A new approach to the classification of muscle health: preliminary investigations

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Abstract

Objective: Upper leg skeletal or lean tissue mass, strength and muscle quality have emerged as time-sensitive indices of muscular health. The aim of this study was to generate a comparative data set based on these indices, in healthy young (n=30, 29.0 ± 3.0 y old) and older (n=32, 58.7 ± 2.8 y old) adults, in order to evaluate their construct validity in establishing cut-points for muscle health. Approach: Whole body and upper leg lean tissue mass was obtained (iDXA^{TM}; GE Healthcare, Madison, WI) prior to the assessment of maximal voluntary isometric torque of the knee extensors and flexors (Cybex Isokinetic Dynamometer; Humac Norm, USA). Main Results: Peak isometric upper leg torque showed the greatest age-related difference (-29.0%), followed by muscle quality (-19.1%) and upper leg lean tissue mass (9.8%). Significance: Cut-points based on Z and T-scores generated from the young adult mean suggest muscle quality demonstrates the greatest construct validity toward the aim of classifying the muscular health of adults. Data generated from large, representative and sex-specific samples are required to adequately classify the muscular health of adults.

Keywords: muscle quality, lean tissue mass, ageing, sarcopenia

Introduction

The decline in muscular strength and associated reduction in functional capability was thought to be caused by a loss of muscle mass [1]. In an approach similar to that used in bone health, diagnostic criteria for sarcopenia has been based on classifying individuals as having high or low indices of muscle mass relative to a healthy young adult norm [2-6]. For example, sarcopenia has been considered to be a loss of muscle mass in an older adult that is greater than or equal to two standard deviations below the mean value obtained from a representative young adult population. These values are known as T-scores [3, 7]. Using this approach to classify young or older adults muscle or lean tissue mass relative to their age-matched peers produces values known as Z-scores. These studies report a prevalence of sarcopenia between ~9 – 34% in adults >65y and ≥50% in those >80y. Prevalence estimates vary widely depending on the health status and ethnicity of the population sampled. Low relative skeletal muscle mass has been found to be predictive of nursing home admission [7] and perhaps can be considered most predictive of functional decline in older (>70y) populations where relative change in muscle mass is accompanied by relative change in muscle quality [8]. However, low relative skeletal muscle mass may be a less valid tool toward the aim of being able to classify muscle health in healthy adults. This is because changes in muscle strength and muscle quality, starting aged ~40 y [9, 10], occur prior to change in muscle cross-sectional area (CSA) [11, 12]. Furthermore, emerging data is beginning to demonstrate a number of muscular indices which demonstrate more time-sensitive responses to the aging process. For example, the thigh region represents a more sensitive index of age-related change in skeletal mass than the whole body [13] and is also more responsive to therapeutic intervention [14-16]. Within the thigh region, the anterior compartment has been shown to account for the majority of age-related change in terms of skeletal mass [17, 18] and strength as represented by the force generating capacity of the knee extensors [19, 20]. Therefore, it would seem logical that indices of muscle quality are based on knee extensor or combined knee extensor and flexor strength per unit skeletal muscle or lean tissue mass (LTM) [21, 22].

In this study, we sought to measure upper leg LTM, maximal voluntary isometric torque of the knee extensors and flexors; and muscle quality (strength per unit tissue) in healthy young (25-35 y) and older (55 – 65 y) adults. The purpose of these measurements was to generate a comparative data set based on time sensitive indices of muscle health. From the young adult mean, cut points can be established where by young and older adult muscle health can be evaluated using Z and T-scores respectively.

Materials and Methods

Participants and experimental procedures

A convenience sample of healthy young (25 – 35 y) and older (55 – 65 y) adults were recruited via email, poster and word of mouth from the Leeds Beckett University campus community. The age range for younger adults was selected to encompass adults who had reached maturity but were not likely to be subject to age-related muscular change. The age range for older adults was selected to encompass healthy older adults who had not yet retired and were prior to more advanced age-related muscular changes. After receiving a complete explanation of the procedures, benefits and risks of the study, all participants gave their written informed consent. The study was approved by the Research Ethics Committee of Leeds Beckett University (Ref: 12768) and carried out in a manner consistent with the Declaration of Helsinki. Figure 1 illustrates the flow chart of study participants from recruitment to participation. From the 74 respondents, 4 were ineligible due to musculoskeletal conditions of the knee which could have impacted upon the measurement of upper leg strength. Three participants dropped out prior to the study beginning due to personal reasons and 5 participants failed to attend all assessments. The number of participants who completed the study (n=62) was deemed sufficient to demonstrate age-related change based on the work of Lanza et al. [23] and Wu et al. [24] who demonstrated age-related difference in muscle function using sample sizes of 24 and 44 respectively.

[**Fig 1.** Study participant flow chart from recruitment to participation]

Participants presented to the laboratory where they had an estimate of current physical activity assessed. This was recorded as the type and frequency of active sessions per week using the Bone Specific Physical Activity Questionnaire [25]. This was not a central focus of our investigation rather a method of estimating the relative physical activity status of our young and older participants. Participants then underwent a measure of whole and regional body composition. In an attempt to standardise test conditions and tissue hydration, participants were instructed to refrain from strenuous exercise in the 12-h period before testing and to avoid eating within 4 hours of testing. Participants consumed 500 ml of water 1-h prior to testing and were instructed to void and defecate, if required, immediately prior to testing. Body composition analysis was followed by an assessment of maximal voluntary isometric contractions of the knee extensors and flexors.

Body Composition

Height was measured to the nearest 0.1 cm by using a stadiometer (Seca) and body mass (BM) was measured to the nearest 0.1kg (MC-180MA; Tanita UK Ltd.). Whole body and regional body composition was estimated using Dual-energy X-ray absorptiometry (iDXA^{TM}; GE Healthcare, Madison, WI) in accordance with procedures used by Harley et al. (2011). The enCORE system software produced estimates of lean soft tissue, fat and bone mineral content and density for the whole body and specific regions. The thigh, representing upper leg LTM, was measured from the inferior side of the lesser trochanter until the tibiofemoral joint as described in Francis et al. [20].

Maximal Voluntary Isometric Torque

Maximal voluntary isometric contractions of the knee extensors and knee flexors of the dominant lower limb were assessed using isokinetic dynamometry (Cybex Isokinetic Dynamometer; Humac Norm, USA). The protocol for assessment including warm up, positioning, familiarisation, number of trials and the criteria for acceptance of an MVC has been adapted from and is described in detail in Francis et al. [20]. Muscle quality was expressed as maximal voluntary isometric knee extensor or combined knee extensor and flexor torque per kilogram upper leg LTM.

Statistical Analysis

A Shapiro-Wilk test was conducted to assess normality of the data for physical characteristics, number of active sessions per week, body composition, peak torque and muscle quality. Mean and standard deviation (SD) and median and interquartile range (IQR) are reported. Age-related difference between young and older adults were analysed using an independent sample t-test or a Wilcoxon-signed-rank test for normal and non-normal data, respectively. For young adults, Z-scores were defined as ≥1 SD or ≥2 SD below the mean of the height adjusted (ht^2) muscular index. For older adults, T-scores were defined as ≥1 SD or ≥2 SD below the young adult mean of the height adjusted (ht^2) muscular index. Statistical analysis was performed by using PASW Statistics 22.0 for Windows (SPSS, Inc.). Significance (2-tailed) was set at $P < 0.05$ for all analyses.

Results

Sixty-two healthy young (n=30) and older (n=32) adults completed all assessments. All participants had similar physical characteristics and body composition. There was no difference in the number of active sessions young and older adults participated in (Table 1). Young and older adults took part in 15 and 18 different activities respectively. Most frequently reported by young adults were running (n=12), cycling (n=7) and walking (n=10). Older adults mainly participated in walking (n=15), Pilates (n=9) and yoga (n=5). Upper leg LTM was lower in the older adults relative to their younger counterparts but this difference was not seen for whole body LTM. Age-related difference in strength was similar for the knee extensors and flexors. On average, younger adults had 29% more upper leg strength relative to older adults (Table 2). As the relative differences in knee extensor and flexor strength were similar between young and older adults so were differences in muscle quality expressed as combined torque or knee extensor torque per kg upper leg LTM (Figure 2; Table 2).

A sex-specific sub-analysis was conducted to determine the influence of gender on differences reported. Compared to the younger adults, strength (combined knee extensor and flexor torque) was lower in both men

(28.6%) and women (30%) (*P*≤0.02), although women appeared to demonstrate greater strength differences in the knee flexors relative to men (-33.7% (*P*=0.02) *vs.* -18.9% (*P*=0.02)). Upper leg LTM was lower in older women (-14.9%, *P*<0.01) but not in older men (-7.7%, *P*=0.271) relative to their younger counterparts. A greater upper leg LTM difference in women but a similar strength difference in both genders led to a smaller muscle quality (combined strength relative to upper leg LTM) difference in older women compared to older men (-17.5% (*P*=0.019) vs. -21.4% (*P*=0.018)).

Based on indices of whole or upper leg LTM none of the younger or older adults had Z or T scores ≥ 2. Knee extensor torque per kg body mass identified a small (n=5; 16.6%) proportion of young adults and a large proportion of older adults (n=13; 40.6%) with Z or T-scores ≥2. Muscle quality expressed as knee extensor torque per kg upper leg LTM identified four (12.5%) older adults with a T-score ≥2 (Table 3).

[**Fig 2.** Age-related median difference (16.4%) in muscle quality defined as knee extensor torque per kg upper leg lean tissue mass]

Table 1. Physical characteristics, body composition and activity levels of healthy young (25 – 35y) and older (55-65y) adults[1.]

	Young (n=30)	Older (n=32)	*P*[2]
Age (years)	29.0 ± 3.0	58.7 ± 2.8	
Height (cm)	172.4 ± 10.7	168.0 ± 9.2	0.082
Body mass (kg)	67.7 (23.0)	70.8 ± 13.9	0.704
BMI kg/m^2	24.3 ± 3.9	24.3 (4.8)	0.473
Body Fat (%)	27.0 ± 9.2	27.9 ± 10.5	0.720
LTM (kg)	46.1 (16.5)	46.5 ± 9.7	0.464
Active Sessions (per week)	4.6 ± 1.5	4.6 ± 2.2	0.877

[1]Values are means ± SDs or medians (IQR). No significant differences were found between groups. [2]P values for the difference between young and older groups analysed by independent t test or Mann-Whitney U test.

Table 2. Upper leg LTM, muscle strength and muscle quality of healthy young (25 – 35y) and older (55-65y) adults[1].

	Young (n=30)	Older (n=32)	Δ[2]	Δ%	*P*[3]
Upper leg LTM (kg)	5.1 (1.6)	4.6 (1.6)	0.5 (0.2 – 1.3)	9.8%	0.045
Knee extensors (N·m)	227.1 ± 88.2	157.9 ± 58.9	69.2 (18) (31.3 – 107.1)	30.5	0.001
Knee Flexors (N·m)	96.4 ± 38.3	58.3 (43.4)	38.1 (5.7 – 42.1)	39.5	0.007
Combined Torque (N·m)	323.5 ± 122.0	229.8 ± 88.3	93.7 (26.9) (39.9 – 147.6)	29.0	0.001
Muscle quality (combined torque N·m kg^{-1})	58.7 ± 14.6	47.5 ± 13.1	11.2 (3.5) (4.2 – 18.3)	19.1	0.002
Muscle quality (knee extensor torque N·m kg^{-1})	41.1 ± 10.4	32.9 ± 10.0	8.2 (2.6) (3.0 – 13.4)	20.0	0.002

[1]Values are means ± SDs or medians (IQR). No significant differences were found between groups. [2]Differences reported as mean difference (std. error difference), 95% confidence interval (CI) or median difference and 95% bootstrap CI. [3]P values for the difference between young and older groups analysed by independent t test or Mann-Whitney U test.

Table 3. Young adult muscle health classified according to z-scores and older adult muscle health classified according to t-scores.

	Whole body LTM/ht^2	**Upper leg LTM/ht^2**	**Knee Extensor Torque (N·m kg^{-1})**	**Muscle Quality (knee extensor torque N·m kg^{-1})**
Z-Score		Younger Adults n (%)		
1	3 (10 %)	4 (13.3 %)	5 (16.6 %)	10 (33.3 %)
2	-	-	3 (10 %)	-
T-Score		Older Adults n (%)		
1	3 (9.4 %)	12 (37.5 %)	13 (40.6 %)	9 (28.1 %)
2	_	_	9 (28.1 %)	4 (12.5 %)

Discussion

The purpose of this study was to generate a comparative data set of time sensitive indices of muscular health between healthy young and older adults. The main reason for this was to enable calculation of Z and T-scores for young and older adults respectively. These data help to make preliminary suggestions as to the most appropriate muscular indices for the assessment of muscle health in adults. Although upper leg LTM was lower (-9.8%) in older adults it did not identify any older adults as having a T score ≥2. By contrast, knee extensor torque per kg body mass seemed to classify ~69% (n=22) of the older adults at least ≥1 (n=13) or ≥ 2 (n=9) T-scores below the young adult mean. In a group of adults of similar physical characteristics and body composition, this index may only reveal that strength normalised to stature is lower in older adults compared to their younger counterparts. In other words, an index based around muscular strength may be highly sensitive but not very specific and as such may not be able to distinguish between those who have lower muscle strength and those at risk of functional decline. Participants in this study were healthy and physically active, to support the construct validity of the index it might be expected that a greater number of participants would be identified as 1 T-score below the young adult mean rather than 2. To this aim, muscle quality seemed to represent a more appropriate index. The number of older adults classified 1 or 2 T-scores below the young adult mean for muscle quality is more conservative. Furthermore, muscle quality appears to have construct validity in a healthy sample of older adults by classifying a greater number as 1 T-score rather than 2 T-scores below the young adult mean (n= 9 *vs.* n =4).

The discussion around whether these indices can establish an accurate prevalence of ‘reduced muscular health’ is of course limited by the small size we have used in this preliminary investigation which is not sex-specific. Furthermore, although muscle quality appears to demonstrate greater construct validity, it is difficult to pass comment on the validity of an index without knowing the consequences for functional performance [26]. The results of this study which appear to support muscle quality as a sensitive index of muscle health are interesting considering our group and others have reported muscle strength to better distinguish functional performance compared to muscle quality in older adults [27, 28]. This has led us to question the validity of the muscle quality index as a marker of functional capability [29], particularly given the increase resource required to quantify skeletal mass via imaging methods. It may be that a combination of muscle quality and functional performance is required to develop an index of ‘reduced muscular health’ that may be predictive of future risk of sarcopenia.

Although, not the main focus of our investigation, it is pertinent to comment on the age-related difference in the muscular indices measured and gender differences observed. Comparison of discrete groups of young and older adults with similar physical characteristics, body composition and a similar number of active sessions per week are less frequent in the literature. The advantage of these groups, whilst acknowledging the limitation of the cross-sectional design, is that the main difference between them is age. From our data, upper leg LTM and strength can be estimated as ~3.3% and 10.1% lower per decade of age respectively. These estimates are consistent with the 3 – 6% and 8 – 15% per decade decline in lower limb skeletal muscle or lean tissue and strength reported in the literature [9, 10, 13, 20].

Contrary to our hypothesis that the knee extensors would demonstrate a preferential age-related difference relative to the knee flexors, strength differences between both muscle groups in the upper leg were similar. In fact, the median age-related difference in knee flexor torque appeared greater than the mean difference in the knee extensors, although this difference disappeared when torque was combined to represent the upper leg. It is possible that the older adults who appear to have maintained or increased their activity in later life have reduced the preferential difference in knee extensor torque which can be as high as 19-20% per decade in cross-sectional study designs [8, 20]. This interpretation must be considered cognisant that while the older adults complete a similar number of active sessions per week, the predominate mode of exercise is of lower intensity and muscular demand than their younger counterparts (walking (n=15) *vs.* running (n=12)). This more conservative strength difference may go some way to explaining why the age-related difference in muscle quality is at the lower end (6.7 % per decade) of the per decade range (5 – 27% per decade) reported previously [29]. Although these are plausible explanations, Wu et al. [24] report similar results to our study in that strength differences occur at a similar rate (~10% per decade) and evenly between the knee flexors and extensors. The finding of an even difference in strength between the knee extensors and flexors is also consistent with the early work of Frontera et al. [1]. It may be that the preferential difference in knee extensor strength we previously reported is confined to those >50y or specific to women [20]. Although, Frontera et al. [19] also reported a preferential decline in knee extensor strength in a longitudinal analysis, it is in a small sample (n=12).

Sub-group analysis by gender revealed that the majority of age-related difference in upper leg LTM was driven by females (-14.9%). The difference between young and older men was not statistically significant (-7.7%, P=0.271). These findings are in agreement with those of Lynch et al. [10] and Janssen et al. [13] who report women to have a greater leg lean or muscle mass decline relative to men between the 3rd and 6th decade respectively. The per decade decline (4.9% (DXA) and 5.7% (MRI)) reported by the authors is similar to that reported in this study (5.0%). The finding that men and women demonstrate a similar difference in leg strength (~30%) with age is in agreement with previous studies. This study appeared to suggest a greater loss of knee flexor torque in women relative to men (-33.7% vs. -18.9%), a finding which has been reported in one other longitudinal study [12]. However, previously we have reported the measurement of maximal voluntary knee flexor torque to be less reliable relative to the measurement of the knee extensors [20]. This may play a role in our study particularly given the small sample used. An even decline in overall lower limb strength for men and women and a greater decline in upper leg LTM for women meant that older women appeared to have a lower difference in muscle quality compared to older men. This gender difference has been reported cross-sectionally and longitudinal in adults in the 7th decade of life [8]. It may also be due to LTM remaining stable in men until age 60y but becoming noticeable different from a young adult in women aged 50y [31]. These gender differences may have had an impact on the Z and T-scores we reported above, however, the 4-older adults classified as having a muscle quality measurement >2SD below the young adult mean were split evenly between genders i.e. 2 male and 2 female. Interpretation of the sex-differences in this study must be made cognisant of the small numbers of young men (n=12) and women (n=18) and older men (n=13) and women (n=19). The age-related difference in upper leg LTM, strength and muscle quality are in line with but toward the lower end of the ranges reported in the literature. This is likely due to the relative health of the older adults as indicated by their maintenance of whole body LTM and activity profile. Nonetheless, the differences between young and older healthy adults are still substantial which is in agreement with data demonstrating that not even masters athletes can avoid the age-related decline in muscular health [30]. A strength of the convenience sample used in this study is that all participants were recruited from within a similar community, were healthy, not retired and had a similar number of active sessions per week. This allowed to us to generate a comparative data set where age was the main difference between groups. Our study is limited by a small size and the cross-sectional nature of the design which cannot account for inter-generational differences or a survival bias toward the healthier older adults. Furthermore, our young adult data is not based on a sex-specific mean which may influence the cut-off points identified. Finally, although the number of active sessions per week were similar, younger adults had a preference for activities of higher intensity and muscular demand which could influence the magnitude of difference reported.

In summary, this preliminary investigation reported muscle quality as the index of greatest construct validity in the measurement of muscle health when assessed via T-scores. Further work is required in a representative, gender specific sample of healthy adults across a greater number of age ranges. The collection of functional performance data in tandem with such measures is required in order to support the criterion validity of an index. Age-related difference in time-sensitive muscular indices between healthy young and older adults were consistent with the literature although at the lower end of that previously reported. This was perhaps demonstrates the relative health of the sample under investigation.

[31]

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Fig 1. Study participant flow chart from recruitment to participation.

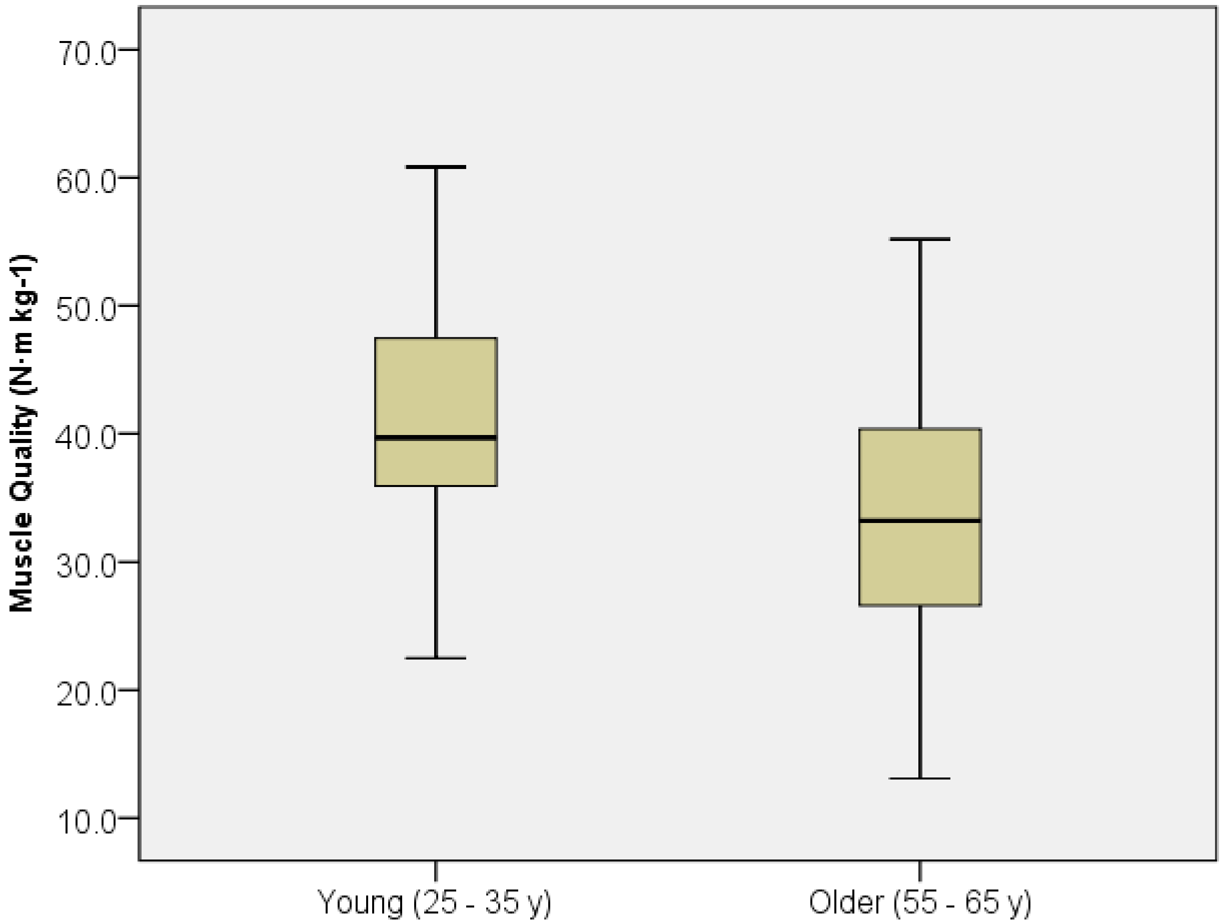

Fig 2. Age-related median difference (16.4%) in muscle quality defined as knee extensor torque per kg upper leg lean tissue mass.