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Muscle Strength: A Better Index of Mortality and Low Physical Performance than Muscle Mass in Elderly

근력: 노인에서 근육량보다 사망과 신체 실행기능 저하에 대한 더 나은 지표

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The Department of Medicine

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College of Medicine

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by

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ABSTRACT

Introduction: Sarcopenia is defined by a loss of muscle mass and strength. This study was performed to investigate the associations between muscle index (mass and strength) and 5-year mortality or low physical performance.

Methods: We included 396 subjects aged 65 years or older in the analysis. Muscle mass and fat mass were assessed by dual energy X-ray absorptiometry. Leg muscle strength and grip strength were measured using dynamometers. The 5-year mortality and low physical performance (Short Physical Performance Battery score < 9) were clinical outcome measures. Associations between muscle index and clinical outcomes were analyzed. Cox proportional hazard models for mortality and logistic regression models for low physical performance were built.

Results: Leg muscle strength and grip strength were significantly associated with 5-year mortality and low physical performance in men and women. Total muscle mass and appendicular skeletal mass in men and women and appendicular skeletal mass divided by height squared in men were associated with 5-year mortality. No association was found between muscle mass indices and 5-year low physical performance. Leg muscle strength was an independent predictor for low physical performance in men (OR = 0.971; 95% CI = 0.945-0.999; *P* = 0.041) after adjustment for age, fat, cognition and depression. Grip strength was an independent predictor for mortality (HR = 0.959; 95% CI = 0.928-0.991; *P* = 0.014) and low physical performance (OR = 0.950; 95% CI = 0.912-0.989; *P* = 0.012) in men after adjustment for age, fat, cognition and depression.

Conclusions: Muscle strength is a better indicator for 5-year adverse clinical outcomes of mortality and low physical performance than muscle mass. In men, muscle strength is an independent predictor of 5-year adverse clinical outcome.

Keywords: muscle strength, elderly, physical performance, mortality, sarcopenia

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INTRODUCTION

Sarcopenia is defined by a loss of muscle mass and strength with aging (1, 2). Sarcopenia is significantly associated with low physical performance, disability, hospitalizations, frailty and mortality (3-5). The muscle mass or strength (quality) related indices with various definitions have been considered as muscle indices. In the researches, sarcopenia has been conventionally defined by using only muscle mass index with different definitions (6) Several studies, however, have reported muscle strength declines faster than muscle mass in elderly, indicating the non-linear relationship between muscle mass and strength in old people (7, 8). Moreover, the age-associated loss of muscle strength is not completely explained by the loss of muscle mass (9, 10). Although there has been a conceptual definition for sarcopenia in terms of loss of muscle mass, the most appropriate muscle index for the definition of sarcopenia has not been agreed upon (2, 6, 11, 12).

From the clinical point of view, the proper indicator should be closely associated with clinical outcomes, and can predict adverse outcomes such as functional limitation, disability and mortality. It is unclear which muscle index is the most reliable indicator for adverse clinical outcomes in elderly. A recent cross-sectional study with 1,705 elderly revealed that muscle strength is the single best measure of age-related muscle change (12). In our previous study, we found that muscle mass is not associated with physical performance in weak older adult, emphasizing muscle strength as a better index from a clinical perspective (13). Several longitudinal studies have reported that low muscle strength is predictive of functional limitation and physical disability in older people (14, 15). To our knowledge, this is the first longitudinal study to investigate causal relationships of both muscle indices and adverse clinical outcomes with adjustment of possible covariates such as sex (16), obesity (17), cognition (18) and depression (19).

The present study, which was part of a prospective observational cohort study with 5-year follow-up, was conducted to investigate the relationship between muscle index and 5-year clinical outcomes in a population of community-dwelling elderly, and to determine independent predictors for adverse clinical outcomes after adjustment for potential confounders. We hypothesized that muscle strength would be a better predictor for clinical outcomes than muscle mass. The results may help identify a better indicator of sarcopenia in clinical practice.

MATERIALS AND METHODS

1. Study population

The analysis in this study was performed using data obtained during the Korean Longitudinal Study on Health and Aging (KLoSHA), a population-based prospective cohort study conducted on residents aged 65 years or older in Seongnam, South Korea. Seongnam is an urban area with a population composition similar to that of the South Korean population. A detailed description of the KLoSHA was published elsewhere (20). Briefly, a random sample of people aged 65 years or older was drawn among citizens of Seongnam, which had a total population of 931,019 in 2005, and 61,730 (6.6%) aged 65 years or older. Finally, 1000 subjects (561 women, 439 men) agreed to participate in the study. All subjects were ethnic Koreans. The baseline examination was conducted from September 2005 to September 2006. A total of 560 people (274 women, 286 men) for whom all of the baseline anthropometric parameters, body composition, and muscle strength measurement data were available were included. Among 560 subjects, 41 subjects died, and 355 completed the

5-year follow-up examinations between May 2010 and March 2012. The causes of drop-out were incomplete data (n = 22), and decline to follow-up (n = 142). All assessments were carried out at Seoul National University Bundang Hospital located in Seongnam. The study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital. Informed consent was obtained from all of the participants.

2. Demographic and anthropometric data

Trained and certified nurses, using standardized questionnaires, recorded age, gender, and comorbidities including hypertension, heart disease, stroke, parkinsonism, diabetes mellitus, cancer, chronic lung disease, arthritis and fracture. Regular exercise was defined as an exercise regimen of at least 30 min for 3 times or more per week. Physical activity levels were estimated by summing times spent walking, gardening, woodworking, lifting, or shoveling over a typical 24-hour period.

Height and body weight were measured to the nearest 0.1 cm or 0.1 kg, respectively, with subjects wearing light garments. Body mass index was calculated as weight divided by height squared (kg/m^2). Waist circumference was measured at the narrowest point between the lower limit of the rib cage and the iliac crest.

3. Muscle mass index

Dual energy X−ray absorptiometry (DXA) is an efficient method for research and clinical use to estimate muscle mass with minimal radiation (2). Total muscle mass (total lean mass) was measured by DXA (Lunar Corporation, Madison, WI, USA). Appendicular skeletal muscle mass (ASM) was calculated as the sum of the muscle mass of the 4 extremities. We used ASM divided by weight (ASM/Wt), and by height squared (ASM/Ht^2) as muscle mass indices (2).

4. Muscle strength index

As muscle strength indices, isokinetic knee extensor strength and grip strength were measured. The isokinetic muscle strength of the right knee extensors was measured using an isokinetic dynamometer (Biodex Isokinetic Tester; Biodex Medical Systems, Shirley, NY, USA) at an angular velocity of 60°/sec. Subjects performed two sets of 5 repetitions, with a 30-sec rest between sets, by exerting maximum pressure on the arm of the isokinetic device. The concentric peak torque values (Nm) obtained from five torque-angle curves in each set were used to evaluate the strength of knee extensors. Grip strength of right hand was measured with a hand dynamometer (Hand Evaluation Kit; Sammons Preston, Bolingbrook, IL, USA).

5. Evaluation of clinical outcomes

The study outcomes were 5-year all-cause mortality and low physical performance. All-cause mortality data over the 5-year period were obtained from the Ministry of Public Administration and Security national database. Follow-up duration was obtained from the difference between the date of baseline visit and the date of death or the end date of the follow-up. To evaluate physical performance, the Short Physical Performance Battery (SPPB) was evaluated at the 5-year follow-up visit. The SPPB is a standard functional outcome measure both for research and clinical outcomes (21). A total possible score of 12 was created using the sum of 4 possible points for 3 tests of chair stands, gait speed, and standing balance. Subjects were first asked to balance in a standing position with their feet side by side, semi-tandem, and fully tandem for 10 sec each. Subjects were next asked to walk a distance of 4 m as fast as possible. Finally, subjects were asked to stand from a sitting position in a chair and return to the seated position five times as quickly as possible while keeping their arms folded across their chest. Low physical performance was defined as an SPPB score of less than 9 (13, 22).

6. Covariates

We included fat mass, cognitive and depressive evaluations as covariates among the broad range of geriatric evaluations performed in KLoSHA (20) as potential confounders. Total fat mass was measure by DXA. Percentage fat mass was calculated as total fat mass x 100/body weight. Assessment of cognition was done using the validated mini-mental state examination (MMSE) of the Korean version of the CERAD-K assessment packet (23). The MMSE consists of 30 questions that assess orientation, attention, immediate- and short−term recall, language function, and the ability to follow simple verbal and written commands. MMSE scores range from 0 to 30 with a higher score indicating better global cognition. Severity of depression was evaluated using the Korean version of the geriatric depression scale (GDS) (24). The GDS is a questionnaire in which participants are asked to respond to the 30 questions by answering yes or no. GDS scores range from 0 to 30 with a higher score indicating more depressive state.

7. Statistical analysis

Statistical significance for the differences between the subjects with different clinical outcomes were assessed using an independent *t*−test or Mann−Whitney *U* test for continuous variables and Pearson's chi−square test or Fisher's exact test for categorical variables, as appropriate. Spearman's rho correlation between each variable was tested before the multivariate analyses. Significant variables from the univariate analyses and possible covariates were included in the final multivariate models. Adjusted Cox proportional hazard models were employed to evaluate the relationships between muscle index and mortality. To identify the independent predictors for low physical performance, a multivariate logistic regression analysis was performed. All tests were two-sided and a *P* value less than 0.05 were taken as statistically significant. The PASW statistics version 18.0 (SPSS Inc., IBM Corporation, Chicago, IL, USA) was used for statistical calculations.

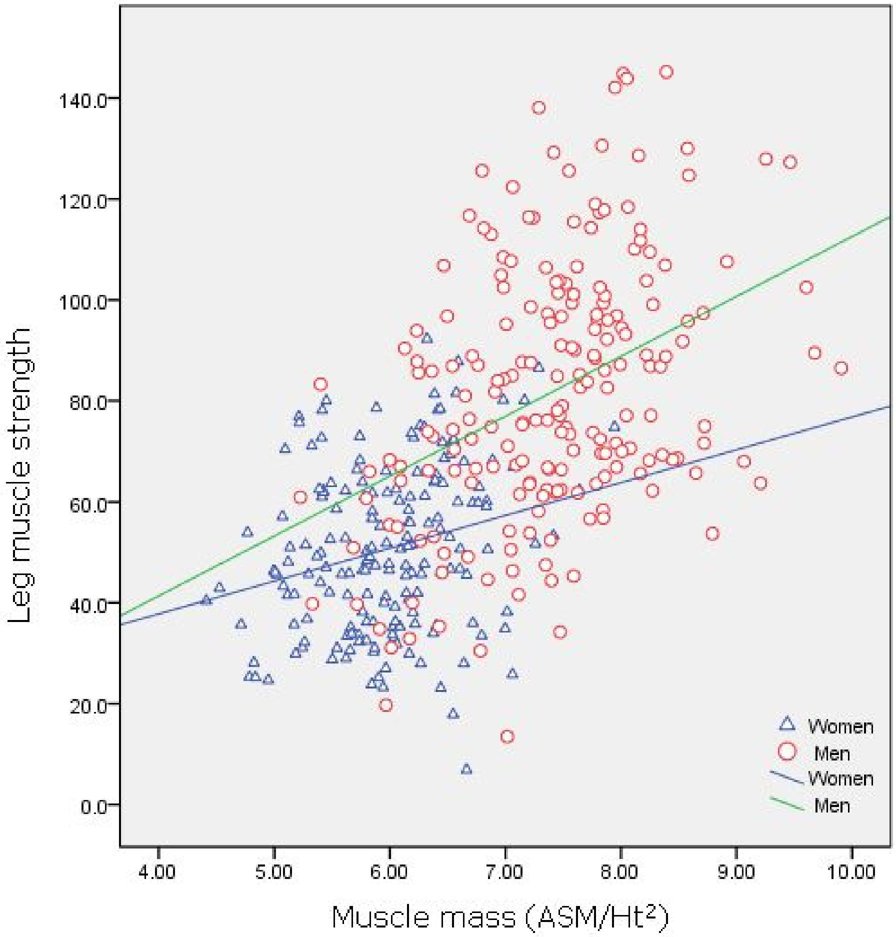
RESULTS

1. Study participants

Among 560 subjects who performed all of the baseline evaluations, 355 subjects (171 women, 184 men) completed the 5-year follow-up examination. During 5 years, 41 subjects (7.3%) of the cohort died. The 205 subjects who did not complete 5-year follow-up examination were older (P < 0.001), and had lower body weight (P = 0.048), higher waist to hip ratio (P = 0.003), lower total muscle mass (P = 0.035), lower ASM (P = 0.020), lower leg muscle strength (P < 0.001), lower grip strength (P < 0.001), lower MMSE (P < 0.001), and higher GDS (P < 0.001).

The correlations between baseline muscle mass and muscle strength in each gender were shown in Fig. 1. Men showed stronger linear correlation than women (R^2 = 0.06 in women; R^2 = 0.152 in men).

Fig. 1. Correlation between muscle mass and muscle strength by gender



2. Baseline factors associated with mortality

Table 1 shows the characteristics of the subjects alive and dead. Subjects who died were significantly older ($P < 0.001$ in women; $P < 0.001$ in men), and had lower total muscle mass ($P = 0.028$ in women; $P = 0.027$ in men), lower ASM ($P = 0.004$ in women; $P = 0.010$ in men), lower leg muscle strength ($P = 0.001$ in women; $P < 0.001$ in men), lower grip strength ($P < 0.001$ in women, $P < 0.001$ in men), and lower MMSE scores ($P = 0.001$ in women; $P = 0.001$ in men) in both men and women. In women, no regular exercise ($P = 0.032$), lower body weight ($P = 0.016$), lower body mass index ($P = 0.048$), lower fat mass ($P = 0.002$), lower percentage body fat ($P = 0.029$) were significantly associated with 5-year mortality. In men, higher serum cholesterol level ($P < 0.001$), lower ASM/Ht^2 ($P = 0.036$) and higher GDS scores ($P = 0.014$) were significantly associated with 5-year mortality.

Table 1. Characteristics of the subjects alive and dead

	Women (n = 186)			Men (n = 210)		
	Alive (n = 171)	Dead (n = 15)	*P* value	Alive (n = 184)	Dead (n = 26)	*P* value
Age (yr)	70.94±5.43	79.47±8.73	< 0.001	72.10±6.66	79.35±9.19	< 0.001
No regular exercise	86 (51.2)	12 (80.0)	0.032	58 (31.5)	11 (42.3)	0.273
Physical activity (hours)	3.94±1.56	3.73±1.52	0.630	4.32±1.89	3.84±1.64	0.254
Serum cholesterol (mg/dL)	199.85±35.15	198.36±34.26	0.878	196.62±34.53	221.96±27.85	<0.001
Serum albumin (g/dL)	4.03±0.27	4.01±0.20	0.512	4.09±0.27	4.05±0.31	0.790
Serum triglycerides (mg/dL)	124.78±54.82	159.86±84.29	0.066	130.13±73.45	154.42±97.05	0.054
Serum hsCRP (mg/dL)	0.27±0.73	0.20±0.26	0.807	0.26±0.76	0.30±0.66	0.931
Comorbidities						
Hypertension	78 (45.9)	9 (60.0)	0.294	76 (41.3)	15 (57.7)	0.114
Heart disease	29 (17.1)	6 (40.0)	0.041	21 (11.4)	4 (15.4)	0.524
Stroke or Parkinsonism	5 (2.9)	2 (13.3)	0.102	7 (3.8)	3 (11.5)	0.112
Diabetes mellitus	28 (16.5)	1 (6.7)	0.473	30 (16.3)	9 (34.6)	0.033
Cancer	15 (8.8)	1 (6.7)	1.000	15 (8.2)	4 (15.4)	0.266
Chronic lung disease	16 (9.4)	2 (13.3)	0.644	17 (9.2)	3 (11.5)	0.720
Arthritis	95 (55.9)	7 (46.7)	0.491	36 (19.6)	6 (23.1)	0.675
Fracture	30 (17.6)	3 (20.0)	0.734	25 (13.6)	4 (15.4)	0.764
Weight (Kg)	57.06±7.77	51.02±11.22	0.016	66.23±9.445	63.90±11.44	0.271
Body mass index (Kg/m^2)	24.63±2.95	22.77±3.76	0.048	24.32±3.16	23.90±3.74	0.544

Waist circumference (cm)	84.73±9.28	84.18±12.91	0.879	87.67±8.61	89.57±8.79	0.319
Waist to hip ratio	0.91±0.10	0.90±0.08	0.734	0.92±0.07	0.95±0.06	0.102
Total muscle mass (kg)	34.27±3.57	32.14±3.47	0.028	47.40±5.29	44.91±5.75	0.027
ASM (kg)	13.85±1.77	12.51±1.56	0.004	20.32±2.73	18.81±3.02	0.010
ASM/Wt (%)	24.47±2.46	25.07±3.06	0.373	30.87±2.99	29.83±3.83	0.195
ASM/Ht^2 (Kg/m^2)	5.99±0.61	5.81±0.59	0.255	7.45±0.85	7.08±0.87	0.036
Total fat mass (kg)	19.83±5.50	15.08±7.00	0.002	15.83±6.08	15.67±6.86	0.904
Percentage fat mass (%)	36.09±6.01	31.53±8.72	0.029	24.29±6.77	24.90±7.43	0.673
Leg muscle strength (Nm)	51.80±16.02	37.32±15.34	0.001	84.59±24.30	61.33±27.16	< 0.001
Grip strength (lbf)	31.52±12.54	19.27±13.84	< 0.001	58.24±17.85	42.54±15.35	< 0.001
MMSE (points)	24.30±3.49	19.20±5.87	0.001	26.35±2.50	23.50±5.78	0.001
GDS (points)	11.51±7.10	13.29±6.82	0.425	8.00±6.26	11.60±7.23	0.014

Values are means ± SD or *n* (%), as appropriate. CRP, C-reactive protein; ASM, Appendicular skeletal mass; ASM/Wt, Appendicular skeletal mass divided by weight; ASM/Ht^2, Appendicular skeletal mass divided by height squared; MMSE, Mini-Mental Status Examination; GDS, Geriatric depression scale.

3. Baseline factors associated with low physical performance

The characteristics of subjects with high physical performance (SPPB ≥ 9) and with low physical performance (SPPB < 9) are presented in Table 2. Older age (P < 0.001 in women; P < 0.001 in men), lower leg muscle strength (P < 0.001 in women; P < 0.001 in men), and lower grip strength (P = 0.040 in women; P < 0.001 in men) were associated with lower physical performance after 5 years in both gender. No regular exercise (P = 0.012), higher waist circumference (P = 0.014), lower MMSE (P < 0.001), higher GDS (P < 0.001) were associated with low physical performance only in women.

Table 2. Characteristics of the subjects with high performance and with low performance

	Women (n = 171)			Men (n = 184)		
	High performance (n = 130)	Low performance (n = 41)	*P* value	High performance (n = 162)	Low performance (n = 22)	*P* value
Age (yr)	70.70±5.35	75.43±7.80	< 0.001	71.22±5.79	78.55±8.97	< 0.001
No regular exercise	58 (45.7)	28 (68.3)	0.012	51 (31.5)	7 (31.8)	0.975
Physical activity (hours)	4.07±1.55	3.52±1.53	0.051	4.41±1.92	3.68±1.52	0.089
Serum cholesterol (mg/dL)	198.76±35.66	203.40±33.64	0.467	196.76±34.50	195.64±35.54	0.887
Serum albumin (g/dL)	4.02±0.28	4.08±0.24	0.258	4.09±0.27	4.14±0.28	0.364
Serum triglycerides (mg/dL)	126.14±57.98	120.35±43.30	0.830	128.76±74.18	140.05±68.65	0.248
Serum hsCRP (mg/dL)	0.26±0.49	0.33±1.21	0.183	0.28±0.81	0.09±0.10	0.327
Comorbidities						
Hypertension	61 (47.3)	17 (41.5)	0.514	68 (42.0)	8 (36.4)	0.616
Heart disease	25 (19.4)	4 (9.8)	0.154	19 (11.7)	2 (9.1)	1.000
Stroke or Parkinsonism	1 (0.8)	4 (9.8)	0.012	6 (3.7)	1 (4.5)	0.596
Diabetes mellitus	19 (14.7)	9 (22.0)	0.277	25 (15.4)	5 (22.7)	0.366
Cancer	13 (10.1)	2 (4.9)	0.527	13 (8.0)	2 (9.1)	0.696
Chronic lung disease	14 (10.9)	2 (4.9)	0.363	14 (8.6)	3 (13.6)	0.434
Arthritis	70 (54.3)	25 (61.0)	0.451	28 (17.3)	8 (36.4)	0.045
Fracture	19 (14.7)	11 (26.8)	0.077	23 (14.2)	2 (9.1)	0.743

Weight (Kg)	56.87±7.51	57.64±8.60	0.583	66.37±9.12	65.18±11.91	0.589
Body mass index (Kg/m2)	24.45±2.96	25.18±2.87	0.169	24.40±3.03	23.70±4.07	0.455
Waist circumference (cm)	83.78±9.21	87.84±8.97	0.014	87.46±8.38	89.09±10.10	0.431
Waist to hip ratio	0.90±0.10	0.94±0.12	0.102	0.92±0.07	0.94±0.06	0.133
Total muscle mass (kg)	34.33±3.67	34.08±3.28	0.700	47.55±5.10	46.30±6.55	0.299
ASM (kg)	13.92±1.78	13.63±1.78	0.376	20.39±2.61	19.80±3.54	0.463
ASM/Wt (%)	24.66±2.40	23.87±2.58	0.074	30.93±2.81	30.41±4.16	0.573
ASM/Ht^2 (Kg/m2)	6.00±0.62	5.96±0.60	0.699	7.49±0.80	7.17±1.10	0.202
Total fat mass (kg)	19.54±5.35	20.77±5.94	0.212	15.76±5.72	16.31±8.40	0.770
Percentage fat mass (%)	35.73±5.97	37.23±6.09	0.164	24.23±6.40	24.74±9.25	0.803
Leg muscle strength (Nm)	54.52±15.32	43.15±15.29	< 0.001	87.20±23.62	66.01±21.16	< 0.001
Grip strength (lbf)	32.64±12.82	28.02±11.04	0.040	60.24±17.25	43.50±15.33	< 0.001
MMSE (points)	25.04±3.03	21.98±3.83	< 0.001	26.50±2.38	25.23±3.05	0.051
GDS (points)	10.30±3.58	15.32±7.41	< 0.001	7.77±6.01	9.68±7.82	0.403

Values are means ± SD or *n* (%), as appropriate. ASM, Appendicular skeletal mass; ASM/Wt, Appendicular skeletal mass divided by weight; ASM/Ht^2, Appendicular skeletal mass divided by height squared; MMSE, Mini-Mental Status Examination; GDS, Geriatric depression scale.

4. Independent predictors of mortality

The Cox regression models to identify mortality risks for muscle indices are shown in Table 3. For each of muscle strength index, leg muscle and grip strength, separate model was constructed (Model 1 and 2). Because strong correlations were found between total muscle mass, ASM, and ASM/Ht^2 (Spearman ρ = 0.685 to 0.960), only ASM/Ht^2 was included in the final model as muscle mass index. ASM/Wt was also not included in the model because of moderate to strong correlation with fat index such as total fat mass and percentage fat mass (Spearman ρ = −0.626 to −0.758). All models were adjusted for age, percentage fat mass, MMSE and GDS. In women, regular exercise was included in model, and serum cholesterol level was included in men.

In women, there was no relationship between muscle indices and mortality risk. In men, the subjects with lower grip strength showed a higher risk of death (HR = 0.959; 95% CI = 0.928−0.991; P = 0.014) after adjusting for age, percentage fat mass, MMSE, GDS and serum cholesterol. Muscle mass index, ASM/Ht^2, was not associated with higher mortality risk in men.

5. Independent predictors of low physical performance

The logistic regression models to identify independent predictors for low physical performance are shown in Table 3. As with Cox regression models for mortality, separate models were constructed for each of muscle strength index (Model 1 and 2). Considering strong correlations between muscle mass indices (Spearman ρ = 0.705 to 0.956), only ASM/Ht^2 was included in the final model. ASM/Wt was also not included in the model because of moderate to strong correlation with fat index (Spearman ρ = −0.614 to −0.772). All models were adjusted for age, percentage fat mass, MMSE and GDS. The models of women were additionally adjusted for regular exercise.

In women, both of muscle strength and mass indices were not independent predictors for low physical performance in 5 years adjusting for covariates. In men, lower leg muscle strength (OR = 0.971; 95% CI = 0.945−0.999; P = 0.041) and grip strength (OR = 0.950; 95% CI = 0.912−0.989; P = 0.012) were independent predictors for low physical performance after adjustment for covariates. Muscle mass index, ASM/Ht^2, was not an independent predictor for low physical performance in men.

Table 3. Predictors for adverse clinical outcomes of mortality and low physical performance

	Women		Men	
	HR or OR (95% CI)*	*P* value	HR or OR (95% CI)*	*P* value
Predictors of mortality, Model 1 (Leg muscle strength)				
Leg muscle strength	0.995 (0.947–1.046)	0.856	0.986 (0.965–1.007)	0.189
ASM/Ht^2	0.595 (0.225–1.573)	0.295	0.928 (0.543–1.584)	0.784
Age	1.072 (0.984–1.169)	0.111	1.055 (0.998–1.115)	0.060
Percentage fat mass	0.918 (0.844–0.999)	0.048	1.012 (0.957–1.070)	0.678
MMSE	0.859 (0.733–1.005)	0.058	0.933 (0.832–1.047)	0.239
GDS	1.015 (0.915–1.127)	0.772	1.060 (0.997–1.127)	0.063
Regular exercise	0.593 (0.103–3.405)	0.558	NA	
Serum cholesterol	NA		1.013 (1.000–1.027)	0.043
Predictors of mortality, Model 2 (Grip strength)				
Grip strength	0.986 (0.935–1.041)	0.615	0.959 (0.928–0.991)	0.014
ASM/Ht^2	0.608 (0.239–1.548)	0.297	0.890 (0.550–1.440)	0.634
Age	1.066 (0.978–1.162)	0.149	1.031 (0.974–1.091)	0.293
Percentage fat mass	0.913 (0.841–0.991)	0.029	0.993 (0.942–1.047)	0.803
MMSE	0.867 (0.742–1.012)	0.071	0.968 (0.876–1.070)	0.528
GDS	1.019 (0.924–1.124)	0.708	1.081 (1.020–1.147)	0.009
Regular exercise	0.955 (0.200–4.563)	0.954	NA	
Serum cholesterol	NA		1.018 (1.005–1.030)	0.005

Predictors of low performance, Model 1 (Leg muscle strength)				
Leg muscle strength	0.968 (0.937–1.000)	0.053	0.971 (0.945–0.999)	0.041
ASM/Ht^2	1.118 (0.524–2.386)	0.772	1.004 (0.521–1.936)	0.989
Age	1.082 (1.000–1.171)	0.050	1.103 (1.029–1.183)	0.005
Percentage fat mass	1.060 (0.988–1.138)	0.105	1.028 (0.963–1.097)	0.413
MMSE	0.871 (0.762–0.995)	0.043	0.980 (0.797–1.206)	0.851
GDS	1.089 (1.022–1.159)	0.008	1.042 (0.966–1.124)	0.285
Regular exercise	0.720 (0.303–1.713)	0.458	NA	
Predictors of low performance, Model 2 (Grip strength)				
Grip strength	0.998 (0.963–1.036)	0.933	0.950 (0.912–0.989)	0.012
ASM/Ht2	0.929 (0.439–1.966)	0.847	0.956 (0.521–1.754)	0.884
Age	1.095 (1.010–1.187)	0.028	1.083 (1.012–1.159)	0.021
Percentage fat mass	1.051 (0.980–1.126)	0.162	1.024 (0.959–1.093)	0.481
MMSE	0.830 (0.726–0.948)	0.006	0.930 (0.768–1.127)	0.461
GDS	1.089 (1.024–1.158)	0.007	1.053 (0.976–1.135)	0.180
Regular exercise	0.767 (0.325–1.808)	0.545	NA	

* HR for predictors of mortality or OR for predictors of low performance; ASM/Ht^2, Appendicular skeletal mass divided by height squared; MMSE, Mini–Mental Status Examination; GDS, Geriatric depression scale.

DISCUSSION

The results of the current study suggest that muscle strength index is a better indicator of 5-year adverse clinical outcomes than a muscle mass index. Muscle strength indices were more closely associated with 5-year mortality and low physical performance than muscle mass indices. Muscle mass indices were not independent predictors for 5-year clinical outcomes in both genders. In men, muscle strength indices were independent predictors for 5-year clinical outcomes after adjustment for muscle mass, age, fat, cognition, and depression. In women, muscle strength indices were not independent predictors for 5-year clinical outcomes.

Several studies have indicated that muscle strength is associated with mobility decline (25), physical performance (12, 26, 27). Most of these evidences, however, were the results of cross-sectional analysis. Therefore, the causal relationship between muscle strength and clinical outcomes have been undisclosed. Our longitudinal study showed that muscle strength, evaluated by isokinetic knee extensor strength and grip strength, was significantly associated with 5-year mortality and low physical performance of both men and women in univariate analyses. After the adjustment for potential confounders, muscle strength was an independent predictor for 5−year clinical outcomes in men

Multiple definitions of muscle mass are used across studies (6). There is still controversy regarding the most proper muscle mass index according to the outcome measures (2, 16, 28). Among these definitions, we assessed total muscle mass, ASM, ASM/Wt, ASM/Ht^2. Our study showed that total muscle mass and ASM were associated with 5−year mortality. ASM/Ht^2 was correlated with 5−year mortality only in men. No association was found between muscle mass index and 5−year physical performance. The muscle mass index was not an independent predictor for mortality and low physical performance.

Our results demonstrate that the muscle strength indices are better indicators of mortality and physical function than muscle mass indices. Based on these results, the alogorithm for sarcopenia case finding suggested by European Working Group on Sarcopenia should be modified (2). In this algorithm, sarcopenia is excluded if the muscle mass is normal in an older subject with slow gait speed (≤ 0.8m/s). Our findings suggest that muscle strength should be measured instead of muscle mass to find a clinically meaningful sarcopenic subject.

In the current study, each gender showed a series of different relationships between body composition data including muscle indices and clinical outcomes. Many previous studies regarding sarcopenia and body composition have employed stratified analysis by gender (6, 16, 27). Non-linear correlation between muscle mass and muscle strength in women (shown in Fig. 1) partially explains the poorer association between muscle mass indices and clinical outcomes in women. Considering that both of muscle mass and strength were not longitudinally associated with clinical outcomes in women, another index beyond muscle mass or strength is necessary in older women.

A few study reported that physical activity was associated with physical mobility decline and mortality in older persons (25, 29). The proportions of the subjects who did not exercise regularly were higher in 5-year mortality group and low physical performance group in women. In men, however, this association was not found. Although regular exercise was not an independent predictor for clinical outcomes, clinicians may recommend regular exercise in elderly women. Because we used only a simple questionnaire to assess regular exercise, future studies with more objective measure of physical activity should be performed to unravel the exact association between physical activity, exercise and clinical outcomes.

The associations between high fat index and low physical performance have been suggested mostly in women (17, 30, 31). In current study, however, low total fat mass and percentage fat mass were associated 5-year mortality in women. We found no association between fat index and low physical performance. A cross-sectional study using the same cohort with ours reported similar results of no association between fat index and low physical performance (16). These inconsistent results across each study might be due to variable definition of fat index. Whereas we used fat index with a continuous variable as one of covariates, most of the studies categorized the fat index into a discrete variable. In addition, a study reported ethnic difference of fat infiltration between black and white (30). Therefore, ethnicity may be a possible confounder for these inconsistent associations across studies.

Previous studies have demonstrated that cognitive impairment and depression are associated with low physical performance (18, 19). In the current study, cognitive impairment, evaluated by MMSE, was associated with mortality in both genders, and with low physical performance in women. Depressive state was significantly associated with 5-year mortality in men, and with low physical performance in women. A prospective cohort study reported that depressive symptoms were predictive of greater decline in physical performance (19). Although the stratified analysis according to gender was not performed in this study, our study showed a similar result in women. In the multivariate models, depression was an independent predictor for mortality in men, and for low physical performance in women. Cognitive impairment was an independent predictor for low performance in women. Therefore, screening and proper management of these symptoms may be important to prevent death and functional decline.

The present study has certain limitations. A large number of subjects were lost to follow-up. There were significant differences in the baseline factors between the subjects who followed through and those who dropped out. The poorer baseline scores for those who dropped out may have caused a healthy survivor bias effect on the results of this study. Because we employed stratified analysis according to the gender, the number of subjects was further decreased in each subgroup. In addition, we did not classify the study subjects according to the definitions of sarcopenia or obesity. The categorization of subjects may provide another glimpse of the complex relationships between body composition and clinical outcomes.

In conclusion, muscle strength is a better indicator of 5-year mortality and low physical performance than muscle mass. Muscle strength was significantly associated with 5-year clinical outcomes in both genders. In men, most importantly, muscle strength was an independent predictor of 5-year clinical outcomes. Future researches should define sarcopenia by measuring the muscle strength and/or muscle mass.

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국문 초록

서론: 근감소증은 근육량과 근력의 감소로 정의된다. 본 연구는 근육 연관 지수 (근육량 및 근력)와 5 년 후 사망 및 신체 실행기능 저하의 관련성을 조사하기 위해 시행되었다.

방법: 65 세 이상 396 명을 대상으로 하여 연구를 시행하였다. 근육량과 지방량은 이중에너지 방사선 흡수계측법(dual energy X-ray absorptiometry)을 사용하여 평가하였다. 하지 근력과 악력은 역량계(dynamometer)를 사용하여 측정하였다. 5 년 후 사망과 신체 실행기능 저하 (간편신체수행검사, Short Physical Performance Battery < 9)를 임상적 결과 측정 기준으로 하였다. 근육 연관 지수와 임상적 결과 사이의 연관성을 분석하였다. 사망에 대한 콕스 비례 위험 모형 (Cox proportional hazard model)과 신체 실행기능 저하에 대한 로지스틱 회귀 모형 (logistic regression model)을 만들었다.

결과:

남녀 모두에서 하지 근력과 악력은 5년 후 사망 및 신체 실행기능 저하와 유의한 연관이 있었다. 여성과 남성에서 총근육량과

사지골격 근육량 (appendicular skeletal mass) 및 남성에서 사지골격 근육량을 키의 제곱으로 나눈 지표는 5년 후 사망과 연관되어 있었다. 근육량 연관 지수와 5년 후 신체 실행기능저하 사이에는 연관성이 발견되지 않았다. 하지 근력은 남성에서 나이, 지방량, 인지, 우울증을 보정한 이후에도 신체 실행기능저하 (OR = 0.971; 95% CI = 0.945–0.999; P =0.041)에 대한 독립적인 예측 인자였다. 악력은 남성에서 나이, 지방량, 인지, 우울증을 보정한 후에도 사망 (HR = 0.959; 95% CI = 0.928–0.991; P = 0.014)과 신체 실행기능저하 (OR = 0.950; 95% CI = 0.912–0.989; P = 0.012)의 독립적 예측 인자였다.

결론: 근력은 근육량보다 5 년 후 사망 및 신체 실행기능저하와 더 큰 연관을 보이는 지표이다. 남성에서는 근력이 5 년 후 사망 및 신체 실행기능저하에 대한 독립적인 예측인자이다.

주요어 : 근력, 노인, 신체 실행기능, 사망, 근감소증

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