Journal of Aging Research & Clinical Practice©
Volume 1, Number 1, 2012

CORRELATES OF THIGH MUSCLE INDEX WITH PHYSICAL PERFORMANCE IN AMBULATORY GERIATRIC PATIENTS

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Abstract: *Objective:* 1) to validate the correlation between the estimated dominant thigh muscle volume using anthropometric measurements and the physical performance of lower limbs in elderly adults at ambulatory clinics; 2) to examine the association between dominant thigh muscle index and frailty. *Design:* Longitudinal observational study. *Setting:* Outpatients at family or geriatric medicine clinics. *Participants:* One hundred forty-eight elderly adults aged 65-90. *Measurements:* The anthropometric measurements (including weight and thigh circumference), appendicular skeletal muscle mass by bioelectrical impendence analysis (BIA), quadriceps muscle strength, physical performance (including timed Up & Go test, 5-meter walking time, and handgrip strength) were examined at baseline and 1-year follow-up with the Fried Frailty Index evaluated concurrently. *Results:* The estimated dominant thigh muscle volume was correlated positively with quadriceps muscle strength and the predicted appendicular skeletal muscle mass but negatively with physical performance (timed Up&Go and 5m walking time) ($p \leqq 0.01$). Dominant thigh muscle index (quadriceps muscle strength per estimated thigh muscle volume*1000 of the dominant leg) was marginally different between genders ($p=0.06$). Additionally, older age, weaker quadriceps muscle strength, lower dominant thigh muscle index, and longer time for TUG (timed Up & Go) test were associated with frailty status (all p-values < 0.05). Dominant thigh muscle index was an independent and protective factor associated with frailty after age adjustment. *Conclusion:* Using the equation with anthropometric measurements to estimate thigh muscle volume is a simple and noninvasive method. Moreover, dominant thigh muscle index helps detect frailty at an early stage and minimize the impacts of gender difference on frailty.

Key words: Anthropometrics measurements, thigh muscle volume, older adults.

Introduction

Sarcopenia is the medical term for muscle loss (1). Along with the aging process, skeletal muscle mass related to exercise and movement undergoes constant quantitative and qualitative decline that leads to immobility (2-5). As previous studies suggest, sarcopenia represents an impaired state which may cause poor health outcomes like frailty, disability, increased risk of falls, and even death (5-7).

The Fried Frailty Index (FFI) proposed by Fried et al. following the Cardiovascular Health Study is one of the most extensively used instruments in the frailty research setting with emphasis on physical function (8, 9). In FFI, mobility is the core to evaluate frailty in elderly. Maintaining mobility is one of the most effective ways to prevent and delay frailty in elderly. Simply speaking, the degradation of musculoskeletal system is a geriatric sign called respectively osteoporosis and sarcopenia in the skeletal and muscular systems (10). Fall caused by mobility dysfunction is a classical geriatric syndrome as it seldom results in serious outcome in young adults but may lead to fracture, trauma, and other serious adverse consequences (disability, hospitalization, institutionalization and mortality) in older adults (11). Sarcopenia is closely related to immobility and frailty, which give rise to adverse outcomes. How to prevent sarcopenia is thus an important issue for disability prevention in the elderly. In contrast to osteoporosis, sarcopenia is still under-explored in clinic and basic researches (12).

The parameters of sarcopenia are the amount of muscle and its functions. The measurable variables are mass, strength and physical performance. According to the literature, sarcopenia denotes one of following situations: (1) change of muscle structure (loss in muscle volume and muscle mass); (2) weak muscle strength; and

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Received June16, 2011
Accepted for publication September 8, 2011

(3) less physical performance as well as endurance (13-15). According to the recommendation of the European Working Group on Sarcopenia in Older People (EWGSOP), diagnosis of sarcopenia requires documentation of low muscle mass plus that of either low muscle strength or low physical performance (13).

Computerized tomography (CT) and magnetic resonance imaging (MRI) are gold standards for estimating muscle mass in research (13, 16). They are, however, expensive, invasive, and impractical in community survey.

Since poor physical performance in the lower limbs of older adults is one of the indicators for frailty and other adverse health effects, in our previous study, we developed a prediction equation model using anthropometric measurements for thigh muscle volume estimation based on MRI-results. The estimated thigh muscle volume was highly correlated with the MRI-measured thigh volume (R^2 = 0.745) (17). This anthropometric measurement is a relatively simple, easy and noninvasive method for regular clinical practice and follow-up.

In this paper following the previous result, we aim to validate the correlation between estimated dominant thigh muscle volume and quadriceps muscle strength and physical performance in lower limbs. Additionally, we attempt to examine the association between thigh muscle loss and frailty.

Material and methods

Subjects

From January 2007 to August 2009, the research team recruited 189 ambulatory patients aged 65-90 from family medicine or geriatric clinics in the districts surrounding Taipei City of Taiwan for a multidimensional, inter-disciplinary comprehensive geriatric assessment. All the enrolled subjects received a long term follow-up. Subjects were required to meet one of the following inclusion criteria: functional decline in recent one year; cognitive impairment; depressive symptom; mobility impairment; fall in recent one year; eating or feeding problem; comorbid conditions ≧5; tracking by different physician ≧3 in recent half year; polypharmacy ≧8 in recent 3 months; hospitalization ≧1 in recent one year; emergency visit ≧2 in recent one year and aged ≧80. Exclusion criteria included bed-ridden patients; long-term residents at nursing homes; patients with a life expectancy shorter than 6 months; or impairment in vision, hearing or communicative ability.

148 out of the 189 enrolled subjects completed the first year comprehensive geriatric assessment and were included for analysis. There were 14 and 15 cases marked respectively with withdrawal of agreement and failure of being reached during follow-up. One case moved to nursing home after enrollment, six subjects passed away during the study, and five cases lost the physical performance data due to mobility impairment.

The estimated thigh muscle volume was calculated by the previously developed equation, which includes age, gender, body weight and thigh circumference predictors (17). Body weight was measured with subjects dressed in light clothing and barefoot. Additionally, thigh circumference was measured from a point 15 cm proximal to the superior pole of the patella (18, 19).

Quadriceps muscle strength of the lower extremities was measured using a commercially available isometric force dynamometer (Micro FET; Hoggan Health Industries, Draper, Utach) during a 5-s maximal force contraction of the dominant quadriceps muscle by knee extension described in the previous study (17).

The BC-418 (Tanita Corporation, Tokyo, Japan) for bioelectrical impedance analysis (BIA) was used to calculate skeletal muscle mass, fat free mass and fat mass of each arm, each leg and trunk. All manipulation was under the standard procedure (20, 21). Appendicular skeletal muscle mass was the sum of muscle mass of right arm, right leg, left arm and left leg according to the previous study (21).

Dominant thigh muscle index was defined to be quadriceps muscle strength of the dominant leg divided by the estimated dominant thigh muscle volume and then times 1000 to examine the association between physical performance of lower limbs and frailty. Therefore, dominant thigh muscle index in this study was represented as quadriceps muscle strength per unit of thigh muscle volume (Newton/cm^3).

Timed Up & Go (TUG) test was performed in the manner prescribed in a previous study (22). Basically, subjects were timed while they rose from arm chairs, walked three meters, turned and walked back to the chair, and sat down.

The FFI proposed by Dr. Fried and her colleagues incorporates five indicators: unintentional weight loss, self-reported exhaustion, low physical activity level, slowness in walking time, and weak grip strength following the Cardiovascular Health Study (8). One point is scored for each indicator when a specific target is reached (8). Subjects scored 0 are defined as robust, cases scored 1-2 are classified as prefrail, and cases scored 3-5 are defined as frail. In order to examine the associated factor of early stage of frailty, subjects in prefrail and frail states were grouped as non-robust cases for further analysis. The five indicators were operationalized as follows in our study:

1) "Weight loss" was defined as self-reported unintentional weight loss more than 3 kg, or greater than 5% of body weight in the previous year.
2) "Exhaustion" was indicated by a self response as "a moderate amount of the time" or "most of the time" to

either of the following two statements: "I felt everything I did was an effort" or "I could not get going" from the Center for Epidemiological Studies-Depression Scale (23).

3) "Low physical activity" was defined by gender specific low weekly energy expenditure measured by the Taiwan IPAQ-SF (International Physical Activity Questionnaire-Short Form) (24).
4) "Slow walking time" was defined as usual walking speed for 5m below the criterion-specific thresholds adjusting for gender and height that were the same as the Cardiovascular Health Study Group (8).
5) "Weakness" was defined as mean grip strength of the dominant hand measured by 3 times below the criterion-specific thresholds adjusting for gender and body mass index (BMI) the same as the Cardiovascular Health Study Group (8).

Statistics

Gender differences in age, muscle volume, strength, and physical performance were examined by student's t-test. Differences in characteristics among the categories of the FFI were compared by student's t-test (continuous variables) or X^2-test (categorical variables). The relationships between estimated dominant thigh muscle mass and physical performance, quadriceps muscle strength, and appendicular skeletal muscle mass were examined by Pearson correlation analysis.

Furthermore, in order to examine the association between thigh muscle related variables and frailty, the generalized linear model was adopted for analysis. Variables include age, estimated dominant thigh muscle volume, predicted appendicular skeletal muscle mass, quadriceps muscle strength, and dominant thigh muscle index.

Results

Characteristics of subjects at baseline and 1-Year follow-up

There was a total of 148 subjects (72 men and 76 women) recruited for study. The mean age was 76.72±6.09 (range 65-88 years). The baseline characteristics are listed in Table 1. Dominant thigh muscle index is generated by quadriceps muscle strength/estimated thigh muscle volume*1000 of the dominant leg.

Of the 148 subjects, 39 (26.4%) reported a score of 0, 53 (35.8%) a score of 1, 32 (21.6%) a score of 2, 18 (12.2%) a score of 3, and 6 (4.1%) a score of 4 at baseline while there were 19 (12.8%) scoring 0, 64 (43.2%) scoring 1, 39 (26.4%) scoring 2, 22 (14.9%) scoring 3, and 4 (2.7%) scoring 4 as defined by the FFI after 1-year follow-up.

Men tended to have stronger quadriceps muscle strength and greater estimated dominant thigh muscle volume as well as predicted appendicular skeletal muscle mass than women ($p < 0.001$). Dominant thigh muscle index was marginally different between genders (p=0.06) (Table 2).

Table 1
Characteristics of subjects at baseline and 1-year follow-up

Variables	Statistics [a]
Gender	
Male	72 (48.6%)
Female	76 (51.4%)
Age (year)	76.72 ± 6.09
Education	
Less than 6 years	75 (50.7%)
Junior High	23 (15.5%)
Senior High	20 (13.5%)
College or more	30 (20.3%)
Marriage Status	
Married	98 (66.2%)
Single (widowed, divorced)	50 (33.8%)
Baseline: Quadriceps Muscle Related Variables	
Predicted appendicular skeletal muscle mass (kg)	16.73±3.93
Muscle strength (Newton)	127.77 ± 28.84
Estimated thigh muscle volume (cm^3)	4966.8± 998.1
Dominant thigh muscle index [b] (newton/cm^3)	26.19 ± 6.00
Time1: Physical Performance	
Timed Up&Go Test (sec)	12.77 ± 8.35
5m walking time (sec)	6.37 ± 5.77
Baseline Fried frailty score	
0	39 (26.4%)
1	53 (35.8%)
2	32 (21.6%)
3	18 (12.2%)
4	6 (4.1%)
Time2:	
1yr follow-up Fried frailty score	
0	19 (12.8%)
1	64 (43.2%)
2	39 (26.4%)
3	22 (14.9%)
4	4 (2.7%)

Note a: n (%) for categorical data, Mean ± SD for continuous data. b: Dominant thigh muscle index = 1000* (quadriceps muscle strength/ thigh muscle volume) of the dominant leg

Table 2
Gender differences in age and muscle (quadriceps) related variables

Variables	Male Mean ± SD	Female Mean ± SD	t (p) [a]
Age	77.60 ± 5.82	75.88 ± 6.25	1.73 (0.087)
Estimated thigh muscle Volume (cm^3)	5666.8 ± 750.1	4303.6 ± 709.7	11.36 (< 0.001) *
Quadriceps muscle strength (Newton)	141.44 ± 21.85	114.82 ± 28.79	6.31 (< 0.001) *
Dominant thigh muscle index (newton/cm^3)	25.23 ± 4.06	27.09 ±7.30	-1.93 (0.056)
Appendicular skeletal muscle mass (kg)	20.15 ± 2.38	13.54 ± 1.85	18.73 (< 0.001) *
Appendicular skeletal muscle mass / height^2 (kg/ cm^2)	7.61 ± 0.84	5.93 ± 0.69	13.23 (< 0.001) *
Timed Up&Go test (sec)	11.63 ± 5.29	13.84 ± 10.38	-1.62 (0.108)
5m walking time (sec)	5.64 ± 2.47	7.07 ± 7.65	-1.52 (0.131)

Note a: by Student's t-test; * : p-value < 0.05

Correlation of estimated dominant thigh muscle volume with muscle related variables and physical performance in lower limbs

The correlation between estimated dominant thigh muscle volume and muscle related variables in lower limbs are summarized in Table 3. The estimated dominant thigh muscle volume was significantly positively correlated with quadriceps muscle strength of the dominant leg and predicted appendicular skeletal muscle mass but negatively correlated with the TUG test, and 5m walking time significantly (all p-values <0.05).

Distribution of age and baseline muscle related variables in lower limbs between subjects with different frailty status

The distribution of thigh muscle related variables and physical performance in lower limbs among subjects with different frailty status at baseline are presented in Table 4. According to this cross-sectional data, frailer subjects tended to be older, spend a longer time in the TUG test, and had a weaker quadriceps muscle strength and dominant thigh muscle index ($p<0.05$ for each comparison). It seems that being older, spending a longer time for the TUG test, and having a weaker quadriceps muscle strength and dominant thigh muscle index are major indicators helping distinguish frailty from robustness. Though the mean of estimated dominant thigh muscle volume, appendicular skeletal muscle mass decreased in subject with frailer status, the decline was not statistically significant (p=0.521 and 0.467, respectively).

Factors associated with frailty scores following generalized linear model

Furthermore, owing to frailty scored 0, 1-5 primarily, the generalized linear model was used to explore correlates of frailty. In model I of Table 5(a), decreasing dominant thigh muscle index was associated with frailty scores at baseline. After age adjustment, decreasing dominant thigh muscle index emerged to be independently associated with frailty scores in Model II. After 1-year follow-up, decreasing dominant thigh muscle index was marginally associated with frailty scores after age adjustment in Model II of Table 5(b).

Table 4

The distribution of variables (age and muscle related variables) among subjects with different frailty status (N=148)

Fried	Robust (n = 39)	Non-robust (n = 109)	p [a]
Female	20 (51.3%)	56 (51.4%)	0.992[b]
Age (year)	74.62±6.43	77.47±5.81	0.012 *
Estimated thigh muscle volume (cm^3)	5055.1±921.8	4935.2±1026.2	0.521
Quadriceps muscle strength[a] (Newton)	139.28±20.06	123.65±30.43	0.003 *
Dominant thigh muscle index (newton/cm^3)	28.15±5.15	25.49±6.15	0.017 *
Appendicular skeletal muscle mass (kg)	17.13±3.91	16.59±3.94	0.467
Appendicular skeletal muscle mass/height^2 (kg/ cm^2)	6.79±0.99	6.72±1.19	0.738
Timed Up&Go Test (sec)	8.70±2.15	14.22±9.23	<0.001 *

Note a: by Student's t-test; b: X^2-test; * : p-value< 0.05

Discussion

As far as the measurements of muscle mass are concerned, MRI is one of the gold standards thanks to its ability to separate fat from other soft tissues of the body (16). However, it is invasive and expensive for regular practice. There are several alternative methods for muscle mass measurements, such as dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), and anthropometric measurements. Each method has its advantages and limitations. By BIA, the volume of fat and lean body mass could be separated for estimation. The greatest challenge of using BIA for muscle mass estimation is that there are diverse models of BIA. Efforts are required to convert data among various models used by different machines. Tanita BC-418, the model used in this study, is equipped with eight polar electrodes capable of separating the muscle mass and non-fat mass, as well as performing fat mass readings for the right arm, right leg, left arm and left leg. In the arms and legs segments, non-bone, non-fat tissues are assumed to be appendicular skeletal muscle mass, that is relatively highly correlated with mobility and physical

Table 3

Correlation of estimated dominant thigh muscle volume with muscle related variables in lower limbs

Characteristics	Quadriceps muscle strength (kg)	Timed Up&Go Test (sec) time (sec)	5m Walking time (sec)	Predictive skeletal muscle mass (kg)
Correlation	0.504	-0.224	-0.215	0.896
p value	<0.001 *	0.006 *	0.009 *	<0.001 *

* P<0.05, indicating a significant variable in the two-tail Pearson correlation test.

performance. Another advantage of using this model is that the correlation between BIA Tania BC-418 and DXA machines for appendicular skeletal muscle mass estimation was high from a previous study (r=0.96, p<0.001) (21).

Table 5
Association between dominant thigh muscle index and frailty by generalized linear model

(a) At Baseline

	Model 1		Model 2	
	β (95% CI)	**P [a] <**		**P [a] <**
Dominant thigh muscle index	-0.031 (-0.061 ~ -0.002)	0.037	-0.038 (-0.067 ~ -0.009)	0.011
Age	--		0.039 (0.011 ~ 0.068)	0.007

(b) at 1-year Follow-up

	Model 1		Model 2	
	β (95% CI)	**P [a] <**		**P [a] <**
Dominant thigh muscle index	-0.016 (-0.037 ~ 0.006)	0.155	-0.021 (-0.042 ~ $1.079*10^{-5}$)	0.050
Age	–		0.047 (0.022 ~ 0.072)	< 0.001

β(95% confidence interval) of dominant thigh muscle index for frailty score at (a) baseline; (b) 1-year follow-up; Note: a: by generalized linear model

Several anthropometric measures for muscle mass estimation have been reported, including mid-upper arm circumference, skin fold thickness, calf circumference (13, 25, 26). One report from Rolland et al. showed that calf circumference < 31 cm was associated with muscle-related disability and self-reported physical function (26). However, some arguments pointed out that changes in age-related body composition may contribute to the errors in muscle mass estimation (13). In our previous study for thigh muscle volume estimation, the result obtained by anthropometric measurements, including age, weight and thigh circumference, was correlated with the MRI-result (r^2=0.745, p <0.001) (17). Moreover, the current study shows that dominant thigh muscle volume estimated by anthropometric measurements is positively correlated with quadriceps muscle strength of the dominant leg and appendicular skeletal muscle mass measured by BIA but negatively correlated with the TUG test, and the 5m walking time. This study is one of the few studies validating the effectiveness of anthropometric measurements in estimating thigh muscle volume in elderly. Consequently, using this anthropometric method for thigh muscle volume estimation might be an alternative way for usual practice and follow-up in future studies.

Several studies did not support the direct association between skeletal muscle mass and physical function impairments in elderly subjects. One study by Rolland et al. on community-dwelling elderly women showed that sarcopenia alone was not associated with self-reported physical difficulties; however, sarcopenic obese women tended to add difficulty for some physical functions (27). Another study by Visser et al. on well-functioning older adults suggested that muscle strength and muscle attenuation (a measure of fat infiltration) were stronger predictors of mobility limitation than lower muscle mass (28). However, more and more papers have supported a wider definition of sarcopenia that takes into consideration of low muscle mass, muscle strength, and physical performance (12, 13). Sarcopenia represents an impaired health status that increases the risk of functional impairment, physical disability and death. A recently published study by Chien et al. reported that sarcopenia was associated with physical disability in Taiwanese community-dwelling elderly men (29).

The fact that muscle mass, like muscle function, decreases with age is well established in previous studies (2-5). Muscle function (peak torque during knee extension) per unit of cross-sectional area of the quadriceps femoris was found to decline with age in men but not women in previous studies (30-32). However, it might be considered a more meaningful indicator of using the whole muscle volume than using a single cross sectional area (33). Though there were several studies exploring the correlates of maximal muscle strength per muscle mass or muscle volume, defined as muscle quality (34-37), this study, to the best of our knowledge, might be the first one to compare dominant quadriceps muscle strength per unit of estimated thigh muscle volume, dominant thigh muscle index, between different frailty statuses. Several advantages of using dominant thigh muscle index are described below.

First of all, either muscle strength in quadriceps or estimated thigh muscle volume is significantly different between men and women (Table 2). However, there is only a marginal difference between genders in dominant thigh muscle index in our study, indicating that the reduced influence of gender on the association between dominant thigh muscle index and frailty.

Secondly, the parameters of sarcopenia are the amount of muscle and its functions [ref (13-15)]. However, when the muscle mass or volume is considered, there are various cut-off points in reference for sarcopenia definition [ref (38-43)]. Moreover, some studies used appendicular skeletal muscle to define sarcopenia whereas some used total skeletal muscle as a measurement. Therefore, dominant thigh muscle volume, muscle mass, and quadriceps muscle strength were adopted as the measurements in this study so as to reduce bias coming from inconsistent definitions and outcome measures of sarcopenia.

Nevertheless, this study may have its limitations (1). Quadriceps muscle strength measured by the isometric force dynamometer produced by Hoggan Health Industries may be variable when the machine was operated by different examiners. Though quadriceps muscle strength was measured by the same staff during the whole period of study, more precise measurement of isometric or isokinetic dynamometers, such as Cybex, for muscle strength examination in lower limbs will be performed in the future. (2) It is arduous to analyze the risk factors of frailty after 1-year follow-up due to the sample size limitation and follow-up duration. There were only 49 (33.1%) subjects with worse Fried Frailty scores after 1-year follow-up. Additionally, in our study, deterioration in handgrip strength was the leading factor of getting frailer scores in the five frailty indicators (shirking, exhaustion, weak hand grip strength, low physical activity and slowness in walking speed). We need more subjects and longer time for observation in the future to examine the prognosis of thigh muscle loss.

Conclusions

According to the study results presented in the paper, the estimated dominant thigh muscle volume using anthropometric measurements appears to be significantly correlated with appendicular skeletal muscle mass, quadriceps muscle strength and physical performance in lower limbs of older adults. Additionally, dominant thigh muscle index can help detect frailty at an early stage and minimize the impacts of gender difference on frailty.

Acknowledgments: This study was supported by PH-099-PP-51 grand "A Pilot Study on Frailty Phenotypes Defined by Pro-inflammatory and Novel Aging Biomarkers" from the National Health Research Institutes, Zhunan, Taiwan. Authors of the paper are grateful to all the participants in this study.

Conflict of interest: None of the authors had a conflict of interest in relation to this manuscript.

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