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

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Abstract

Objectives: Peripheral arterial disease and intermittent claudication (PAD-IC) negatively affects physical activity and function. There is evidence for plantarflexor muscle dysfunction and weakness, however, the extent to which this dysfunction can be attributed to reduced muscle size and/or quality is not yet known. This study investigated whether *in vivo* plantarflexor muscle quality during static and dynamic contractions are altered by PAD-IC and whether such changes are associated with impaired walking endurance (according to initial and absolute claudication distances). **Methods:** A total of 22 participants were recruited, consisting of 10 healthy controls and 12 claudicants with occlusion of the superficial femoral artery (seven unilateral and five bilateral). Muscle quality of the combined gastrocnemius muscles during static contractions was calculated by normalising the estimated maximal potential muscle force to the physiological cross-sectional area of both lateral and medial gastrocnemius. Muscle quality during dynamic contractions of the combined plantarflexor muscles was calculated as the ratio of peak voluntary concentric plantarflexor power and the summed volume of lateral and medial gastrocnemius. **Results:** Dynamic muscle quality was 24% lower in both the claudicating-limb and asymptomatic-limb groups compared to controls (P=.017 and P=.023). The differences were most apparent at the highest contraction velocity (180°/s). Dynamic muscle quality was associated with reduced walking endurance (R=.689, P=.006 and R=.550, P=.042 for initial and absolute claudication distance, respectively). The claudicating-limb group demonstrated a trend towards reduced static muscle quality compared to controls (22%, P=.084). The relative contribution of the soleus muscle to plantarflexion maximum voluntary contraction was significantly higher in both claudicating-limb and asymptomatic-limb groups compared to controls (P=.012 and P=.018). **Conclusions**: The muscle strength of the plantarflexors in those with PAD-IC appears to be impaired at high contraction velocities. This may be

explained by some reduction in gastrocnemii muscle quality and a greater reliance on the prominently type I fibred soleus muscle. The reduced dynamic capability of the plantarflexor muscles was associated with disease severity and walking ability, therefore efforts to improve plantarflexor power through dynamic exercise intervention are vital to maintain functional performance.

Introduction

Peripheral arterial disease and intermittent claudication (PAD-IC) refers to a chronic lower-limb atherosclerotic disease that primarily affects the older population[1]. The disease negatively impacts on functional ability[2], physical activity levels[3] and quality of life[4]. The most frequent site of claudication pain is in the plantarflexor (triceps surae) muscles[5], where there are clear signs of dysfunction, such as reduced ankle power generation during gait[6,7]. However, the few previous studies directly investigating plantarflexor function are inconsistent about whether strength is diminished in claudicants compared to healthy controls[8-10]. Plantarflexor strength is a strong predictor of mortality in men with PAD-IC[11,12], 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 [13]. 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 [13]. In PAD-IC voluntary joint moments have been measured previously[8-10] 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[14] and increase in response to resistance training[15]. It is reasonable to assume muscle quality would be altered in claudicants given that the disease primarily affects the elderly[1] and is associated with reduced physical activity[3]. Additional factors associated with PAD-IC that may further affect muscle quality include intra-muscular fat infiltration[16], 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)[17-19] and conversely to more type I fibres (slow-twitch)[20,21]. As specific tension differs between fibre types[22] 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[5]. This may contribute to the inconsistent effects reported following progressive resistance training in claudicants[23].

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 plantarflexion moments and concentric plantarflexion 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 plantarflexion moment, concentric plantarflexion power, and static and dynamic muscle quality.

Methods

Participants

Ethical approval was granted by the National Health Service Research Ethics Committee (REC reference: 11/YH/0335). A total of 22 participants were recruited consisting of 12 claudicants (seven unilateral, five bilateral) and ten healthy controls (Table I). Claudicants were recruited via consultant referral from a local outpatient vascular clinic. Male and female participants aged between 55-80 years who were diagnosed with Rutherford Grade 1 Chronic Limb Ischemia[24] with an arterial narrowing of the superficial femoral artery were considered for inclusion. 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 controls were recruited from the local community via email and word of mouth. Individuals deemed to have severe or acute cardiovascular, musculoskeletal or pulmonary illness were excluded along with those with a previous lower-limb joint replacement. Any individuals with a history of neurological disorders, stroke, myocardial

infarction or life-limiting diseases, such as cancer, were also excluded. All participants gave written informed consent prior to testing

Disease severity

Disease severity was determined using the ankle brachial pressure index/ratio (ABPI). 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 at 2.5km/h at 10% incline)[5]. Those unable to complete 5 minutes were able to stop at the point of maximum claudication pain. 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[5]. The post-exercise ABPI was subsequently used to categorise the limbs of the participants as well as classify disease severity. Any limb with an ABPI <0.9 was classified as claudicating and represents the 'claudicating-limb' group. The asymptomatic limb of the unilateral claudicants was identified (ABPI ≥0.9) and represents the 'asymptomatic-limb' group. Control participants also undertook the exercise protocol to determine ABPI values, confirming the absence of PAD-IC.

Walking endurance

The 6-minute walk test was modified to be performed on level ground and combined with a pain rating based on the ACSM claudication pain scale[25]. This method is a reliable

alternative to treadmill walk tests[26] and allows participants to walk for longer than 6-minutes

if they are able. Patients walked continuously along a 10m walkway at a self-selected pace

and informed the investigator of the level of pain and position on the pain scale every 20m.

Initial claudication distance was classed as level 1 on the pain scale and signified the onset of

pain. Absolute claudication distance was classed as level 4 on the pain scale, represented

maximal pain and signified the end of the test.

Experimental protocol

The static muscle quality (specific tension) of the combined gastrocnemii muscles was

defined as maximal potential Achilles tendon force (equation 1) normalised to the reduced

gastrocnemii physiological cross-sectional area (equation 2)[2];

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

2) Reduced gastrocnemii PCSA $= \left(\dfrac{GL\ V}{GL\ FL_{MVC}}\right)*cos \cdot GL\theta_{MVC} + \left(\dfrac{GM\ V}{GM\ FL_{MVC}}\right)*cos \cdot GM\theta_{MVC}$

where *PCSA* is physiological cross-sectional area, *GL* is lateral gastrocnemius, *GM* is medial

gastrocnemius, *V* is muscle volume, *FL* is fascicle length and *θ* is pennation, both quantified

during maximum voluntary contraction (MVC).

The methods used to determine each component of these equations are detailed below.

Measurements and calculations for maximal Achilles tendon force

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 plantarflexion to maximum dorsiflexion. Verbal encouragement was given throughout all trials. Three maximal isometric plantarflexion 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[28]. All further trials to establish voluntary and antagonist activation, soleus contribution, fascicle length and pennation were performed in this joint position.

Antagonist co-activation

The contribution of antagonist muscle activity to the measured joint moment was estimated from the surface electromyography (EMG) (Telemyo 2400T, Noraxon, Arizona, USA) of the tibialis anterior, to represent the ankle dorsiflexors. Electrode placement and skin preparation were according to standardised guidelines[29]. The EMG of the tibialis anterior was recorded at 2000Hz synchronously with joint moments during the isometric plantarflexion contractions (working as an antagonist) and then combined with the EMG-moment relationship during dorsiflexion contractions (working as an agonist) to estimate the antagonist co-activation moment[27].

Soleus contribution

The contribution of soleus to plantarflexion moment was quantified with additional plantarflexion contractions with the knee flexed where gastrocnemii muscle does not contribute to the measured joint moment[28]. Activation changes between the two positions were corrected using the EMG-moment relationship in two joint configurations using equation 3;

3) Soleus moment Knee 0°= $\dfrac{\textit{Soleus moment Knee 90°* Soleus EMG Knee 0°}}{\textit{Soleus EMG Knee 90°}}$

Activation capacity

The level of muscle activation achieved during voluntary contraction was calculated using the interpolated twitch technique[30]. 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. 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 torque. 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 4[31]:

4) Voluntary activation= $\left(1-\dfrac{\textit{Superimposed twitch}}{\textit{Resting twitch}}\right)x\ 100$

Measurement of moment arm length

Achilles tendon moment arm length was calculated using the tendon travel method[32] and using ultrasound imaging (50-mm probe length, MyLab50 x-vision, Esaote Biomedica, Genoa, Italy) to quantify linear myotendinous junction displacement.

Measures of muscle size at rest and architecture during MVC

Participants were asked to lie prone on a plinth with their ankle plantarflexed and supported on the bed with the musculature relaxed. To quantify lateral and medial gastrocnemius 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 which is a reliable and valid alternative to MRI imaging[15]. Lateral and medial gastrocnemius volume were combined for total gastrocnemii muscle volume.

Optimum fascicle length and pennation angle during MVC were measured from synchronised sagittal-plane ultrasound video-recordings of the muscle belly of lateral and medial gastrocnemius , 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)[27].

Measures of dynamic muscle quality

Isokinetic plantarflexion 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[33]. 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[34]. Dynamic muscle quality was defined as peak power normalised to gastrocnemii muscle volume. Adequate rest (>1 min) was provided between trials.

Statistical analysis

A linear relationship exists between advancing age and dynamic muscle quality[35] 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) and gastrocnemii physiological cross-sectional area, 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[36]. Since low ABPI values indicate high disease severity a positive relationship indicates a decrease in the respective parameter with worsening disease.

Results

No significant differences were found between groups in height (P=.230) or mass (P=.167) (Table I). 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[35] and there is no reason to believe gender differences influenced our measures of muscle quality[27]. 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 I. 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	Healthy 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)	0.99 (0.10)
ABPI post-exercise	0.55 (0.21)	0.90 (0.06)	1.00 (0.13)
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

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 II, and III). A trend was observed for smaller gastrocnemii physiological cross-sectional area with higher disease severity (P=.073) (Table II).

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

Table II. 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 III. 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

1   *Between group comparisons*

2   There were no differences between groups in isometric joint MVC, however the soleus

3   contribution to this joint moment was significantly greater in both the claudicating-limb and

4   asymptomatic-limb groups than in healthy controls (P=.008 and P=.012, respectively). The

5   claudicating-limb group demonstrated trends towards reduced static muscle quality compared

6   to healthy controls (P=.084) (Table IV).

7

8   At 120°/s the asymptomatic-limb group demonstrated trends towards reduced power (P=.071)

9   with similar trends observed at 180°/s in the claudicating-limb group compared to healthy

10   controls (P=.100). When normalised to gastrocnemii muscle volume, the asymptomatic-limb

11   group had significantly reduced power/volume at 120°/s (P=.036) compared to healthy

12   controls and both the asymptomatic-limb (P=.023) and claudicating-limb (P=.017) groups

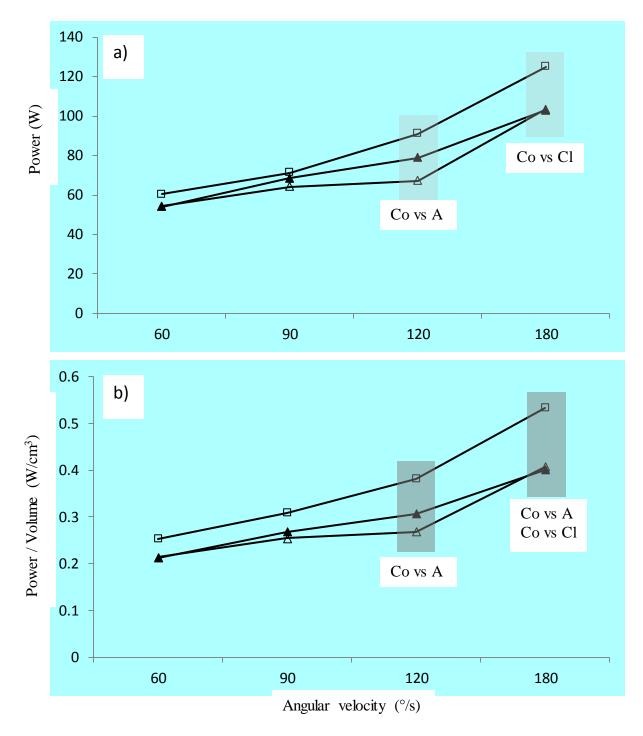13   had significantly reduced power/volume at 180°/s (dynamic muscle quality) (Figure 1).

14

15

Table IV. 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.

	Claudicating-limb	Asymptomatic-limb	Healthy 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)[Co]	62.1 (1.4)[Co]	55.6 (7.9)
Gastronemii 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			
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)[Co]	28.8 (8.3)	34.5 (10.4)

Cl = vs Claudicating-limb group, A = vs Asymptomatic-limb group Co = vs Healthy control group

1

Figure 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 = vs Claudicating-limb group, A = vs Asymptomatic-limb group Co = vs Healthy control group.

1 **Discussion**

2 The aim of the study was to investigate the effects of peripheral arterial disease and

3 intermittent claudication (PAD-IC) on the strength, power, size and *in vivo* whole muscle

4 quality of the plantarflexors. We found no effects of disease on external measures of

5 "strength" during static or low speed contractions, but the claudicants relied on the

6 predominantly type I-fibred soleus to develop overall strength more than healthy controls.

7 Significant strength differences between claudicants and controls were apparent during higher

8 speed ($\geq 120°$/s) contractions. These data support our hypotheses that the dynamic muscle

9 quality of claudicants was reduced compared to healthy controls, and this was associated with

10 poorer walking endurance. These novel findings suggest that impaired muscle quality and a

11 greater reliance on the soleus muscle contribute to reduced dynamic strength of claudicants at

12 high speeds, which in turn contributes to the impaired functional ability seen in this

13 population.

14

15 Previous studies investigating plantarflexor strength in individuals with PAD-IC are

16 inconsistent[8-10] and comparisons between studies are confounded by differing methods of

17 strength assessment. This study quantified plantarflexor strength across a range of contraction

18 speeds, and observed no between-group differences at low velocities. However, the power

19 generating capacity of the claudicants was 13-26% lower than controls at speeds of 120-

20 180°/s. Interestingly, this was the case for both claudicating-limb and asymptomatic-limb

21 groups. This indicates either the presence of systemic effects of ischemia in the

22 'asymptomatic'-limb or that deleterious adaptations were driven by the relative inactivity

23 caused by the symptomatic limb. Isometric plantarflexor strength has previously been

24 reported as a strong predictor of mortality in men with PAD-IC[11,12]; however the current

1   data suggest that dynamic contractions at higher velocities may be more sensitive to

2   functional deteriorations, which was not apparent in previous sub-group analyses[37]. Future

3   functional assessments and measures of plantarflexor strength should consider the use of

4   dynamic, concentric tests in order to detect strength losses early in diagnosis and to identify

5   those with greater strength impairments.

6

7   Whilst voluntary joint moments and powers are simple and time-efficient measures, they do

8   not provide information regarding the underlying mechanisms contributing to the externally

9   measured strength. Despite minimal between-group differences in isometric MVC, a

10   substantially lower (25%, but non-significant) tendon force was found in both claudicating-

11   limb and asymptomatic-limb groups compared to controls. Combined with similar

12   physiological cross-sectional areas, this led to a trend towards reduced static muscle quality

13   (21%) in the claudicating-limb group, and a non-significant reduction of 16% in the

14   asymptomatic-limb group, compared to controls. These effects were not mirrored in the

15   correlations with ABPI, suggesting other stimuli must exist, such a physical activity levels, to

16   drive these reductions in static gastrocnemii muscle quality of claudicants.

17

18   The reduced tendon force in the claudicating-limb group, despite similar joint moments

19   between groups, can be attributed to a greater (12%) contribution of the soleus to the overall

20   joint moment, compared to healthy controls. This increased reliance on the soleus during

21   plantarflexion contractions may be linked to the proposed shift in fibre type in claudicants[17-

22   21]. Therefore, the increased contribution from the slower, type I-dominant soleus muscle[38]

23   may act as a means to reduce the metabolic cost of the task. However, during dynamic

1   contractions, a greater contribution from soleus would have a detrimental effect on the ability

2   to generate power, particularly at high speeds, which is consistent with the present data.

3

4   When muscle power was normalised to volume (dynamic muscle quality) between-group

5   differences became larger and significant associations with walking endurance and disease

6   severity were apparent. This corroborates previous reports of reduced ankle plantarflexor

7   power per kg body mass in gait[6,7] and demonstrates the importance of plantarflexor power

8   for functional performance. The reductions in dynamic muscle quality were associated with

9   changes in walking performance that have previously been reported as clinically meaningful

10   (>50m)[39]. Long-term efforts to monitor the implications of this appear warranted, and

11   quantification of dynamic muscle quality may provide a useful outcome measure in these

12   efforts. Exercise prescription is a primary treatment option in PAD-IC to improve mobility

13   and to combat muscle weakness[5]. It appears that such training interventions should target

14   improvements in plantarflexor power by redressing the relative contribution from the soleus

15   and gastrocnemii muscles through dynamic exercise programmes (high-velocity resistance

16   training). Future work should endeavour to assess how these important musculoskeletal

17   parameters respond to (exercise-based) interventions and whether they lead to the predicted

18   improvements in walking capacity.

19

20   Correlation analysis revealed that variations in activation capacity amongst the claudicating-

21   limb group significantly affected walking endurance. This would increase the perceived effort

22   of walking, possibly leading to altered gait mechanics to redistribute joint kinetics, and

23   consequently alter movement efficiency and endurance. Activation level was not quantified

24   during the isokinetic trials because muscle stimulation during dynamic contractions is

1 technically very challenging, particularly for the plantarflexors where the muscle group

2 works almost exclusively on the ascending limb of the force-length relationship, so

3 stimulation at optimal muscle length is not possible. Future work should endeavour to

4 investigate the activation capacity of the plantarflexor muscles during dynamic contractions,

5 since it may be different to that in isometric conditions and could contribute to the specific

6 power deficits at high velocities. This would provide greater understanding of the

7 neuromuscular adaptations caused by PAD-IC and their influence on functional performance.

8

9 Some limitations to the present study must be acknowledged. It is recognised that the present

10 sample is small with a wide range of disease severity. Nonetheless we were able to detect

11 between-group differences and meaningful associations with walking endurance, as such we

12 consider this sample adequate to confirm the hypotheses. Static muscle quality should be

13 calculated with measures of truly optimal muscle force and length, i.e., plateau of the force-

14 length relationship. As is typical for the plantarflexors, this plateau was not observed[28] and

15 we do not know whether participants reached optimal fascicle length. However, previous

16 work has shown that small changes in joint position do not significantly affect estimates of

17 muscle quality[27]. By calculating the quality of the entire gastrocnemii muscle group, errors

18 associated with distributing tendon force between the lateral and medial gastrocnemii

19 muscles were avoided. However, it was necessary to assume that once soleus contribution

20 was removed, the Achilles' tendon force reflected only that produced by the gastrocnemii

21 muscle. Dynamic muscle quality was calculated as plantarflexor joint power normalised to

22 gastrocnemii muscle volume only, assuming the relative size of these muscles remains

23 constant, as is the case in ageing[34]. Claudicants relied on the soleus more than healthy

24 controls did, meaning any error associated with this assumption will most likely

25 underestimate the true between-group difference in dynamic muscle quality. Additionally,

1   moment arm length was determined during passive joint rotations at rest[32] and it is known to

2   change during contraction[40]. However, there is no reason to assume the change from rest to

3   contraction would be different between controls and claudicants; consequently, we consider

4   the comparisons presented in this study to remain valid.

5

6   **Conclusions**

7   The present study quantified the intrinsic quality of *in vivo* claudicant muscle for the first

8   time. Dynamic plantarflexion strength, particularly at the highest velocity, was lower in

9   claudicants compared to healthy controls and was significantly associated with disease

10   severity and impaired walking endurance. When dynamic strength was normalised to muscle

11   size (to calculate muscle quality) between group differences were larger and relationships

12   with walking endurance were stronger. The impaired function at high velocities may be

13   related to a reduction in maximal (static) muscle quality and an increased reliance on the

14   predominantly type-I fibred soleus muscle. Efforts to monitor strength at high velocities

15   appear the most appropriate way to detect functional losses early, and improving the dynamic

16   capabilities of the plantarflexors is likely to help maintain walking endurance in claudicants.

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