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ORIGINAL ARTICLE

Relationship between thigh muscle mass and augmented pressure from wave reflections in healthy adults

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Abstract Skeletal muscle may be viewed as an endocrine organ that releases numerous factors with the potential to influence vascular tone. Previous cross-sectional studies have shown an inverse relationship between muscle mass and arterial stiffness. We examined the relationship between muscle mass, arterial pressure in the aorta and brachial artery, and pressure from wave reflections [characterized as heart rate corrected augmentation pressure (AP)] and augmentation index (AIx). Twenty-seven (13 male, 14 female) subjects who were non-smokers and had no known cardiovascular or metabolic diseases visited the laboratory for two sessions of testing. Upon arriving for the first session, mid-thigh muscle (mCSA) and fat (fCSA) cross-sectional area were assessed using peripheral Quantitative Computed Tomography. Following this, concentric one-repetition maximum (1-RM) testing was completed to assess knee extensor strength. The second visit consisted of taking brachial and aortic blood pressure measurements. A significant positive relationship was found between mCSA and brachial systolic blood pressure ($r = 0.47$, $p = 0.02$), but not between mCSA and aortic systolic blood pressure ($r = 0.35$, $p = 0.09$). There was an inverse association between mCSA and AP75 (-0.49, $p = 0.01$) and AIx75 (-0.49, $p = 0.01$). In conclusion, muscle mass is associated with brachial systolic blood pressure and inversely associated with pressure from wave reflections. Our findings suggest a link between global musculo-skeletal integrity and cardiovascular hemodynamics in young healthy adults.

Keywords Resistance training · Cardiovascular · Blood pressure · Muscle cross-sectional area · Fat mass · Strength

Introduction

Skeletal muscle mass may be considered a global marker of musculo-skeletal health. Skeletal muscle functions as the largest disposal site of ingested glucose (Holloszy 2005), plays an important role in lipid oxidation (Helge et al. 2006; Sahlin et al. 2007), and is a significant contributor to resting energy expenditure (Bosy-Westphal et al. 2004), highlighting the importance of maintaining skeletal muscle quantity and quality for overall health. Further, greater lean soft tissue mass attenuates age-related increases in arterial stiffness (Sanada et al. 2009, 2010; Snijder et al. 2004; Ochi et al. 2010). Increased arterial stiffness results in an earlier return of reflected blood pressure (BP) waves back to the aorta during systole which can augment aortic systolic and pulse pressures. This reflected pressure can either be described in absolute terms of augmented pressure (AP) or relative to aortic pulse pressure as the augmentation index (AIx). AIx is a strong marker for coronary artery disease (Weber et al. 2004) and associated with cardiovascular risk (Nurnberger et al. 2002). Whether AIx is associated with muscle mass remains unexplored.

There can be large differences in BP between the aorta and brachial artery, especially with increased arterial

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stiffness causing augmentation of aortic pressure. In many studies, researchers may rely on brachial BP to gauge overall hemodynamic burden given the well-noted association between brachial BP and cardiovascular morbidity and mortality (Collins and MacMahon 1994). However, aortic BP may be a stronger predictor of CV risk (Roman et al. 2007). Brachial BP serves only as a surrogate marker for aortic pressure and previous research suggests that in healthy, younger subjects, conventional peripheral BP estimates may be erroneous as estimates of aortic BP (Siebenhofer et al. 1999).

The purpose of this study was twofold: (1) to determine the relationships between peripheral and aortic BP with mid-thigh muscle cross-sectional area (mCSA); (2) to examine the relationship between the magnitude of aortic pressure augmentation (AP and AIx) and mCSA.

Methods

Subjects

Twenty-seven (13 male, 14 female) subjects who were non-smokers and had no known cardiovascular or metabolic diseases visited the laboratory for two sessions of testing. All subjects were tested at least 2 h post-prandial and were instructed to avoid caffeine, medications, and exercise on the day of their visit. The data for the current manuscript are secondary analyses of a larger investigation that has in part, been previously published (Loenneke et al. 2011). The study received approval from the university's institutional review board, and each subject gave written informed consent before participation.

Study design

Upon arriving at the laboratory for the first session, subjects' height and body mass were measured using a standard stadiometer and an electronic scale (Tanita BWB 800-AS, Tokyo, Japan). Mid-thigh mCSA and fat cross-sectional area (fCSA) of the right thigh were assessed using peripheral quantitative computed tomography (pQCT) as described previously (Loenneke et al. 2011). All pQCT scans were made by a trained pQCT technician whose coefficient of variation for repeated measurements was 1.59 % for mCSA and 1.52 % for fCSA. Our pQCT scanner has been previously shown to be a valid and reliable measurement when compared to magnetic resonance imaging with a correlation between measurements of $r = 0.991$ (Cramer et al. 2007). Following this measurement, concentric one-repetition maximum (1-RM) testing was completed to assess knee extensor strength (Cybex Strength Systems, Medway, MA, USA) using standard 1-RM procedures (Baechle and Earle 2000). The second visit consisted of taking brachial and aortic blood pressure measurements on each participant in the seated position following 5 min of rest. Brachial systolic (bSBP) and diastolic (bDBP) blood pressures were measured using an automatic BP measuring device with an appropriately sized cuff (Omron Healthcare Inc, Vernon Hills, IL). Two BP measurements were taken and, if bSBP measurements were within 5 mmHg, the average of the measurements was used for analysis. If the first two bSBP measurements were not within 5 mmHg, the BP measurement was repeated and the average of the two closest readings used for subsequent analysis. Using applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia) and a high-fidelity strain-gauge transducer (Miller Instruments, Houston, TX, USA), radial artery pulse waveforms were obtained and used for pulse wave analysis (PWA). Aortic BP waveforms were derived from radial BP waveforms using a generalized validated transfer function (SphygmoCor, AtCor Medical, Sydney, Australia). From these waveforms, aortic systolic (aSBP), diastolic (aDBP), and mean (MAP) BPs were obtained. The augmentation index (AIx) was defined as AP divided by aortic PP and expressed as a percentage (Nichols and Singh 2002). Heart rate (HR) was determined from the time between waveforms. AIx and AP values were expressed relative to a HR of 75 bpm (AIx75 and AP75; SphymoCor, AtCor Medical, Sydney, Australia). Pulse pressure amplification (PP amp) was calculated as the difference between brachial and aortic pulse pressures. Systolic pressure amplification (SP amp) was calculated as the difference between brachial and aortic systolic pressures. All measurements were taken by the same investigator who has found no significant day to day differences in AIx75 (ICC = 0.7) or AP75 (ICC = 0.6), $p = 0.572$ and $p = 0.821$, respectively.

Statistical analyses

Data were analyzed using two-tailed Pearson partial coefficient correlations with an alpha level of 0.05. Since sex differences in wave reflection are apparent regardless of body height (Gatzka et al. 2001), partial correlations were used controlling for sex and height. Variables include bSBP, bDBP, aSBP, aDBP, MAP, PP amp, SP amp, mCSA, fCSA, AP75, AIx75, and absolute strength (1-RM). Correlations were listed as strong (±0.50 to 1.0), moderate (±0.30 to 0.49), or weak (±0.10 to 0.29). Analysis of covariance (ANCOVA) was performed to examine the main effects of sex, thigh muscle CSA and the interaction effect of sex × mCSA on AP75 and Aix75. Data are presented as mean ± SD.

Table 1 Descriptive statistics

	Mean	SD
Age (years)	23	3
Height (m)	1.74	0.10
Body mass (kg)	73.8	12.9
BMI (kg/m^2)	24.4	3.0
Knee extensor 1-RM (kg)	97.7	31.0
Brachial SBP (mmHg)	118	10
Brachial DBP (mmHg)	78	8
Aortic SBP (mmHg)	104	10
Aortic DBP (mmHg)	79	9
Mean arterial pressure (mmHg)	91	9
Pulse pressure amplification (mmHg)	15	4
Systolic pressure amplification (mmHg)	14	4
AP75 (mmHg)	0	3
HR (bpm)	65	14
AIx75 (%)	2	10
Thigh circumference (cm)	58.6	4.0
Fat CSA (cm^2)	661.1	265.3
Muscle CSA (cm^2)	1,604.4	357.0
Total CSA (cm^2)	2,320.8	319.3

Augmentation index (AIx75) and Augmentation pressure (AP75) expressed relative to a heart rate (HR) of 75

Results

Participant characteristics are presented in Table 1. Table 2 presents the correlation matrix between hemodynamic and muscular variables. All values shown were adjusted for height and sex. AIx75 and AP75 were inversely correlated with mCSA, but not with mid-thigh fCSA or knee extensor 1-RM. mCSA was also directly related to bSBP, but not aSBP. The relationship between AP and mCSA is presented in Fig. 1 for men and Fig. 2 for women. Unadjusted correlations between mCSA and PP amp ($r = 0.55$; $p = 0.002$) and SP amp ($r = 0.57$; $p = 0.002$) were statistically significant but when adjusting for height and sex they were no longer significant. ANCOVA revealed a significant main effect of thigh muscle CSA on AIx75 ($p = 0.042$) and a trend for AP75 ($p = 0.051$), but no main effect of sex ($p = 0.643$; $p = 0.491$) or sex × mCSA ($p = 0.581$; $p = 0.444$).

Discussion

Our first major finding was an inverse relationship between mid-thigh mCSA and the magnitude of pressure augmentation from wave reflections (AP75 and AIx75). This relationship was stronger in males than females, likely due to a greater range of thigh muscle CSA values among males. In agreement with our findings, studies of older cohorts (Abbatecola et al. 2012) have shown associations between arterial stiffening and the loss of muscle mass. The present data, and previous work (Fahs et al. 2010), suggest that muscular–vascular coupling may also be observed in young individuals before age-related changes in muscle size and function may be apparent. The mechanisms for this association are not clear. One possibility is that greater muscle mass may decrease the tone of small muscular arteries via release of vasoactive agents and the magnitude of augmentation is determined by the tone of the small muscular arterioles (Kelly et al. 2001). Another potential mechanism may be related to a larger vascular network (e.g., angiogenic sprouting) stemming from a larger muscle mass. Skeletal muscle contains more microvessels than any other organ system, thus an increase in mCSA results in a proportional increase in capillary number (McCall et al. 1996). A greater vascular network would, in turn, result in greater waveform dispersion, reducing the apparent magnitude of the reflected pressure waves (Hope et al. 2005). This relationship may also reflect the metabolic benefits of high skeletal muscle mass including increased insulin sensitivity as a higher augmentation index has been observed in insulin-resistant young adults (Urbina et al. 2012).

Our second finding was a direct relationship between bSBP and mCSA, but not between aSBP and mCSA. This suggests that subjects with greater thigh muscle mass have higher peripheral BP. It is interesting to note that in young healthy subjects, conventional peripheral BP is not an accurate surrogate of aortic hemodynamic load (Siebenhofer et al. 1999). This is due to changes in vascular tone, arterial stiffness and pressure from wave reflections altering the amplification of the BP waveform from aortic to peripheral vascular sites. Indeed AIx accounts for approximately 29 % of the variance in pulse pressure amplification (Segers et al. 2009). Moreover, the paradoxical relationship between bSBP and mCSA noted in the present study was likely due to pulse pressure amplification which may be profound in young healthy adults. In the present study, absolute amplification was >14 mmHg. Some have gone so far as to suggest that amplification may even result in a diagnosis of hypertension (i.e. spurious systolic hypertension) (Mahmud and Feely 2003). In line with this is that aSBP was not related to mCSA in the present study. Furthermore, we noted an association between PP amplification and mCSA, although this association did not remain after adjusting for sex and height.

This inverse relationship between muscle and wave reflection is somewhat in contrast to previous resistance training intervention studies which indicate resistance training, a primary means of increasing muscle mass, increases central artery stiffness (Miyachi et al. 2004). A recent meta-analysis has concluded that resistance training

Table 2 Adjusted correlation matrix

Controlling for height and sex	Brachial SBP (mmHg)	Brachial DBP (mmHg)	Aortic SBP (mmHg)	Aortic DBP (mmHg)	Mean arterial pressure (mmHg)	Pulse pressure AMP (mmHg)	Systolic pressure AMP (mmHg)	Muscle CSA (cm^2)	Fat CSA (cm^2)	AP75 (mmHg)	AIx75 (%)	Knee extensor 1-RM (kg)
Brachial SBP (mmHg)												
Correlation	1.000											
p value												
Brachial DBP (mmHg)												
Correlation	0.752	1.000										
p value	<0.001											
Aortic SBP (mmHg)												
Correlation	0.925	0.835	1.000									
p value	<0.001	<0.001										
Aortic DBP (mmHg)												
Correlation	0.734	0.986	0.844	1.000								
p value	<0.001	<0.001	<0.001									
Mean arterial pressure (mmHg)												
Correlation	0.845	0.956	0.944	0.970	1.000							
p value	<0.001	<0.001	<0.001	<0.001								
Pulse pressure AMP (mmHg)												
Correlation	0.181	−0.237	−0.173	−0.242	−0.215	1.000						
p value	0.386	0.255	0.407	0.245	0.302							
Systolic pressure AMP (mmHg)												
Correlation	0.142	−0.257	−0.244	−0.327	−0.301	0.915	1.000					
p value	0.498	0.215	0.240	0.111	0.143	0.000						
Muscle CSA (cm^2)												
Correlation	0.465	0.279	0.350	0.216	0.261	0.166	0.275	1.000				
p value	0.019	0.177	0.087	0.299	0.208	0.428	0.183					
Fat CSA (cm^2)												
Correlation	−0.168	−0.232	−0.172	−0.203	−0.194	0.080	0.018	−0.059	1.000			
p value	0.421	0.263	0.412	0.331	0.353	0.704	0.932	0.778				
AP75 (mmHg)												
Correlation	−0.111	−0.011	0.125	0.058	0.106	−0.501	−0.608	−0.487	0.266	1.000		
p value	0.599	0.960	0.552	0.783	0.612	0.011	0.001	0.014	0.199			
AIx75 (%)												
Correlation	−0.116	0.010	0.115	0.076	0.109	−0.494	−0.596	−0.489	0.290	0.967	1.000	
p value	0.581	0.962	0.584	0.719	0.603	0.012	0.002	0.013	0.160	<0.001		

Table 2 continued

Controlling for height and sex	Brachial SBP (mmHg)	Brachial DBP (mmHg)	Aortic SBP (mmHg)	Aortic DBP (mmHg)	Mean arterial pressure (mmHg)	Pulse pressure AMP (mmHg)	Systolic pressure AMP (mmHg)	Muscle CSA (cm^2)	Fat CSA (cm^2)	AP75 (mmHg)	AIx75 (%)	Knee extensor 1-RM (kg)
Knee extensor 1-RM (kg)												
Correlation	0.327	0.402	0.281	0.380	0.344	0.094	0.104	0.733	−0.039	−0.246	−0.255	1.000
p value	0.110	0.046	0.174	0.061	0.092	0.654	0.621	<0.001	0.855	0.236	0.219	

Systolic blood pressure (SBP); Diastolic blood pressure (DBP); Amplification (AMP); cross-sectional area (CSA); Augmented pressure (AP); Augmentation Index (AIx); One-repetition maximum (1-RM)

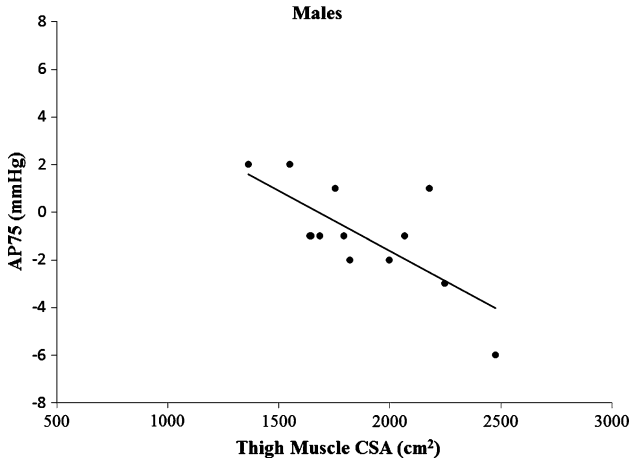

Fig. 1 The relationship between augmented pressure expressed relative to a heart rate of 75 and mid-thigh muscle cross-sectional area (mCSA) in males

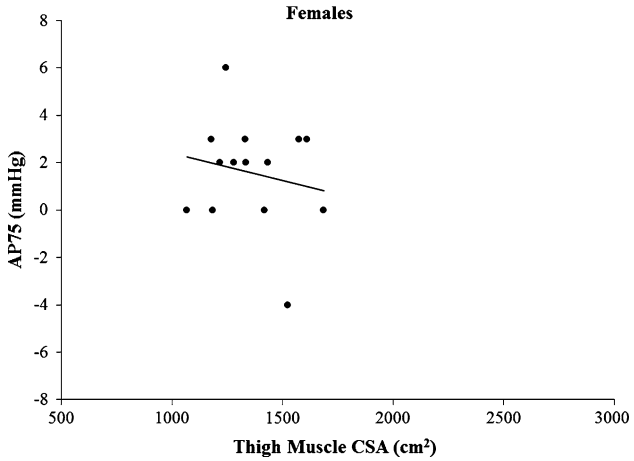

Fig. 2 The relationship between augmented pressure expressed relative to a heart rate of 75 and mid-thigh muscle cross-sectional area (mCSA) in females

causes a relative increase in arterial stiffness of ~11 % (Miyachi 2012). Thus, it appears that although resistance training for muscle mass accretion may also increase arterial stiffness, muscle mass per se may reduce the magnitude of wave reflection. Future studies should examine the impact of muscle mass accretion on wave reflection and the Augmentation Index.

It should also be noted that some investigations have observed sex differences in the determinants of the Augmentation Index. For example, muscle sympathetic nervous system activity (MSNA) has been shown to be positively related to the Augmentation Index in men and negatively related to the Augmentation Index in women (Casey et al. 2011). However, our results suggest that the relationship between mCSA and AP75 is stronger, but

similar in males (Fig. 1) compared to females (Fig. 2). This is likely due to the greater range of mCSA values observed in males compared to females.

Conclusions

In conclusion, a direct relationship was found between mCSA and bSBP, but not between mCSA and aortic pressure. In addition, there was an inverse relationship between mid-thigh mCSA and the magnitude of pressure from wave reflections (AP75 and AIx75). Altered wave reflection with subsequent effects on PP amplification may help explain the paradoxical observation of a positive association between mCSA and bSBP. These data are only correlational and may not necessarily indicate a direct effect of mCSA on augmentation or bSBP. Furthermore, our sample size is limited and these relationships may only be applicable to young, healthy individuals. Future studies should investigate these associations in larger cohorts of different age groups and also determine potential mechanism behind these associations.

Conflict of interest None of the authors had financial or personal conflict of interest with regard to this study.

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