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

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 IV).

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 1).

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

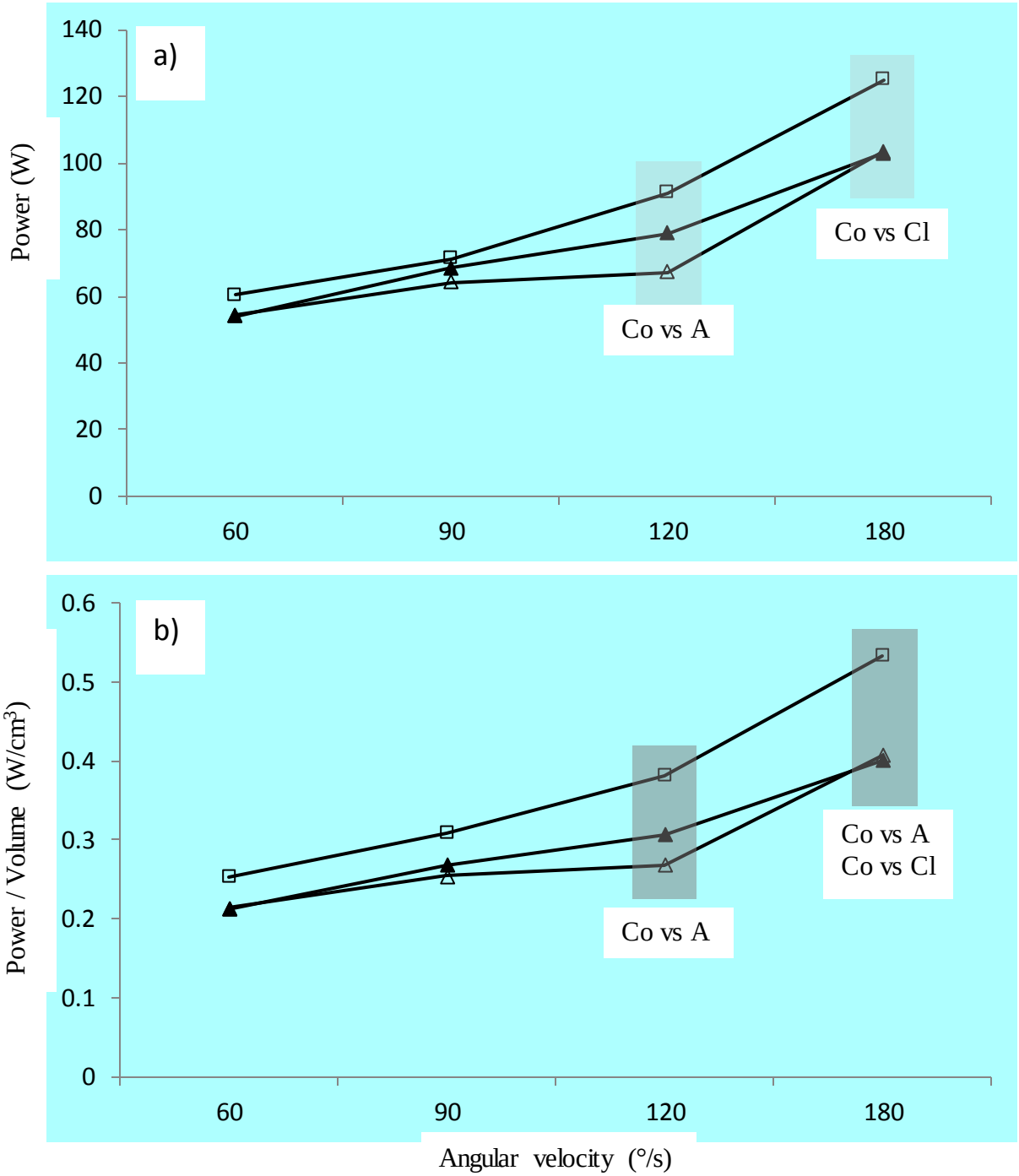

Figure 1. Group mean power-velocity (a) and normalised power-velocity (b) profiles for claudicating-limb (▲), asymptomatic-limb (Δ) and healthy controls (□). Dark shaded values represent those reaching significance (P≤.05) and light shaded values represent those demonstrating trends towards significance (P<.10). Cl = vs Claudicating-limb group, A = vs Asymptomatic-limb group Co = vs Healthy control group.

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[8-10] 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. 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. Isometric plantarflexor strength has previously been reported as a strong predictor of mortality in men with PAD-IC[11,12]; 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[37]. Future functional assessments and measures of plantarflexor strength should consider the use of dynamic, concentric tests in order to detect strength losses early in diagnosis 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 plantarflexion contractions may be linked to the proposed shift in fibre type in claudicants[17-21]. Therefore, the increased contribution from the slower, type I-dominant soleus muscle[38] 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[6,7] 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 (>50m)[39]. 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[5]. 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 because 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. It is recognised that the present sample is small with a wide range of disease severity. Nonetheless we were able to detect between-group differences and meaningful associations with walking endurance, as such we consider this sample adequate to confirm the hypotheses. 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[28] 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[27]. By calculating the quality of the entire gastrocnemii muscle group, errors associated with distributing tendon force between the lateral and medial gastrocnemii muscles 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[34]. 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[32] and it is known to change during contraction[40]. 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.

Conclusions

The present study quantified the intrinsic quality of *in vivo* claudicant muscle for the first time. Dynamic plantarflexion strength, 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 dynamic strength 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 strength 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.

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