, the present study offers a further explanation as PAD-IC appears to "weaken" the Achilles tendon. This emphasises the need to address the shortfalls in the tendon of claudicants; notably increasing stiffness and reducing mechanical hysteresis, which would have a substantial impact on functional ability. This is further compounded by the inclusion of these variables in our regression models to explain walking endurance (Chapter 4,

Tables 4.6 and 4.7), indicating exercise interventions in this clinical population should be targeted at improving these tendon parameters.

We observed that, not only was tendon Young's modulus significantly reduced and tendon hysteresis increased in those with more severe forms of disease, there were also non-significant reductions in tendon stiffness (24-29%) and increases in tendon elongation (17-18%) (Chapter 4, Table 4.5). Interestingly, it was noted that the asymptomatic limb also demonstrated comparable deleterious adaptations to the claudicating limbs (Chapter 4, Table 4.5). Previous research demonstrated asymptomatic PAD patients (ABPI <0.9 but no exertional leg pain) had reduced physical function, smaller calf muscle area and increased calf muscle fat percentage compared to symptomatic PAD patients and healthy controls (McDermott et al., 2008a). Combined with our findings in unilateral claudicants, this suggests that systemic effects of PAD result in deleterious musculoskeletal adaptations. However, whether these changes are solely due to systemic disease or associated with reduced physical activity, or a combination of these factors is not clear. Nonetheless, the fact that the asymptomatic limb is impaired, regardless of the direct cause, can implicate treatment decisions. Even if the symptomatic limb in unilateral claudicants was treated using angioplasty or surgical interventions, the quality of the 'healthy' limb may still be compromised to some extent, therefore mitigating the impact of intervention. This corroborates previous reports that long-term effects of angioplasty are not necessarily sustained compared to exercise therapy (Fowkes & Gillespie, 2000, Spronk et al., 2009). As both unilateral and bilateral claudicants were included in these studies, the role the asymptomatic limb plays in functional deteriorations post-intervention cannot be determined and poses a valuable and important question to answer.

## 8.2 Effect of PAD-IC on the size, architecture and measures of muscle quality of the gastrocnemii

It was hypothesised that the gastrocnemii in claudicants would demonstrate comparable adaptations to those seen with disuse and ageing: reduced muscle size; relatively shorter fascicle lengths; and reduced pennation angles. It was believed that these parameters would explain poorer functional ability. Interestingly, the results disproved this hypothesis.

It was found that muscle size (volume and PCSA) was not different between claudicating or asymptomatic-limbs and healthy controls (Chapter 5, Table 5.4). This was in agreement with the findings of Raval et al. (2012), but in contrast to the previous findings of McDermott et al. (2009b) who reported muscle CSA to be 8.1% smaller in claudicants than controls, and those of Garg et al. (2011) who also reported similar differences (3.5–10.5 %). It seems unlikely that the present results were confounded by the influence of body size, since no differences were found between groups for height, body mass or BMI, or normalised muscle size as represented by volume/tibia length$^3$ (P=.952) and PCSA/tibia length$^2$ (P=.201 (see Table 2 in appendix A3). As such the disparities with previous work likely reflects the dissimilar ways in which muscle size was quantified. Regardless of the reason for the apparent differences to previous research, the magnitude of muscle size difference between controls and claudicants previously reported (McDermott et al., 2009b, Garg et al., 2011) remains small. Moreover, even the previously reported reductions in muscle CSA do not fully account for the larger differences in muscle power previously

observed (Camara et al., 2012) and the clear limitations in both power and normalised power at high contraction velocities identified in Chapter 5.

In those with PAD-IC, remodelling of the muscle architecture towards relatively longer fascicles indicated adaptations towards a larger functional range of motion and velocity. The beneficial effect of this is to reduce the energy consumption of muscle length change during contraction. In an ischemic environment where oxygen supply is at a premium, this adaptation would improve functional ability. However, concomitant increases in hysteresis, suggesting inefficiency in energy utilisation of the Achilles tendon, were also observed. At this stage it is not possible to determine a clear cause and effect relationship between these parameters. The direction of coefficients in our regression model also indicated that shallower pennation angles, indicative of a muscle with longer fibres, play an important role in claudicants' functional ability. This suggests muscle structure favouring length changes (which is also reflected by the observed longer fascicle: tendon length ratios) rather than force production are beneficial for walking endurance. Furthermore, the longer fascicles we observed at rest, notably GM (Chapter 4, Table 4.4), remain long during isometric plantarflexor contraction and is further supported by strong positive correlations between fascicle: tendon length ratios and fascicle length at MVC (see Table 3 in appendix A3). This provides further support that these structural changes have a profound effect on functional capabilities.

The disparity between previous studies and the varied effectiveness of strength-based rehabilitation interventions likely stems from the current lack of understanding of how

factors that contribute to muscle strength are affected by PAD-IC and disease severity. It was demonstrated that, whilst externally measured strength (isometric MVC and concentric peak power at slow velocities) were comparable between groups (Chapter 5), claudicants relied on the predominantly type I-fibred soleus to develop overall strength to a greater extent than healthy controls. This suggests that the need for plantarflexor muscle action at a reduced metabolic cost is paramount, but this also compromises the dynamic quality of the gastrocnemii muscles. Further associations between the previously identified longer fascicle: tendon length ratios, increased soleus contribution and reduced static muscle quality, *independent of disease severity*, (see Table 3 in appendix A5) further support the notion that metabolic efficiency is preferential over maximal force production. This has a substantial effect on the ability to generate fast and strong muscle action, which is consistent with the findings of significantly impaired dynamic muscle quality (Chapter 5) and further associations with disease severity and walking endurance.

The findings in this thesis support previously observed reports of reduced muscle power during strength assessments (Camara et al., 2012) and during level gait (Koutakis et al., 2010a, Wurdeman et al., 2012a) and, for the first time, offer musculoskeletal explanations for these limitations. Whilst lower-limb muscle strength, particularly isometric plantarflexor strength, is associated with mortality (Singh et al., 2010, McDermott et al., 2012), monitoring plantarflexor power at high velocities appears the most appropriate way to detect functional losses. Furthermore, the results provide clear direction for informing exercise-based interventions with a focus on high-velocity resistance training. Future research should focus on the assessment of these measures of static and dynamic muscle quality and investigate

whether appropriately designed interventions will lead to the predicted improvements in functional ability.

### 8.3 Effect of PAD-IC on stair gait biomechanics and relationships with muscle-tendon adaptations

Within PAD-IC, gait mechanics during level walking have previously been investigated with clear signs of plantarflexor dysfunction evident in both the absence and presence of claudication pain (Scott-Pandorf et al., 2007, Chen et al., 2008, Koutakis et al., 2010a, Wurdeman et al., 2012a). However, the muscular demands during stair negotiation are much higher during level gait (Nadeau et al., 2003, Tiedemann et al., 2007) therefore the limitations of the plantarflexors will likely have a substantial influence on the ability to accomplish this task safely. It was hypothesised that, firstly, the previously identified adaptations of the Achilles tendon and gastrocnemii muscle would result in altered kinematic and kinetic profiles of the ankle; and secondly, this would result in claudicants adopting strategies to avoid increasing the functional demand on this muscle group. Whilst there is evidence to support the first hypothesis, compensatory strategies were not clearly present in either stair ascent or stair descent.

During stair ascent, the ability to generate plantarflexor joint moment was comparable in claudicants and healthy controls. However, reduced angular velocities resulted in reduced plantarflexor power generation which, combined with the reduced propulsive and vertical ground reaction forces, provide functional evidence for velocity-dependent limitations of the plantarflexors. These findings mirror the investigations

into plantarflexor strength reported in Chapter 5, with similar isometric MVC and reduced peak power (as well as reduced dynamic muscle quality) compared to healthy controls. These findings are also commensurate with comparable plantarflexor moments yet reduced ankle power generation compared to healthy controls observed during level walking (Wurdeman et al., 2012a).

Compensatory strategies were expected during stair ascent to assist the less powerful plantarflexors during the push-up phase, which could be achieved through increased knee extensor or hip extensor activity during weight acceptance in order to 'pull' the body vertically. This was not evident (Chapter 6, Table 6.4 and Figure 6.3) indicating that either the hip and/or knee extensors lack adequate strength to provide such a compensation; or that the claudicants were actively evading increased muscular effort in an attempt to avoid earlier onset of claudication pain and increased metabolic cost (Mockford et al., 2010). However, given the observed shift towards increased utilisation of the hip extensors during stair descent with concurrent reduced knee moments (Chapter 7, Table 7.4), it seems likely that weak knee extensors were preventing adequate strategies from being adopted to compensate for the impaired plantarflexors during both stair ascent and descent. The typical redistribution of task demand seen in healthy elderly compared to younger counterparts allows the elderly to work within safer limits of maximum joint strength (Reeves et al., 2008a, Reeves et al., 2009b). A comparable study should be performed in claudicants to: firstly, quantify the strength of the hip and knee musculature/extensors to establish whether the lack of compensation is because these muscle are already operating close to maximum; and secondly, to assess the effects of appropriately designed exercise

interventions on the ankle plantarflexors and knee extensors and the subsequent distribution strategies of this task demand.

A greater prevalence of falls in claudicants (Gardner & Montgomery, 2001) and evidence of impaired balance (Gardner & Montgomery, 2001, Mockford et al., 2011, Gohil et al., 2013) have been previously reported. Despite Gardner & Montgomery, (2001) not differentiating between a fall on level ground and a fall on stairs, the increased demands of stair descent would further challenge dynamic stability. Our findings demonstrated a lack of substantial compensatory strategies and the surprising redistribution *towards* the limited ankle plantarflexors could place the claudicants at a greater risk of falls. Additional analysis of the data revealed that those with reduced static muscle quality utilised the ankle plantarflexors more, and the knee extensors less, to contribute to peak support moment during weight acceptance (R=-.635, P=.066, see Figure 1 appendix A5), suggesting those with the most severe impairments in the gastrocnemii were actually more reliant on them. This reinforces the need to address these limitations with appropriate progressive resistance training interventions.

However, some mechanisms to increase stability were observed in unilateral claudicants: greater dorsiflexion and extended controlled lowering (Chapter 7, Table 7.1 and Figure 7.1). Whilst this suggests unilateral claudicants may possess mechanisms to increase stability, it also presents an important question regarding the fate of bilateral claudicants that do not possess an asymptomatic limb capable of compensating. It was beyond the scope of the current programme of research to assess

balance between groups however, detailed investigation of the prevalence of falls between different disease presentations (unilateral vs bilateral) and their coping strategies are essential in order to provide targeted balance-based recommendations.

### 8.4 Study limitations and future directions

Limitations pertaining to specific methodology involved in each Chapter are discussed therein. This section focuses on more global limitations that are applicable to the general methodology and study design employed.

First, it must be acknowledged that our sample size was small which likely influenced the strength of some correlation analyses and introduced some Type-II error for between-group comparisons. Nonetheless, meaningful differences and associations were still identifiable therefore the sample size seems adequate to test our hypotheses and discover clinically relevant adaptations. This was the first study to investigate *in vivo* muscle and tendon properties as well as stair negotiation biomechanics in claudicants and has provided further functional insight into the effect of PAD-IC. However, additional investigations are needed on larger samples with a wider range of disease severity, including adequate numbers of unilateral and bilateral claudicants to elucidate the between-limb relationships, adaptations and compensations. The unilateral claudicants also require special attention in order to comprehensively differentiate whether asymptomatic-limb adaptations are solely due to systemic disease or associated reduced physical activity.

Second, the present study recruited claudicants with a narrowing of the superficial femoral artery but also included those with more extensive disease (such as occlusion of the external iliac artery). However, the vascular imaging determined that the primary stenosis was located in the superficial femoral artery for all participants. Furthermore, the calf was reported as the primary site of claudication pain in all participants which mimics that reported in general PAD-IC population (Norgren et al., 2007), however other sites of less severe pain were also reported. Whilst the calf is the most frequent site of pain, the thighs and buttocks are often implicated, depending on the location and extent of arterial narrowing. This may have consequences for movement patterns and potentially, adaptations in the structure and function of other muscle-tendon units. Future investigations of movement patterns and muscle-tendon adaptations in those with PAD-IC should endeavour to elucidate the impact of multiple stenoses and claudication pain sites by categorising claudicants into appropriate sub-groups.

Third, the present study focused on the gastrocnemii muscle *in vivo* due to its functional importance in such tasks as level walking and stair negotiation. We have suggested that claudicants utilise the soleus muscle more than the gastrocnemii towards plantarflexor contractions as an additional means to reduce the metabolic cost of muscle action. This reasoning assumes that the proportions of fibre-types within these muscles has not been altered and that the gastrocnemii possess primarily type-II fibres and the soleus muscle type-I fibres. Previous literature has revealed contradictory reports of fibre-type shifting in the calf (, Regensteiner et al., 1993, Steinacker et al., 2000, McGuigan et al., 2001b, Askew et al., 2005, Gasparini et al., 2012) with this avenue of assessment being out of the scope of the current programme

of research. Furthermore, the relative size of the gastrocnemii muscles and the soleus remain constant with ageing (Morse et al., 2005a). However, the size of the soleus muscle, in relation to the size of the gastrocnemii in claudicants, is yet to be quantified and is required to fully understand the impact of PAD-IC on the triceps surae group. Future investigation should aim to combine these assessments, both functional and histochemical, in order to provide a comprehensive understanding of these adaptations.

Fourth, the present study did not assess the strength of the hip or knee musculature and we have made inferences regarding the lack of compensatory strategies due to inadequate strength in the proximal muscles. It must be acknowledged that, whilst this may be a valid suggestion based on the previously reported reductions in proximal strength (McDermott et al., 2004b, McDermott et al., 2008b, Camara et al., 2012), this should be confirmed. For these suggestions to be more conclusive, a similar study to that performed by Reeves et al. (2008a) and Reeves et al. (2009b) that quantifies joint moments during functional tasks to maximal strength would be required to establish reasons why compensatory strategies are not being adopted. Furthermore, we also only investigated stair negotiation in a pain-free state. Previous literature demonstrates level gait biomechanics worsens in the presence of claudication pain (Scott-Pandorf et al., 2007, Koutakis et al., 2010a); therefore, it would be reasonable to assume that stair biomechanics may also deteriorate. Of particular interest would be if the presence of claudication pain elicits a re-distribution of the task demands between the joints during stair negotiation. Claudication pain in the calf will likely place an increased demand on the more proximal joints as a means to avoid painful muscle work of the calf. Fully understanding these relationships in both pain-free and pained states are

essential to understand the safety of stair climbing for this group and to develop informed targeted interventions.

Finally, this study has quantified stair biomechanics in claudicants for the first time and has discovered functionally relevant deviations that may affect the ability to safely negotiate stairs. However, we have made assumptions regarding stability and centre of mass control during stair negotiation and indicates that more detailed biomechanical analysis is needed. A full-body model would be necessary to accurately determine the centre of mass location and would provide greater insight of the potential compensatory strategies adopted, notably in the unilateral claudicants. The present study also excluded trials in which the handrail was being used due to the known alterations in gait biomechanics (Reeves et al., 2008b); that was not the focus of our investigations. This avenue should be explored further with instrumented handrails to accurately quantify how the task demand can be re-distributed across the upper and lower-body.

### 8.5 Clinical recommendations

This thesis has identified important changes in the structure and quality of the gastrocnemii muscles and the properties and function of the Achilles tendon, that appear to influence whole body function during demanding and risky physical activities; such as stair negotiation. The following are evidence-based directions for future investigations to optimise exercise interventions:

1) The alterations in Achilles tendon properties and gastrocnemii muscle architecture, and the relationships these parameters have with walking endurance indicate **eccentric exercise interventions** focused the plantarflexors would be beneficial for functional ability.
2) Our findings regarding measures of gastrocnemii muscle quality and joint kinetics during stair negotiation provide a clear indication that the ability to generate plantarflexor strength is not necessarily impaired, but the ability to generate this strength during high speed movements is adversely affected by PAD-IC. This suggests **high-velocity exercise interventions** of the plantarflexors would address this limitation
3) It appears that knee extensor weakness may prevent adequate compensatory strategies from being adopted to prevent increased demand on the limited plantarflexors. This implies exercise interventions also need to target **knee extensor strength**, not only due to the association with mortality, but also because of their role during functional tasks.

## 8.6 Conclusions

This thesis has explored a novel avenue of research within the field of peripheral arterial disease and was the first of its kind to investigate the functional properties of the plantarflexors and stair biomechanics in claudicants. The impact of PAD-IC on walking endurance and functional ability are widely reported, however the biomechanical mechanisms behind such declines were not investigated. The lack of this knowledge partly explains the surprising ineffectiveness of current progressive resistance training interventions reported in the literature. The findings of this thesis

provide new, clinically relevant insights into the musculoskeletal adaptations associated with the disease, how they impact on functional ability and how claudicants negotiate the challenging task of stair climbing with these adaptations. This research has provided clear evidenced-based recommendations for targeted exercise interventions that will likely be of great functional benefit to this population.

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**Appendix (A1)**

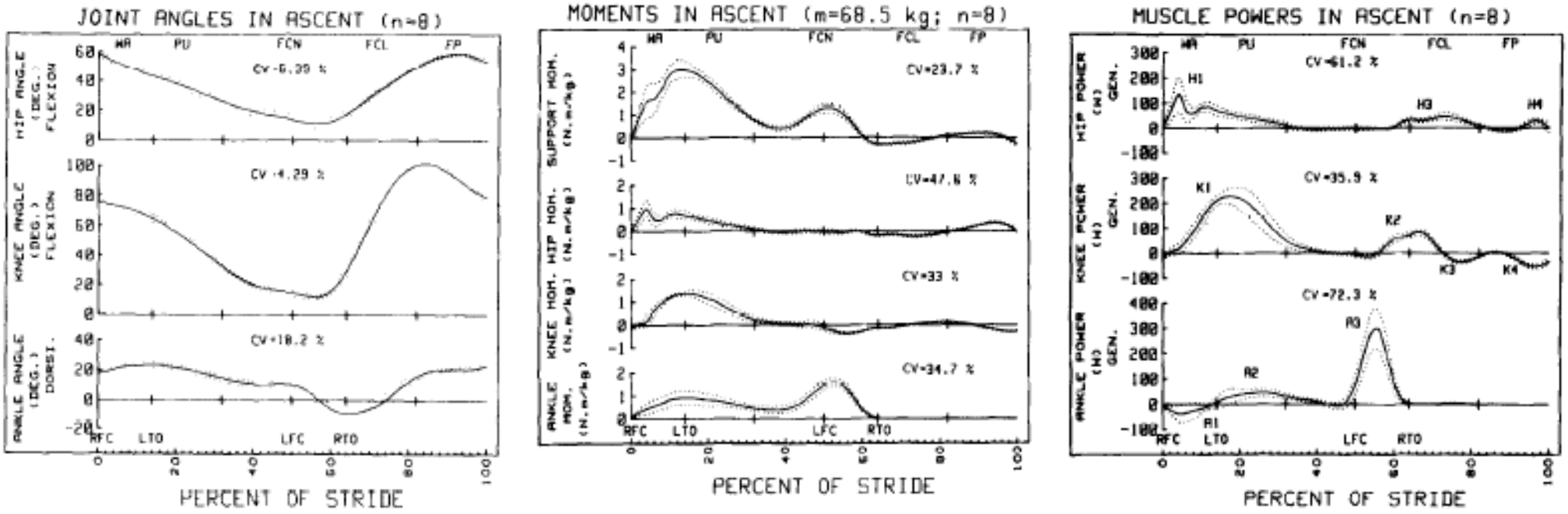


**Figure 1**. Example joint angle, moment and power curves for stair ascent taken from McFayden & Winter (1988) for the hip (top), knee (middle) and bottom (ankle). R/LFC – Right/Left foot contact, R/LTO – Right/Left toe-off, WA – weight acceptance, PU – pull up, FCN – forward continuance, FCL – foot clearance, FP – foot placement.

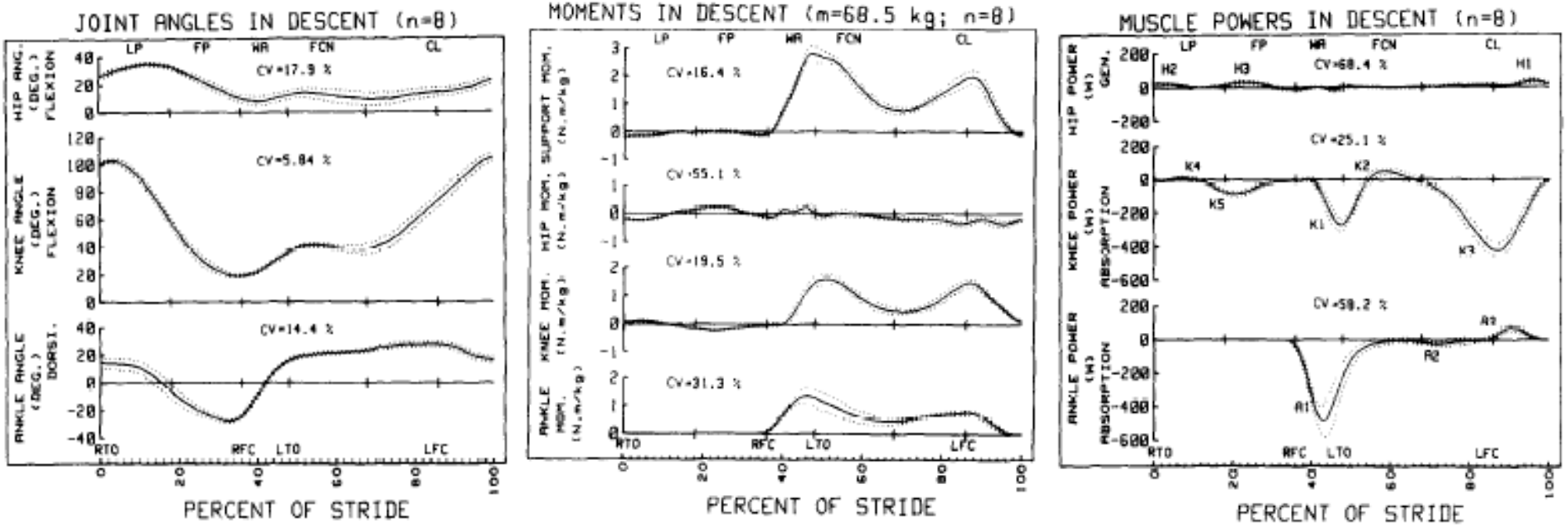


**Figure 2**. Example joint angle, moment and power curves for stair descent taken from McFayden & Winter (1988) for the hip (top), knee (middle) and bottom (ankle). Note – percent of stride is determined from toe-off to the following toe-off (i.e. swing phase followed by stance phase). R/LFC – Right/Left foot contact, R/LTO – Right/Left toe-off, LP – leg pull-through, FP – foot placement, WA – weight acceptance, FCN – forward continuance, CL – controlled lowering.

## Appendix (A2)

**Table 1**. Individual participant characteristics. Dom – Dominant limb, Non-Dom – Non-dominant limb. Asymp – Asymptomatic limb. Symp – Symptomatic limb

| Participant | Group | Right Leg | Left Leg | Sex | Age (years) | Height (m) | Mass (kg) | BMI |
|---|---|---|---|---|---|---|---|---|
| 1 | Control | Non-Dom | Dom | F | 59 | 1.58 | 77.7 | 31.12 |
| 2 | Control | Dom | Non-Dom | F | 61 | 1.59 | 73.1 | 28.91 |
| 3 | Control | Dom | Non-Dom | M | 65 | 1.73 | 68.2 | 22.79 |
| 4 | Control | Dom | Non-Dom | F | 64 | 1.76 | 69.7 | 22.50 |
| 5 | Control | Dom | Non-Dom | F | 55 | 1.61 | 66.9 | 25.81 |
| 6 | Control | Non-Dom | Dom | F | 58 | 1.58 | 73.1 | 29.28 |
| 7 | Control | Dom | Non-Dom | M | 62 | 1.76 | 96.2 | 31.06 |
| 8 | Control | Dom | Non-Dom | F | 61 | 1.54 | 51.9 | 21.88 |
| 9 | Control | Dom | Non-Dom | M | 67 | 1.69 | 73.3 | 25.66 |
| 10 | Control | Dom | Non-Dom | M | 64 | 1.80 | 72.6 | 22.41 |
| 11 | Unilateral | Asymp | Symp | F | 69 | 1.55 | 64.4 | 26.81 |
| 12 | Unilateral | Symp | Asymp | M | 55 | 1.80 | 119.5 | 36.88 |
| 13 | Unilateral | Symp | Asymp | M | 68 | 1.77 | 71.0 | 22.66 |
| 14 | Unilateral | Symp | Asymp | F | 59 | 1.63 | 72.1 | 27.14 |
| 15 | Unilateral | Asymp | Symp | M | 63 | 1.73 | 89.9 | 30.04 |
| 16 | Unilateral | Symp | Asymp | M | 73 | 1.76 | 97.7 | 31.54 |
| 17 | Unilateral | Asymp | Symp | F | 76 | 1.58 | 61.3 | 24.56 |
| 18 | Bilateral | Better | Worse | M | 69 | 1.73 | 72.9 | 24.36 |
| 19 | Bilateral | Worse | Better | M | 60 | 1.76 | 53.7 | 17.34 |
| 20 | Bilateral | Better | Worse | M | 55 | 1.74 | 93.7 | 30.62 |
| 21 | Bilateral | Worse | Better | M | 67 | 1.74 | 86.6 | 28.60 |
| 22 | Bilateral | Better | Worse | M | 66 | 1.70 | 94.1 | 32.56 |
| 23 | Bilateral | Worse | Better | M | 55 | 1.77 | 95.3 | 30.42 |

**Appendix (A3)**

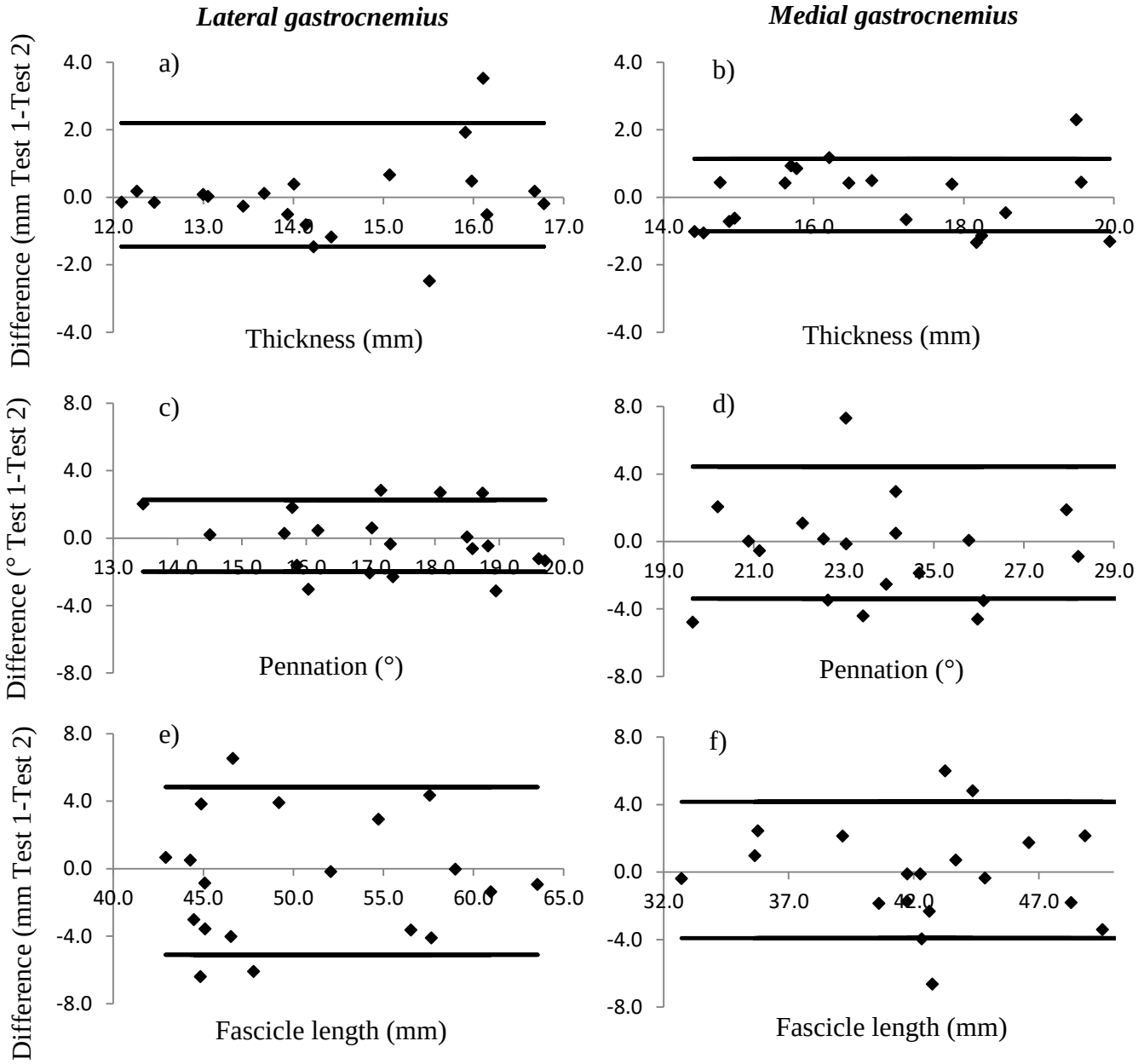


**Figure 1.** Ultrasound reliability between two testing sessions for muscle thickness (a and b), pennation angle (c and d) and fascicle length (e and f) for lateral (a, c and e) and medial (b, d and f) gastrocnemius. Data taken from 20 healthy individuals with solid black line representing limits of agreement.

## Appendix (A4)

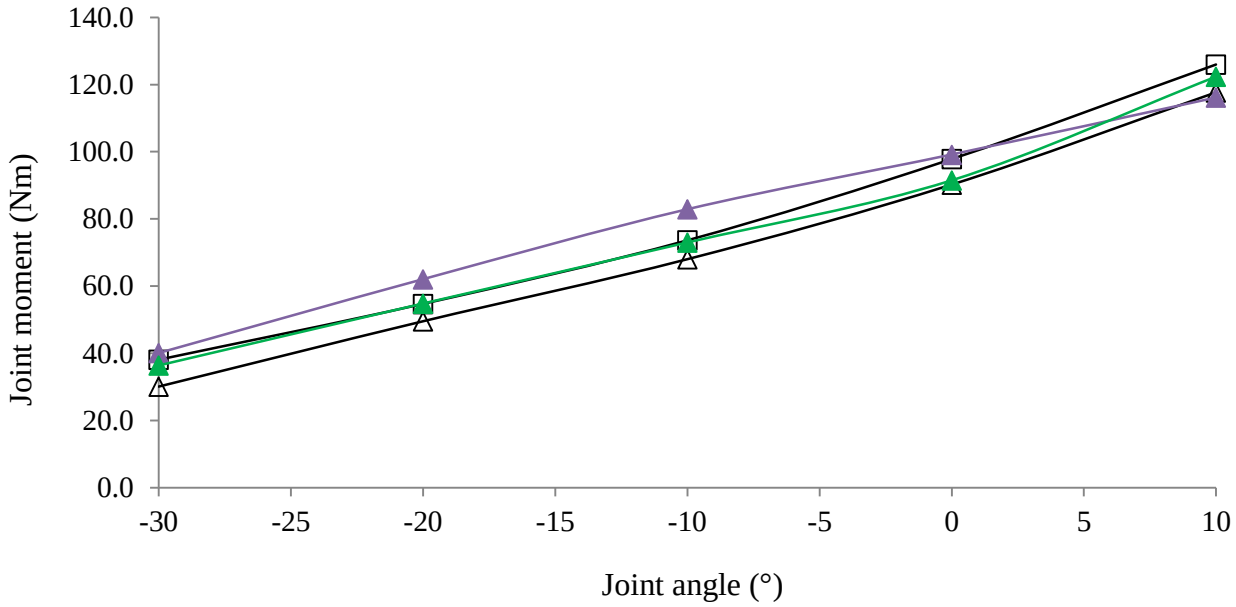


**Figure 1.** Plantarflexor moment-angle relationship from maximal plantarflexion (-ve) to maximal dorsiflexion (+ve) for the low ABPI group (Δ), high ABPI group (Δ), asymptomatic-limb group (Δ) and healthy controls (□). No significant between-group differences were found at any joint angle

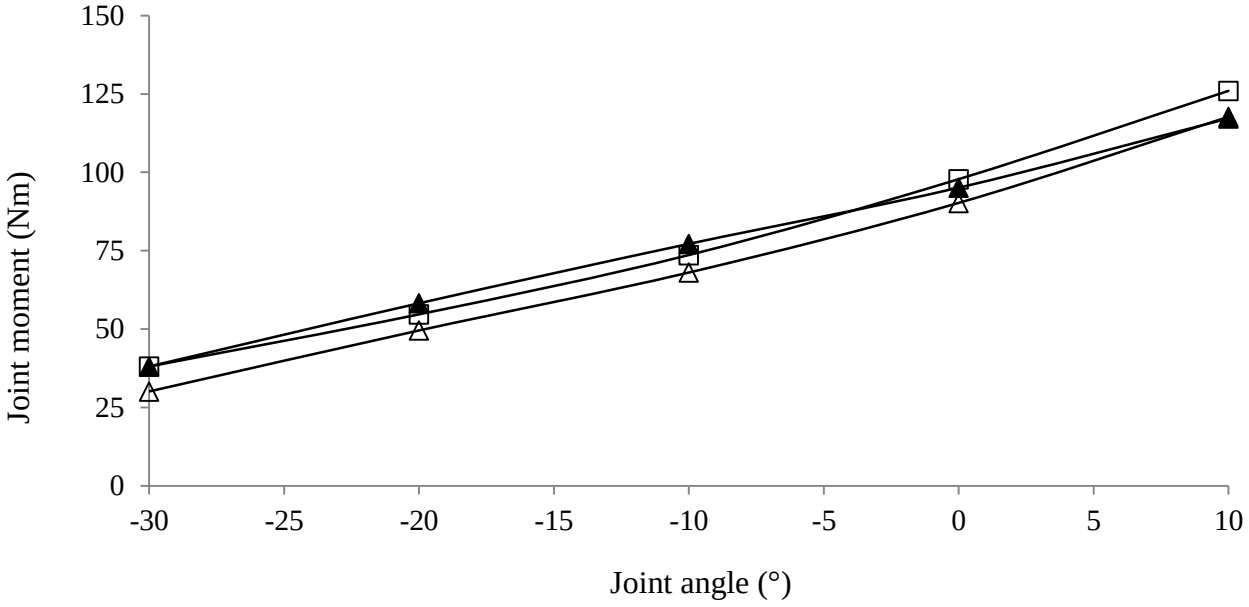


**Figure 2.** Plantarflexor moment-angle relationship from maximal plantarflexion (-ve) to maximal dorsiflexion (+ve) for the claudicating-limb (Δ), asymptomatic-limb (Δ) and healthy control groups (□). No significant between-group differences were found at any joint angle

## Appendix A5

**Table 2**. Group mean (SD) normalised gastrocnemii muscle size.

| | **Claudicating-limb** | **Asymptomatic-limb** | **Control** |
|---|---|---|---|
| PCSA/tibia length$^2$ | 0.034 (0.006) | 0.036 (0.007) | 0.038 (0.006) |
| Volume/tibia length$^3$ | 0.004 (0.001) | 0.004 (0.007) | 0.004 (0.008) |

**Table 3**. Pearson partial correlation, controlled for age and disease severity, between resting fascicle: tendon length ratios and measured fascicle lengths during MVC. Light shaded values indicate trends towards significance (P=≤.10) and dark shaded values indicate significant associations (P=≤.05)

| | | **GL fascicle length at MVC** | **GM fascicle length at MVC** | **Soleus contribution** | **Static muscle quality** |
|---|---|---|---|---|---|
| **GL FL:TL** | Correlation | .524 | .817 | .626 | -.650 |
| | Significance | .066 | .001 | .022 | .016 |
| **GM FL:TL** | Correlation | .082 | .817 | .500 | -.647 |
| | Significance | .790 | .000 | .082 | .017 |

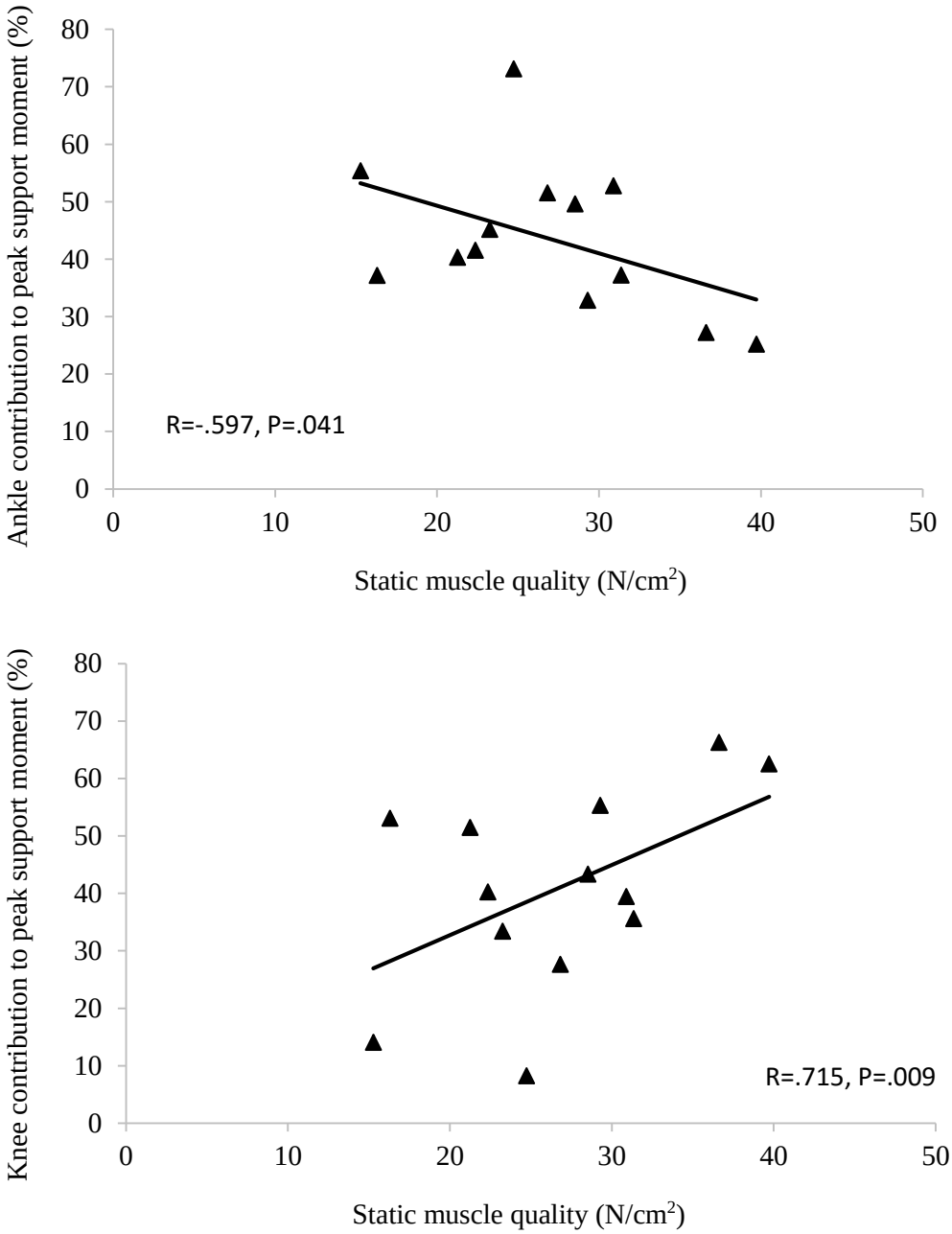


**Figure 1.** Pearson partial correlations (controlled for age, disease severity and walking speed) between static muscle quality and ankle contribution to peak support moment (top), and knee contribution to peak support moment (bottom) for the claudicating-limbs only