Age- and sex-related differences in myosin heavy chain isoforms and muscle strength, function, and quality: a cross-sectional study

Seung-Lyul Oh¹ / Sang Hoon Yoon² / Jae-Young Lim¹,3

1. Aging & Mobility Biophysics Laboratory, Department of Rehabilitation Medicine, Seoul National University Bundang Hospital, Seongnam-si, Republic of Korea
2. Department of Neurosurgery, The Armed Forces Capital Hospital, Seongnam, Republic of Korea
3. Institute on Aging, Seoul National University, Seoul, Republic of Korea

INTRODUCTION

Muscle strength normally declines with aging, and its measurement is an important component of physical examination for the evaluation of physical function. Muscle strength reaches its peak at ages between 25 and 35 years and plateaus until the age of >40 years, although it may slightly decrease and starts to quickly decline starting at the age of 60 years. Although the decline rates of muscle strength after the age of 65 years vary for each individual, it has been reported that an average of 4.5–5.5% of muscle strength is lost every 5 years. Therefore, muscle strength decreases by >30% on average by the seventh and eighth decade of life among the elderly.

Maintenance of muscle mass and strength is an important contributing factor to optimal health and physical functional status in older adults, as the loss in muscle mass and strength with increasing aging results in sarcopenia and ultimately increases susceptibility to injury and prevalence of their mobility limitations. Although many previous studies have shown sex-related differences in muscle mass, strength, and quality with aging, few have reported sex-related differences in these muscle parameters in relation to sarcopenia in the Korean population.

Skeletal muscle mass index (SMI) (appendicular skeletal muscle mass [ASM]/height squared) and muscle strength in Korean men decrease with aging. In contrast, in Korean women, no significant differences between the young and older groups have been observed, who instead showed a tendency toward an increase with aging. Kim et al. reported sex-related differences in muscle mass and SMI using data from the Korean National Health and Nutrition Examination Survey, which is a nationwide population-based cross-sectional study, from 2008 to 2010. Total muscle mass and ASM in men dramatically increased in the third decade of their life and then gradually decreased until the age of 90 years, with a slight acceleration after the age of 60 years. However, changes in SMI and muscle strength with aging occurred quite differently in women, indicating that total muscle mass and ASM in women increased slowly until the fourth decade of their

[Keywords] Myosin heavy chain, Muscle strength, Muscle quality, Sex-related difference, Aging
MHC isoforms and muscle strength and quality

Table 1. Participant characteristics

| Characteristic | Y (n=28) | O (n=25) | YM (n=17) | OM (n=15) | YW (n=11) | OW (n=10) | Interaction (gender X age) |
|----------------|---------|---------|----------|----------|---------|---------|---------------------------|
| Age, yr.       | 29.39±4.57 | 70.36±3.43 | 29.23±4.51 | 71.87±3.42 | 29.64±4.88 | 68.12±9.1 | 478.08*** |
| Height, cm     | 170.42±8.92 | 161.42±6.86" | 176.9±4±2.48 | 165.2±0.9a | 160±35±4.57 | 155.7±6.0±7b | 62.317*** |
| Weight, kg     | 68.2±13.37 | 64.5±8.83 | 75.7±19.04 | 67.9±5.83a | 56.7±10.64 | 59.4±10.33 | 12.6±8*** |
| BMI, kg/m²     | 23.34±3.31 | 24.7±3.18 | 24.17±2.67 | 24.96±2.55 | 22.06±3.89 | 24.5±4.08 | 2.119 |

The data presented as mean±SD. Y, young adult; O, older adult; YM, young men; OM, older men; YW, young women; OW, older women. The body mass index (BMI) was defined as body weight divided by height squared (body weight/height²). *P values were calculated by independent T-test. Significantly different between groups (a, YM vs. OM; b, YW vs. OW). Statistical significance was set at p<0.05.

In total, 53 healthy participants provided informed consent and were included in this study. Participants were divided into two different age groups: young (Y, n=28, 20–40 years) and older (O, n=25, >65 years). Each group was further divided according to sex: men (M, n=32) and women (W, n=21). Finally, the four groups in this study were as follows: young (17 young men, 11 young women) and older (15 older men, SPPB score [M±SD]: 11±6.1±0.6; 10 older women, SPPB score [M±SD]: 11.6±0.7). Participants’ characteristics are shown in Table 1.

Experimental procedures

All participants in this study visited the research laboratory thrice. During the first and second visits, the screening procedure for each participant and the measurement of body composition, muscle strength, and muscle quality were performed, respectively. During the third visit, skeletal muscle specimens were acquired through biopsy from all participants for the analysis of MHC isoforms. Participants were restricted to excessive food intake and strenuous physical activity 24 h before each visiting time.

Body composition

Total and regional lean mass and total fat mass were assessed using dual-energy X-ray absorptiometry (DEXA) (PIXI; GE Medical Systems Lunar, Madison, WI, USA). The legs were defined using a line bisecting the femoral neck. Bone mineral content was subtracted from the total and regional lean mass to calculate the quantity of total non-bone lean mass, which primarily represents the skeletal muscle. Fat mass was estimated for the whole body as well and was examined for these analyses. Moreover, body mass index (weight divided by height squared) in kg/m² was used to measure body composition. SMI was defined as ASM divided by height squared.

Muscle strength, function, and quality

We measured grip strength using a hand dynamometer (Jamar 5030J; Bolingbrook, IL, USA) and maximal voluntary isokinetic/isometric strength and isotonic power of the dominant knee extensor and flexor using an isokinetic dynamometer (Primus RS; BTE, Hanover, MD, USA). Grip strength was measured twice on each hand, with the elbow flexed at a right angle and the forearm in neutral position. The maximum of the four readings generated was considered the maximal grip strength. Maximal voluntary concentric isokinetic torque was assessed in Newton-meters (Nm) at angular velocities of 60 deg/s,
and it also presented as relative isokinetic strength which is a value divided by body mass (Nm/kg, %). For at least three times but no more than six, maximal efforts were allowed to produce three overlying curves, and peak maximal torque production was recorded. Peak isometric knee extensor torque at 90° of knee flexion was measured following the same procedure. For this test, participants were asked to extend their knee as fast and hard as they could to maintain force production for 3 s. Maximal isotonic power of the muscle was measured in watts (W). Muscle quality was evaluated using the strength-to-muscle mass ratio\textsuperscript{27}. We defined the upper- and lower-body muscle qualities as the ratio of the grip strength (in kg) and isokinetic torque (in Nm) at the arm and knee to the lean mass (in kg) in the arm and leg, respectively, as measured using DEXA.

Muscle biopsy

Muscle specimens were percutaneously obtained under local anesthesia from the vastus lateralis using a modified Bergström needle (11750-06 and 11750-07; Dixons Surgical Instruments, Wickford, UK) biopsy technique with suction. We performed muscle biopsy under ultrasound guidance to minimize vessel and nerve damage. Muscle samples were embedded in O.C.T. compound (Tissue-Tek; CA, USA), frozen with liquid nitrogen-cooled isopentane, and stored at -80°C for electrophoretic determination of MHC isoform composition.

Myosin heavy chain

We performed separation and identification of MHC isoforms following a previously described method\textsuperscript{28}. Briefly, muscle blocks were cut into cryosections of 10 µm thickness in a cryostat (Thermo Electronic) cooled to -20°C. Myosin isoforms were separated using 6% sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) on a Bio-Rad Mini-PROTEAN gel system (Bio-Rad, Hercules, CA, USA). Electrophoresis was performed at 140 V for 10 h. The gels were subsequently stained with Bio-Safe Coomassie blue (Bio-Rad, Hercules, CA, USA). In the MHC isoform region, three major bands were separated in order of migration to MHC I or Ila and IIX depending on their molecular masses compared with those of marker proteins. Each MHC isoform was expressed as percentage of total densitometry. Densitometry was performed using ImageJ software (National Institutes of Health, MD, USA) (Figure 1).

Statistical analysis

All data are presented as mean±SD. A two-way analysis of variance was used to determine the main effects of sex and age and age-by-sex group interaction on muscle mass, strength, and quality. Subsequent comparisons of age groups were performed using post-hoc analysis by independent t-test. Pearson’s correlation (r) coefficients were used to assess the relationship between MHC isoforms and muscle strength with respect to sex and age. All statistical analyses were performed using SPSS version 20.0 (IBM, Armonk, NY, USA), and p-values of <0.05 were considered statistically significant.

RESULTS

Anthropometric characteristics

The anthropometric characteristics of participants are summarized in Table 1. Older men were significantly smaller ($p<0.001$) and lighter ($p=0.007$) than young men. In contrast, older women were significantly smaller in height than young women ($p=0.044$), but no significant difference in weight was observed, with older women even showing a strong tendency.

Body composition

Data on body composition including skeletal muscle mass (SMM), lean body mass (LBM), fat mass, and SMI according to age and sex are presented in Table 2. There were significant interactions between age-by-sex effects on SMM ($F=19.553$, $p<0.001$), LBM ($F=38.763$, $p<0.001$), percentage of body fat ($F=7.817$, $p<0.001$), and SMI ($F=15.294$, $p<0.001$). The SMM and LBM did not differ between young and older adults. However, these parameters were significantly greater in young men than in older men (SMM: 18.6%, $p=0.026$; LBM: 10.1%, $p=0.014$). In contrast, there were no significant differences in women according to age groups.
### Table 2. The differences in body composition between younger and older adults

| Characteristic | Y  (n=28) | O  (n=25) | YM (n=17) | OM (n=15) | YW (n=11) | OW (n=10) | Interaction (gender X age) |
|----------------|-----------|-----------|-----------|-----------|-----------|-----------|---------------------------|
| Skeletal muscle mass, kg | 29.48±6.82 | 24.81±3.96 | 34.02±4.28 | 27.71±2.52 | 23.8±4.71 | 21.18±1.69 | 19.55*** |
| Lean body mass, kg | 41.69±11.02 | 45.04±6.80 | 55.36±6.0 | 49.77±31.36 | 35.48±5.65 | 37.95±38.47 | 38.76*** |
| Fat mass, kg | 17.51±6.25 | 16.88±6.33 | 15.46±4.53 | 15.62±4.84 | 18.44±6.88 | 18.77±2.98 | 0.793 |
| % body fat, % | 30.19±8.53 | 26.98±8.02 | 21.66±4.43 | 23.59±6.31 | 34.06±6.95 | 32.06±7.84 | 7.817*** |
| SMI, kg/m² | 0.07±0.01 | 0.07±0.01 | 0.08±0.94 | 7.97±0.71 | 5.86±1.12 | 6.37±0.79 | 15.294*** |

The data presented as means±SD. Y, young adult; O, older adult; YM, young men; OM, older men; YW, young women; OW; older women. The skeletal muscle mass index (SMI) was defined as the ratio of appendicular skeletal muscle mass (ASM) by height squared. P values were calculated by independent T-Test. Significantly different between groups (a, YM vs. OM; b, YW vs. OW). Statistical significance was set at p<0.05.

### Table 3. The differences in muscle strength, function and quality between younger and older adults

| Characteristic | Y  (n=28) | O  (n=25) | YM (n=17) | OM (n=15) | YW (n=11) | OW (n=10) | Interaction (gender X age) |
|----------------|-----------|-----------|-----------|-----------|-----------|-----------|---------------------------|
| Grip strength, kg | 41.92±14.09 | 29.43±7.13* | 51.35±8.84 | 33.21±6.32 | 27.34±5.06 | 23.76±3.73 | 18.751*** |
| Isometric strength, kg | 168.83±50.24 | 136.1±43.83* | 221.9±9.39 | 156.16±40.75a | 139.88±37.18 | 106.09±29.49b | 12.446*** |
| Isotonic power, W | 104.00±42.90 | 72.33±26.57* | 152.62±25.78 | 87.76±20.8a | 77.48±20.5 | 49.18±14.74b | 33.423*** |
| Isokinetic extensor strength, Nm | 137.65±53.18 | 87.75±21.70* | 173.84±31.57 | 96.79±17.0a | 81.72±19.32 | 74.19±21.59 | 21.286*** |
| Relative isokinetic extensor strength, Nm/kg (%) | 197.88±60.45 | 136.85±32.25* | 232.62±50.1 | 144.17±31.46a | 144.19±25.04 | 125.87±31.78 | 24.350*** |
| Isokinetic flexor strength, Nm | 69.67±25.52 | 44.41±15.80* | 86.3±17.32 | 50.56±16.03a | 43.97±9.06 | 35.18±10.39 | 10.395*** |
| Relative isokinetic or strength, Nm/kg (%) | 101.15±29.18 | 68.79±22.85* | 115.72±26.41 | 75.07±25.64a | 78.65±16.3 | 59.36±14.33b | 16.089*** |
| Upper-body muscle quality, kg/kg | 15.49±2.32 | 11.60±2.09* | 13.61±2.07 | 11.13±1.87a | 16.35±1.95 | 12.31±2.3b | 14.758*** |
| Lower-body muscle quality, Nm/kg | 14.38±2.79 | 12.33±2.78* | 16.09±3.23 | 12.12±2.18a | 13.61±2.32 | 12.67±3.62 | 2.843 |

The data presented as means±SD. Y, young adult; O, older adult; YM, young men; OM, older men; YW, young women; OW; older women. Muscles quality was defined as the ratio of strength by lean mass. P values were calculated by independent T-Test. Significantly different between groups (a, YM vs. OM; b, YW vs. OW). Statistical significance was set at p<0.05.

### Table 4. The differences in myosin heavy chain isoforms between younger and older adults

| MHC isoforms | Y  (n=28) | O  (n=25) | YM (n=17) | OM (n=15) | YW (n=11) | OW (n=10) | Interaction (gender X age) |
|---------------|-----------|-----------|-----------|-----------|-----------|-----------|---------------------------|
| MHC-I | 43.84±16.84 | 56.56±14.18* | 36.72±15.74 | 54.44±16.04a | 54.21±12.9 | 59.53±11.19 | 6.677*** |
| MHC-IIa | 43.66±11.80 | 34.45±11.85* | 47.68±12.73 | 38.21±11.97a | 37.82±7.45 | 29.19±9.95b | 5.965*** |
| MHC-IIx | 12.50±10.22 | 9.00±9.27 | 15.62±10.56 | 7.36±9.61a | 7.97±8.11 | 11.3±8.73 | 2.329 |

The data presented as means±SD. Y, young adult; O, older adult; YM, young men; OM, older men; YW, young women; OW; older women. P values were calculated by independent T-Test. Significantly different between groups (a, YM vs. OM; b, YW vs. OW). Statistical significance was set at p<0.05.

### Table 5. The association of myosin heavy chain isoform composition with muscle strength and function

| MHC isoforms | lIa | lIa | lI |
|--------------|-----|-----|---|
| Age | -0.206 | -0.369** | 0.399** |
| Skeletal muscle mass | 0.188 | 0.521** | -0.487* |
| Total fat mass | 0.287 | -0.289 | 0.042 |
| SMI | 0.242 | 0.163 | -0.262 |
| Grip strength | 0.231 | 0.462** | -0.483*** |
| Isometric strength | 0.226 | 0.607*** | -0.593*** |
| Isotonic power | 0.282 | 0.455** | -0.512** |
| Isokinetic extensor strength | 0.199 | 0.511*** | -0.500*** |
| Isokinetic flexor strength | 0.215 | 0.492** | -0.495*** |
| Relative isokinetic extensor strength | 0.110 | 0.524*** | -0.459*** |
| Relative isokinetic flexor strength | 0.114 | 0.508*** | -0.448*** |
| Upper-body muscle quality | -0.201 | 0.042 | 0.088 |
| Lower-body muscle quality | 0.063 | 0.358* | -0.299 |

Pearson’s correlation coefficients are shown and statistical significant was set at p<0.05.
Differences in MHC isoforms and muscle strength and quality

Fig. 2. The association of myosin heavy chain isoform composition with muscle strength and function
(A) Association between MHC I and muscle strength, muscle function (B) Association between MHC IIa and muscle strength, muscle function
YM, young men; OM, older men; YW, young women; OW, older women. Pearson’s correlation coefficients are shown and statistical significant was set at \( p<0.05 \).
Differences in MHC isoforms and muscle strength and quality

Muscle strength, function, and quality

We assessed grip strength, isometric/isokinetic strength, and isotonic power as objective measurements of muscle strength and quality. The results of sex-related differences in muscle strength and quality with aging are presented in Table 3. Except for lower-body muscle quality ($F=2.843$, $p=0.051$), which showed no significant interaction between age-by-sex effects, there were significant interactions between the effects of grip strength ($F=18.751$, $p<0.001$), isometric strength ($F=12.446$, $p<0.001$), isometric power ($F=33.423$, $p<0.001$), isokinetic extensor ($F=21.286$, $p<0.001$) and flexor ($F=10.395$, $p<0.001$), strength, relative isokinetic extensor ($F=24.35$, $p<0.001$) and flexor ($F=16.089$, $p<0.001$) strength, and upper-body muscle quality ($F=14.758$, $p<0.001$). Older men showed significantly lower muscle strength, including grip strength (35.3%, $p<0.001$), isometric strength (29.6%, $p=0.001$), isometric power (42.5%, $p<0.001$), isokinetic extensor (44.3%, $p<0.001$) and flexor (41.4%, $p<0.001$) strength, and relative isokinetic extensor (38%, $p<0.001$) and flexor (35.1%, $p<0.001$) strength, than young men. The muscle quality was poorer in older men than in young men (upper-body: 18.2%, $p=0.022$; lower-body: 24.8%, $p=0.005$). In contrast, older women had significantly lower values for isometric strength (24.2%, $p=0.034$), isometric power (36.5%, $p=0.002$), relative isokinetic flexor strength (24.5%, $p<0.001$), and upper-body muscle quality (24.7%, $p<0.001$) only than young women, and other parameters of muscle strength and quality were not significantly different between age groups.

Myosin heavy chain isoforms

The results for the MHC isoforms from the vastus lateralis and the correlations of these isoforms with muscle strength and quality are presented in Tables 4 and 5 and Figure 2. The proportion of MHC I was significantly higher in older adults than in young adults ($p=0.005$), whereas the proportion of MHC Ila was significantly lower in older adults than in young adults ($p=0.008$). Moreover, the proportion of MHC IIX appeared lower in older adults than in young adults, albeit without significant difference. Although the proportion of MHC IIX ($F=2.329$, $p=0.087$) did not show significant interactions between age-by-sex effects, there were significant interactions between the effects of MHC I ($F=6.677$, $p=0.001$) and MHC IIX ($F=5.965$, $p=0.002$). The proportion of MHC I was significantly higher in older men than in young men ($p=0.005$); however, there were no significant differences in the case of women. The proportion of MHC Ila was significantly lower in older men and women than in young men and women ($p=0.045$ and $p=0.04$, respectively), whereas significant differences in MHC IIX between the young and older groups were observed in men ($p=0.033$), but not in women. In addition, in all groups except for young men, the proportion of MHC I was found to be 42.5–103.9% higher than that of MHC Ila, whereas the proportion of MHC IIX was 29.8% higher than that of MHC I in young men. As shown in Table 5 and Figure 2, there was a negative correlation between MHC I and SMM ($r=-0.487$, $p<0.05$), grip strength ($r=-0.483$, $p<0.001$), isometric strength ($r=-0.593$, $p<0.001$), isotonic power ($r=-0.512$, $p=0.001$), isokinetic strength (extensor: $r=0.500$, $p=0.001$; flexor: $r=0.495$, $p=0.001$), and relative isokinetic strength (extensor: $r=0.459$, $p=0.001$; flexor: $r=0.448$, $p=0.001$). In contrast, MHC Ila positively correlated with SMM ($r=0.521$, $p<0.01$), grip strength ($r=0.462$, $p=0.001$), isometric strength ($r=0.607$, $p<0.001$), isotonic power ($r=0.455$, $p=0.003$), isokinetic strength (extensor: $r=0.511$, $p<0.001$; flexor: $r=0.492$, $p<0.001$), relative isokinetic strength (extensor: $r=0.524$, $p<0.001$; flexor: $r=0.508$, $p<0.001$), and lower-body muscle quality ($r=0.358$, $p=0.023$). There was no significant association between MHC IIX and muscle mass, strength, function, and quality.

**DISCUSSION**

In the present study, we found sex-related differences in body composition (SMM, LBM), muscle strength (grip strength, isokinetic extensor and flexor strength, isometric strength, isotonic power), muscle quality, and MHC isoforms with aging in Korean men and women. During the aging process, age plays a major role in the correlation between MHC isoforms and body composition and muscle strength and quality in men, but it does not seem to have a significant effect on several measures of muscle parameters in women. These differences seem to occur because muscle strength and quality in men decrease with aging, with young and older women showing no difference. In particular, grip strength (27.34±5.06 vs. 23.76±3.73), isokinetic extensor (81.72±19.32 vs. 74.19±21.59) and flexor (43.97±9.06 vs. 35.18±10.39) strength, and lower-body muscle quality (13.61±3.22 vs. 12.67±3.62) were not significantly greater in young women than in older women. With respect to MHC isoform distributions, the proportion of MHC Ila and IIX and that of MHC I were significantly higher and lower, respectively, in young men than in older men. Only the proportion of MHC IIX was lower in older women than in young women, with no difference in the proportion of MHC I and IIX between the two groups.

Numerous studies have suggested that the decrease in SMM and muscle strength due to aging was characterized by a decline in the number of muscle fibers and, in particular, the atrophy of MHC Ila fibers\(^{15-20, 29-31}\). Landi et al.\(^{32}\) reported that older adults aged >75 years lose approximately 60% of their muscle strength. Further, they showed a similar linear pattern of age decline in both men and women across their entire life course. Interestingly, our study showed that these reductions differed by sex. In women, there were no significant differences in SMM, grip strength, and isokinetic knee strength between the young and older groups. Similarly, previous studies reported that the reduction in muscle quality\(^{36}\) and strength with weight loss was more pronounced in men than in women\(^{33}\). In the Survey of National Physical Fitness\(^{36}\), the grip strength was 44.5 kg in Korean men in their 20s.
(25–29 years of age) and 34.4 kg in men in their 70s (70–75 years of age), which was a difference of approximately 22.7%. In contrast, there was no significant difference in the grip strength between young and older women, with a difference of 13.1% (26 kg vs. 22.6 kg). Kim et al. also showed that the muscle mass and SMI were not significantly higher in Korean young women, indicating that the age-related difference was not significant in Korean women. In fact, the decline in muscle function including muscle strength attenuation is well known to be more remarkable in men than in women. However, we could explain the possible reasons for this sex-difference difference based on the muscle parameter findings in the present study. The level of muscle mass and strength in Korean young women is not considerably different from that in older women, compared with the differences in men. When it comes to analyses of data on MHC isoforms from the vastus lateralis, the proportion of MHC IIa fibers in young men was 29.8% higher than that of MHC I fibers, whereas the proportion of MHC I fibers in older men was 42.5% higher than that of MHC IIa fibers, suggesting the dominant reduction in fast-twitch type II fibers due to aging. Surprisingly, MHC IIa fibers were 30.2% less in Korean young women than MHC I fibers. We consider that low muscle strength and quality in Korean young women may be associated with low proportion of MHC IIa fibers. Interestingly, we showed that the proportion of MHC IIX in men significantly decreased with aging, whereas those in women tended to increase. The MHC IIX isoform increases in pathological conditions such as cerebral palsy and even in disuse-induced muscle wasting, and it overshoots during detraining after the heavy-load resistance exercise training period. However, in this study, the standard deviation for MHC IIX isoform might be too large to be associated with muscle strength and quality, unlike MHC IIa and I isoforms. MHC IIX isoform was not expressed in 18 of 53 participants (34%) in our study, who only had MHC I and IIa isoforms. In fact, MHC IIX is not often expressed in the human skeletal muscle.

This study has potential methodological limitations. Firstly, this is a cross-sectional study, and longitudinal studies are ideally required to be performed to validate our results. Secondly, our study has a limited sample size; hence, future studies with larger sample size and increased sampling areas are needed to confirm our findings. Finally, although muscle weakness due to aging is caused by various problems, we did not investigate metabolism, physical activities and lifestyle, living environment, and so on. In particular, this study did not investigate nutritional intake, which has an important effect on muscle function with aging. Nevertheless, this study is the first to report sex-related differences in MHC isoform compositions and muscle strength and quality with aging in the Korean population.

In conclusion, the results of this study indicate the existence of sex-related differences in muscle mass, strength, and quality with increasing age. The effects on muscle strength and quality with aging were significant in men, but not in women. Higher and lower proportions of MHC I and MHC IIa fibers, respectively, were inversely associated with muscle strength and quality. In particular, Korean young women showed lower muscle strength and quality, and the proportion of MHC isoforms was similar to that in the muscles of older women.

ACKNOWLEDGEMENTS

This study was supported by Seoul National University Bundang Hospital Research Fund (SNUBH-04-2011-005).

REFERENCES

1. Gómez-Cabello A, Carnicero JA, Alonso-Bouzón C, Tresguerras JÁ, Alfaro-Acha A, Ara I, Rodriguez-Mañas L, García-García FJ. Age and gender, two key factors in the associations between physical activity and strength during the ageing process. Maturitas. 2014;78:106-12.
2. Pedrero-Chamizo R, Gomez-Cabello A, Delgado S, et al. Physical fitness levels among independent non-institutionalized Spanish elderly: the elderly EXER-NET multi-center study. Arch Gerontol Geriatr. 2012;55:406–16.
3. Doherty TJ. Invited review: aging and sarcopenia. J Appl Physiol. 2003;95:1717–27.
4. Auyeung TW, Lee SW, Leung J, Kwok T, Woo J. Age-associated decline of muscle mass, grip strength and gait speed: a 4-year longitudinal study of 3018 community-dwelling older Chinese. Geriatr Gerontol Int. 2014;14:76-84.
5. Bai HJ, Sun JQ, Chen M, Xu DF, Xie H, Yu ZW, Bao ZJ, Chen J, Pan YR, Lu DJ, Cheng S. Age-related decline in skeletal muscle mass and function among elderly men and women in Shanghai, China: a cross sectional study. Asia Pac J Clin Nutr. 2016;25:326-32.
6. Bouchard DR, Héroux M, Janssen I. Association between muscle mass, leg strength, and fat mass with physical function in older adults: influence of age and sex. J Aging Health. 2011;23:313-28.
7. Daly RM, Rosengren BE, Alwis G, Ahlborg HG, Sernbo I, Karlsson MK. Gender specific age-related changes in bone density, muscle strength and functional performance in the elderly: a 10-year prospective population-based study. BMC Geriatrics. 2013;13:71.
8. Danneskiold-Samsøe B, Bartels EM, Bülow PM, Lund H, Stockmarr A, Holm CC, Wätjen I, Appleyard M, Bliddal H. Isokinetic and isometric muscle strength in a healthy population with special reference to age and gender. Acta Physiol. 2009;197:1-88.
9. Germain CM, Batsis JA, Vasquez E, McQuoid DR. Muscle Strength, Physical Activity, and Functional Limitations in Older Adults with Central Obesity. J Aging Res. 2016;2016:8387324.
10. Kasai T, Ishiguro N, Matsu i Y, Harada A, Takemura M, Yuki A, Kato Y, Otsuka R, Ando F, Shimokata H. Sex and age-related differences in mid-thigh composition and muscle quality determined by computed tomography in middle-aged and elder-
Differences in MHC isoforms and muscle strength and quality

Journal of Exercise Nutrition & Biochemistry


dy Japanese. Geriatr Gerontol Int. 2015;15:700-6.
11. Kimura M, Mizuta C, Yamada Y, Okayama Y, Nakamura E. Constructing an index of physical fitness age for Japanese elderly based on 7-year longitudinal data: sex differences in estimated physical fitness age. Age (Dordr). 2012;34:203-14.
12. Lindle RS, Metter EJ, Lynch NA, Fleg JL, Foard JL, Tobin J, Roy TA, Hurley BF. Age and gender comparisons of muscle strength in 654 women and men aged 20-93 yr. J Appl Physiol (1985). 1997;83:1581-7.
13. Milanović Z, Pantelić S, Trajković N, Sporiš G, Kostić R, James N. Age-related decrease in physical activity and functional fitness among elderly men and women. Clin Interv Aging. 2013;8:549-56.
14. Yanagawa N, Shimomitsu T, Kawanishi M, Fukunaga T, Kanehisa H. Sex difference in age-related changes in knee extensor strength and power production during a 10-times-repeated sit-to-stand task in Japanese elderly. J Physiological Anthropology: 2015:34:40.
15. Kim KM, Jang HC, Lim S. Differences among skeletal muscle mass indices derived from height, weight, and body mass index adjusted models in assessing sarcopenia. Korean J Intern Med. 2016;31:643-50.
16. Ministry of Culture, Sports and Tourism. The survey of national physical fitness. 2017.
17. Lexell J. Human aging, muscle mass, and fiber type composition. J Gerontol A Biol Sci Med Sci. 1995;50:11-6.
18. Short KR, Vittone JL, Bigelow ML, Proctor DN, Cohen-Schimke JM, Rys P, Nair KS. Changes in myosin heavy chain mRNA and protein expression in human skeletal muscle with age and endurance exercise training. J Appl Physiol (1985). 2005;99:95-102.
19. Trappe S, Gallagher P, Harber M, Carrithers J, Fluckey J, Trappe T. Single muscle fibre contractile properties in young and old men and women. J Physiol. 2003;552:47-58.
20. Aagaard P, Andersen JL. Correlation between contractile strength and myosin heavy chain isoform composition in human skeletal muscle. Med Sci Sports Exerc. 1998;30:1217-22.
21. Konopka AR, Trappe TA, Jemiolo B, Trappe SW, Harber MP. Myosin heavy chain plasticity in aging skeletal muscle with aerobic exercise training. J Gerontol A Biol Sci Med Sci. 2011;66:835-41.
22. Trappe S, Harber M, Creer A, Gallagher P, Slikva D, Minchev K, Whitsett D. Single human muscle fiber adaptations with marathon training. J Appl Physiol. 2006;101:721-7.
23. Gallagher P, Trappe S, Harber M, Creer A, Mazzetti S, Trappe T, Alkner B, Tesch P. Effects of 84-days of bedrest and resistance training on single muscle fibre myosin heavy chain distribution in human vastus lateralis and soleus muscles. Acta Physiol Scand. 2005;185:61-9.
24. Trappe S, Trappe T, Gallagher P, Harber M, Alkner B, Tesch P. Human single muscle fibre function with 84 day bed-rest and resistance exercise. J Physiol. 2004;557:501-13.
25. Slikva D, Rauz U, Hollon C, Minchev K, Trappe S. Single muscle fiber adaptations to resistance training in old (>80 yr) men: evidence for limited skeletal muscle plasticity. Am J Physiol Regul Integr Comp Physiol. 2008;295:273-80.
26. Visser M, Fuerst T, Lang T, Salamone L, Harris TB. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study—Dual-Energy X-ray Absorptiometry and Body Composition Working Group. J Appl Physiol. 1999;87:1513-20.
27. Newman AB, Haggerty CL, Goodpaster B, Harris T, Kritchevsky S, Nevitt M, Miles TP, Visser M; Health Aging And Body Composition Research Group. Strength and muscle mass quality in a well-functioning cohort of older adults: The Health, Aging and Body Composition Study. J Am Geriatr Soc. 2003;51:323-30.
28. Widrick JJ, Maddalozzo GF, Lewis D, Valentine BA, Garner DP, Stelzer JE, Shoepe TC, Snow CM. Morphological and functional characteristics of skeletal muscle fibers from hormone-replaced and nonreplaced postmenopausal women. J Gerontol A Biol Sci Med Sci. 2003;58:3-10.
29. Lexell J, Henriksson-Larsen K, Winblad B, Sjostrom M. Distribution of different fiber types in human skeletal muscles: effects of aging studied in whole muscle cross sections. Muscle Nerve. 1983;6:588-95.
30. Lexell J, Taylor CC, Sjostrom M. What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. J Neurol. 1988;84:275-94.
31. Lexell J, Downham D. What is the effect of ageing on type 2 muscle fibres? J Neurol Sci. 1992;107:250-1.
32. Landi F, Calvani R, Tosato M, Martone AM, Fusco D, Sisto A, Ortolani E, Savaresi G, Salini S, Marzetti E. Age-Related Variations of Muscle Mass, Strength, and Physical Performance in Community-Dwellers: Results From the Milan EXPO Survey. J Am Med Dir Assoc. 2017;18:17-24.
33. Norman K, Stobäus N, Reiss J, Schulzke J, Valentini L, Pirlich M. Effect of sexual dimorphism on muscle strength in cachexia. J Cachexia Sarcopenia Muscle. 2012;3:111-6.
34. Gantelius S, Hedström Y, Pontén E. Higher expression of myosin heavy chain IIX in wrist flexors in cerebral palsy. Clin Orthop Relat Res. 2012;470:1272-7.
35. Pontén EM1, Stål PS. Decreased capillarization and a shift to fast myosin heavy chain IIX in the biceps brachii muscle from young adults with spastic paresis. J Neurosci. 2007;253:25-33.
36. Andersen JL, Schiaffino S. Mismatch between myosin heavy-chain mRNA and protein distribution in human skeletal muscle fibers. Am J Physiol. 1997;272:1881-9.
37. D’Antona G, Pellegrino MA, Adami R, Rossi R, Carliuzzi CN, Canepari M, Saltin B, Bottinelli R. The effect of ageing and immobilization on structure and function of human skeletal muscle fibres. J Physiol. 2003;552:499-511.
38. Andersen JL, Aagaard P. Myosin heavy chain IIX overshoot in human skeletal muscle. Muscle Nerve. 2000;23:1095-104.