Observational Study

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Interrelationship among thigh intermuscular adipose tissue, cross-sectional area, muscle strength, and functional mobility in older subjects

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Abstract

The aim of this cross-sectional study was to investigate the association between lower limb strength, muscle mass and composition, and balance ability in elders.

Thirty-four older participants (Age: 65.6 ± 4.73 years; male = 10 and female = 24) were assessed for muscle strength (maximal isometric strength of knee extensors and one repetition maximum by leg press, the one repetition maximum [1RM]), balance and gait capacity (Mini-BESTest), body composition by whole-body dual energy x-ray absorptiometry (obtaining Appendicular Skeletal Muscle Mass Index, ASMMI), and magnetic resonance imaging of thigh to evaluate Intermuscular Adipose Tissue (IMAT) and muscle Cross Sectional Area (CSA).

Positive correlations between 1RM and ASMMI (r_s = 0.64, P < .0001) and thigh CSA (r_s = 0.52, P = .0017), but not with thigh IMAT, were found. In addition, significant correlations between knee extensors strength and ASMMI (r_s = 0.48, P = .004) and thigh CSA (r_s = 0.49, P = .0033) and IMAT (r_s = -0.35, P = .043) were observed, whereas no significant correlations between the Mini-BESTest with ASMMI, thigh CSA, and IMAT were observed.

Lower limb strength positively correlated with appendicular muscle mass. Further, the maximal isometric strength of knee extensors negatively correlated with thigh IMAT in elderly patients, whereas the dynamic balance ability did not correlate with any of the morphological variables of the muscle (i.e., ASMMI, CSA, and IMAT). A reduced muscle size and strength could affect movement and reduce physical function in older patients. Improving the composition and size of muscle in elder subjects could reduce frailty and risk of falls.

Abbreviations: ASMMI = appendicular skeletal muscle mass index, BMI = body mass index, BESTest = the mini-balance evaluation systems test, CSA = cross-sectional muscle area, DXA = whole-body dual energy x-ray absorptiometry, IMAT = intermuscular adipose tissue, MIS = maximal isometric strength, MRI = magnetic resonance imaging, 1RM = the one repetition maximum, SD = standard deviation, N = newtons.

Keywords: accidental falls, adipose tissue, aging, muscle strength, sarcopenia

1. Introduction

Aging of the human population is one of the phenomena of greatest impact globally during 21st century. The raise of number of people with 60 or more years of age is partly due to increased life expectancy and birth control.[1] Estimates indicate that in 2050 there will be a greater number of elders aged 60 or over (about 2.1 billion) in relation with adolescents aged 10–24 (about 2.0 billion).[2] Advances in medicine and science have led to improved life expectancy in the human population.[3] Although the increase of longevity is gratifying, on the other hand, aging could be an impediment for living a satisfying life, especially for elders who may not have the capacity to maintain themselves as independent, active, and healthy.[4] It has been observed that the 18% of elders, aged over 65 years, are dependent upon others in performing one or more daily activities, and about 30% of people aged 60 or more will fall in any 12-month period.[5,6]

The aging process is accompanied by natural physiological changes. The main body structures that impair movement are muscles and the nervous system. Regarding muscles, aging is associated with a decline in skeletal muscle mass and function, causing an alteration of strength, physical performance, and movement.[7–9] Estimates for the total decline in

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The authors have no conflicts of interest to disclose.

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the muscle mass between 40 and 80 years of age range from 30% to 50%, and the annual decline in functional capacity is reported to be 1% to 2% after the age of 50 increasing to 3% after 60 years.[10] This process begins sooner in women than in men, when comparing levels of isometric strength of the same muscle group.[11] It has been observed that weakness of lower extremity is clinically important as a risk factor for falls.[5,12,13] Studies have shown that low muscle mass is associated with poor functional performance[14,15] and self-reported disability.[16] To this regard, muscle mass is highly correlated with muscle strength.[17]

Moreover, during aging there is a redistribution of fat, with storage sites of fat changing from subcutaneous positions to ectopic positions.[18] Intermuscular adipose tissue (IMAT), found beneath the fascia and within the muscles, increases with aging,[19,20] and recent studies showed that IMAT is a significant predictor of mobility and muscle function in elders.[20–23] Older adults with higher IMAT levels have reduced muscle strength[21,24] and, similarly, Addison et al[25] observed that older adults with increased IMAT in the hip muscles registered lower balance and mobility and higher gait variability.[25] Furthermore, proprioceptive perception decreases with age,[26] and older subjects typically show reduced balance control, which is characterized by the alteration of muscle function, nervous system, and sensory information mainly arriving from the somatosensory, vestibular, and visual systems.[26] This reduction of balance control represents one of the major causes of increased risk of fall in elders.[27]

Therefore, to increase the knowledge on the contribution of different muscle variables (i.e., muscle mass and IMAT) to humans' physical function, the aim of the present cross-over study was to investigate the possible association between lower limb strength, muscle mass and composition, and balance ability in elder subjects. Based on existing evidence, we hypothesized that subjects with the highest levels of muscle mass and lowest IMAT would register greater lower limb strength and higher balance scores.

2. Materials and methods

2.1. Study design

This observational, cross-sectional, study was conducted at the IRCCS Istituto Ortopedico Galeazzi (Milan, Italy), in accordance with the STROBE guidelines[28] for cross-sectional studies, between November 2019 and October 2021. The study was approved by the Ethical Committee of Vita-Salute San Raffaele University (ref. no.: 124/INT/2019), and all procedures were performed in compliance with laws and regulations governing the use of human subjects (Declaration of Helsinki). All participants received explanation of purpose, methods, potential risks, and benefits of the study, and written informed consent was obtained from all participants. The authors have no conflict of interest to declare.

2.2. Participants

Participants were recruited from the outpatient clinic of the Endocrinology and Diabetology Service of IRCCS Istituto Ortopedico Galeazzi, upon invitation by the caring physician. Potential participants were screened for eligibility by an endocrinology disease specialist. The inclusion criteria for the study were: Caucasian ethnicity, aged between 60 and 80 years, sedentary behavior, and ability to walk autonomously. Exclusion criteria were: Body Mass Index (BMI) < 18.5 or > 40.0, active smoking, history of cancer, pace-maker, recent fracture or orthopedic surgery within the past 6 months, neurological or orthopedic pathological conditions potentially affecting movement, and diagnosis of balance disorder. Participants who met the above inclusion criteria were included in the study and completed the following clinical evaluations: 1. Whole-body dual energy X-ray absorptiometry (DXA) to assess total and district body fat-free and fat mass and the Appendicular Skeletal Muscle Mass Index (ASMMI); 2. Thigh Magnetic Resonance Imaging (MRI) to determine the Cross-Sectional muscle Area (CSA) and IMAT of thigh muscles; 3. Risk of fall assessment through the mini-Balance Evaluation Systems Test (BESTest)[29]; 4. Strength assessment by means of: a. the one repetition maximum (1RM) leg press test; b. Hand Grip Strength test; c. dynamometers to assess Maximal Isometric Strength (MIS) of knee extensor muscles.

2.3. Anthropometric measures

Height was rounded to the nearest 1 cm and body mass to the nearest 0.5 kg (Seca 217, Vogel & Halke, Hamburg, Germany). BMI was calculated using the standard formula (weight in kg divided by height in meters squared).

2.4. Total body composition assessment by DXA

DXA (Hologic QDR-Discovery Densitometer; Hologic Inc., Bedford, MA) is considered the gold standard method for the evaluation of body composition.[30–32] Subjects' total body fat mass and ASMMI, indicating the amount of muscle in the upper and lower limbs corrected by the individuals' square of the height and typically used to identify subjects affected by sarcopenia,[33] were calculated and considered as main outcomes for further analysis.

2.5. Magnetic resonance imaging scan

Dixon MRI sequences on axial plane at the middle third of the thigh was performed with a 1.5T MR system (Avanto, Siemens Medical Solution, Erlangen, Germany) to objectively quantify thigh CSA and thigh IMAT.[34,35] For all sequences, 15 slices of a 5-mm thickness were acquired and the segmentation of the thigh muscles was performed, with the use of the ImageJ free software,[36] by an expert investigator; in detail, each slice in which the muscle-tendon junction of the gluteus maximus muscle was clearly visible was analyzed. The whole muscle area was selected as a single unit, while femur, subcutaneous fat, and blood vessels were excluded from the segmentation. CSA is expressed in mm^2, and IMAT is expressed in percentage of the total muscle CSA of thigh muscles.

2.6. Balance and gait assessment

The mini-BESTest is a valid tool, showing very high inter-rater and test-retest reliability,[37] for the evaluation of gait and dynamic balance deficits in older subjects.[29] This instrument includes 14 items evaluating 4 different aspects of dynamic balance: anticipatory postural adjustments, postural responses, sensory orientation, and balance during gait. Each item has a score from 0 (lower score) to 2 (higher score) and the total maximum score is 28, with higher scores indicating better balance. The Mini-BESTest took approximately 12–15 minutes to administer, and it was performed with subjects wearing comfortable sport shoes.

2.7. Strength assessment

Participants warmed up prior to perform the strength tests, by cycling for 5 minutes on a cycle-ergometer and were familiarized with the testing procedures. All strength tests were supervised by 3 expert investigators (JAV, MB, SB).

2.8. One repetition maximum leg press test

The 1RM test is considered the gold standard for assessing muscle strength[38] and the 1RM leg press test was utilized to assess maximal lower limber muscle strength, expressed in Kg. Participants were familiarized with the resistance machine (Leg Press Machine, Technogym, Cesena, Italy) by performing 15 to 20 repetitions with a light load and then performed some repetitions at ~50%, ~70%, and ~80% of the predicted 1RM. After each successful performance, the load gradually increased until a failed attempt occurred. One-minute resting periods were given between each attempt.

2.9. Maximal isometric strength of knee extensors muscles

Knee extensors MIS was measured using a belt-stabilized dynamometer (Sauter FK 1k, Sauter GmbH, Balingen, Germany) with subjects in a setting position and the knee placed at 90° flexion. MIS was specifically recorded in Newtons (N), and 3 repetitions were performed. The participants were instructed to remain seated in an upright position and the upper limbs were placed on the bed to support the body and prevent a fall. A resting period of 1 minute was given after each repetition, and the average of 3 trials for each limb was utilized for further analysis.

2.10. Statistical analysis

Quantitative variables were expressed as mean ± and standard deviation (SD). The normality of the distribution of the outcome measures was checked using graphical methods and the Shapiro–Wilk test. Because only one of the tested variables was normally distributed (ASMMI), nonparametric tests were used for the analysis. The existence of a correlation between the morphological muscle variables (i.e., ASMMI, CSA, IMAT) and the functional parameters (i.e., muscle strength and balance) was tested by the means of the Spearman correlation index. The strength of correlation is described using the following interpretation: .00–.30 "negligible correlation"; .30–.50 "low positive (negative) correlation"; .50–.70 "moderate positive (negative) correlation"; .70 –.90 "high positive (negative) correlation"; .90–1.0 "very high positive (negative) correlation".[39] Correlation were considered significant when $r_s > 0.3$ and $P < .05$. Statistical analysis was performed using Graph Pad Prism Software, version 8.0 for Windows (Graph Pad Software, San Diego, CA).

3. Results

Sixty participants were screened, and 34 were eligible and participated in the study. Twenty-six participants were noneligible for the study because they did not meet the inclusion criteria (n = 23) or declined to participate (n = 3). Table 1 shows the baseline characteristics of the subjects who participated in the study. Four women of the participants were classified as sarcopenic on the basis of their ASMMI.[33]

Multipanel Figure 1 graphically shows the correlation between lower limb strength scores, expressed as 1RM leg press, and ASMMI, CSA, and IMAT. Significant positive correlations between 1RM leg press and ASMMI ($r_s = 0.64$, $P < .0001$) and thigh CSA ($r_s = 0.52$, $P = .0017$) were detected, whereas no

Table 1

Baseline characteristics of the 34 subjects who participated in the study.

	Mean ± SD	Median (Q1–Q3)	Min-Max	95%CI
Age (yr)	65.6 ± 4.73	64.50 (62.00–67.25)	60–78.00	63.97–67.27
Height (m)	1.64 ± 0.09	1.63 (1.57–1.70)	1.48–1.87	1.61–1.67
Body mass (kg)	71.37 ± 12.32	71.00 (61.08–80.70)	54.0–103.0	67.07–75.67
BMI (kg/m^2)	26.56 ± 3.94	26.12 (23.51–29.20)	20.60–37.53	25.19–27.94
Fat mass (%)	36.07 ± 5.71	36.25 (32.08–40.45)	23.40–46.10	34.08–38.06
ASMMI (kg/m^2)	6.83 ± 1.22	6.51 (5.93–7.69)	4.91–9.51	6.40–7.25
CSA (mm^2)	10673 ± 2780	9827 (8844–12671)	7010–18221	9703–11643
IMAT (%)	14.48 ± 3.84	13.64 (12.41–16.37)	9.3–28.6	13.14–15.82
Knee extensors strength (N)	305.3 ± 103.7	285.7 (239.0–368.2)	142.7–721.7	269.2–341.5
Leg press (kg)	141.5 ± 45.34	125.0 (110.0–152.5)	80–260	125.7–157.3
Mini-BESTest	25.06 ± 2.40	25.00 (23.75–27.00)	18–28	24.22–25.90

Values are expressed as mean ± standard deviations (SD), median (Q1–Q3), minimum and maximum (Min-Max), and 95% confidence intervals (CI).
ASMMI: appendicular skeletal muscle mass index; BMI: body mass index; CSA: Cross Sectional Area of thigh; IMAT: Intermuscular Adipose Tissue.

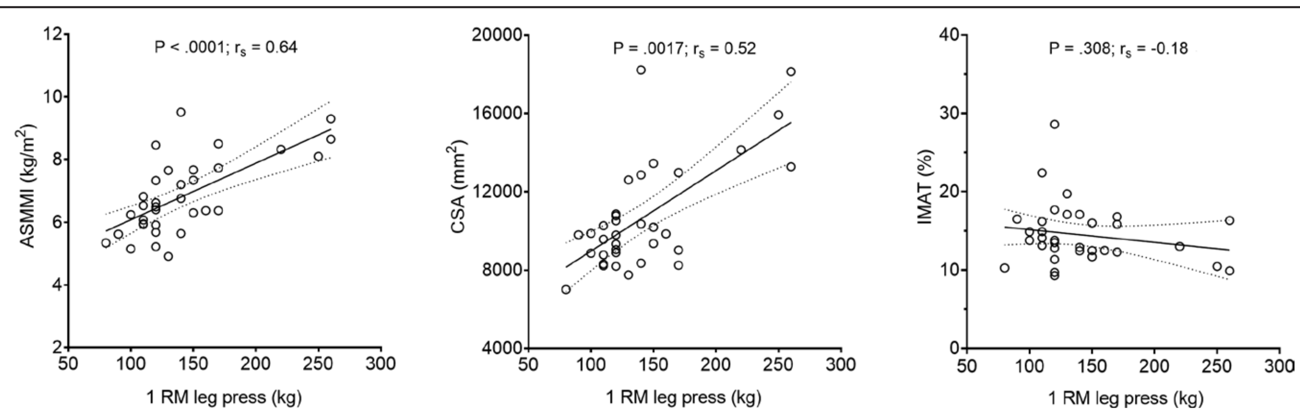

Figure 1. The correlations between 1RM leg press and ASMMI, CSA, and IMAT. 1RM: One Repetition Maximum; ASMMI: Appendicular Skeletal Muscle Mass Index; CSA: Cross-Sectional muscle Area; IMAT: Intermuscular Adipose Tissue.

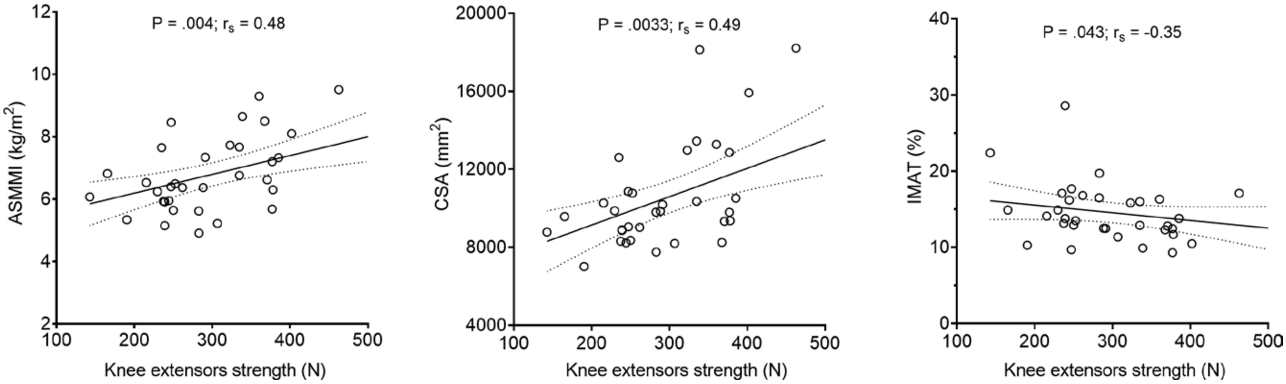

Figure 2. The correlations between knee extensors strength and ASMMI, CSA, and IMAT. ASMMI: Appendicular Skeletal Muscle Mass Index; CSA: Cross-Sectional muscle Area; IMAT: Intermuscular Adipose Tissue.

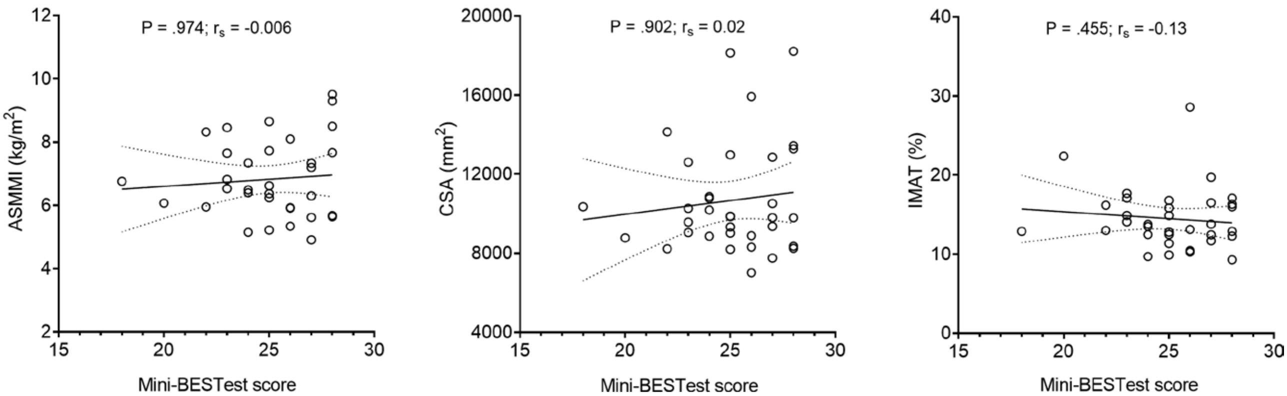

Figure 3. The correlations between Mini-BESTest and ASMMI, CSA, and IMAT. ASMMI: Appendicular Skeletal Muscle Mass Index; CSA: Cross-Sectional muscle Area; IMAT: Intermuscular Adipose Tissue.

significant correlation was observed between 1RM leg press and IMAT (r_s = -0.18, P = .308).

Figure 2 shows significant positive correlations between knee extensors strength and ASMMI (r_s = 0.48, P = .004) and thigh CSA (r_s = 0.49, P = .0033). Further, knee extensors strength was negatively correlated with IMAT (r_s = -0.35, P = .043).

Figure 3 reports graphically the correlations between the Mini-BESTest and ASMMI, CSA, and IMAT. No significant correlation between Mini-BESTest and ASMIMI (r_s = -0.0057, P = .974) and thigh CSA (r_s = 0.022, P = .902) and IMAT (r_s = -0.132, P = .455) were detected.

4. Discussion

This study explored the possible association between lower limb strength, muscle mass and composition, and balance ability in elder subjects in order to better understand the contribution of different muscle variables to the physical function within population. The main findings of this study were: 1. lower limb strength, both assessed by the 1RM leg press and the dynamometry, positively correlated with ASMMI and thigh CSA; 2. thigh IMAT showed a negative correlation with knee extensors but not with 1RM leg press; 3. dynamic balance ability did not correlate with ASMMI, thigh CSA and IMAT. Our initial hypotheses were partially confirmed.

The positive correlation between lower limbs muscle mass and strength highlights that muscle size is an important factor to generate force; it is indeed assumed that muscle strength growths with an increase of muscle mass.[40] To confirm this, Chen et al[41] quantified the positive association between muscle mass and muscle strength in older adults, and found that muscle mass explained about 13% of variance in muscle strength, independent of age and gender.[41] Further, the positive correlation between the maximal isometric strength of knee extensors and thigh CSA in our study is in accordance with the study of Goodpaster et al,[24] where they demonstrated that muscle CSA is positively associated with strength of knee extensors in elderly women and men and that lower muscle strength with age can be largely attributed to a reduction of skeletal muscle.[24] Nevertheless, Beliaeff et al[42] observed that leg muscle mass is not the main contributor to quadriceps muscle strength in older men and women: leg muscle mass accounted for 5% of the variance in quadriceps muscle strength in men and 4% in women, 95% of this variance in men and 96% in women remain to be explained by factors other than lower limb muscle mass.[42] Addison et al[18] observed that a loss of lean muscle mass in older adults does not directly translate into a loss of strength,[18] and other studies demonstrated that aging is also characterized by a decrease in nervous system function, which is a factor that influence muscle strength and power in elders.[12,42,43]

The growing interest in ASMMI assessed by DXA, due to its great characteristics of reproducibility and precision, represents the basis of the majority of the operational definitions of muscle mass in older subjects.[44] In our study, 4 of the participants were classified as sarcopenic on the basis of the DXA-based ASMMI, but we observed that lower limbs' strength, evaluated both by the leg press and with the dynamometer, positively correlates with ASMMI. It is well known that aging is associated with a reduction of ASMMI[45]; therefore the maintenance of a great muscle mass of lower and upper limbs could be considered a key factor to counteract the negative effect of aging. Muscle health is a key variable for healthy aging, and physical activity and diet could be considered 2 nonpharmacological methods to prevent muscle loss.[45–47] Another result of our study is the absence of correlation between balance, assessed by Mini-BESTest, and ASMMI or thigh CSA. This suggests that DXA-based ASMMI is not able to discriminate subjects with higher or lower balance capacity and, consequently, the risk of fall among healthy elders. The relationship between muscle mass and balance in older subjects is not fully understood in literature. A study of Gouveia et al[48] emphasizes a great positive relationship between muscle mass and balance (measured by dynamic and static activities) in 802 elders aged 60 to 79 years.[48] On the contrary, the study of Bijlsma et al[49] observed that muscle mass is not associated with the ability to maintain standing balance in most balance conditions.[49] However, both studies demonstrated the association between muscle strength and balance in older people. Therefore, it seems that muscle strength rather than muscle mass can be considered an important factor to maintain good balance in old age.

Other measures than absolute muscle quantity or muscle CSA are needed to fully understand skeletal muscle composition and performance. IMAT is recognized as a key factor able to affect strength and mobility function in older adults.[21] Increased levels of IMAT have been linked with decreased strength and composition of muscle, decreased mobility, and an increased risk of future limitations of mobility.[23] In the present study, we reported a significant correlation between thigh IMAT and knee extensors but not with the 1RM assessed by the leg press; therefore, our results are partially in contrast with the previous studies that demonstrated that IMAT is a key factor able to affect strength in elders.[18,20] Marcus et al[20] reported that higher levels of IMAT in the thigh are predictive of loss of physical function in 109 older subjects.[20] Decreases in muscle quantity and composition may lead to functional activities' complications in elders,[50] like decrease in balance capacity and an increase of risk of fall.[21] To this regard, dynamic and standing balance show age-related changes, condition that increase at around the 6th decade but becomes more significant after the age of 60 years.[27] A study of Gouveia et al.[48] detected a strong positive relationship between muscle strength, muscle mass, and balance.[48] Gouveia et al. observed that muscle mass and strength seem to have a more important contribution to balance capacity in later life, approximately after the age of 70 years.[48] Our results are in contrast with this study since a relationship between CSA and Mini-BESTest was not detected. Regarding Mini-BESTest, Magnani et al.[51] suggested the cutoff scores for predicting falls.[51] The risk of fall growth under a score of 25 in elders aged between 60 and 69 years and under a score of 23 in elders aged from 70 to 79 years. Eight of our subjects made a score under these values. This means that about 76.47% of our sample has a good physical condition, with a reduced risk of fall. A study of Jeon et al.[52] demonstrated that muscle strength in the upper and lower limbs, dynamic balance and static balance were higher in a group of elders with no previous falls than other groups of elders with antecedent falls.[52] To this regard, it could be concluded that muscle health is a key factor to maintain good physical performance in elder people, reducing risk of fall and improving the quality of life.

Some limitations need to be acknowledged. First, no power analysis was performed and the small sample does not allow drawing exhaustive conclusions. Second, the design of the study allows only to describe associations among clinical variables of the subjects with no cause–effect relationships. Lastly, gender distribution was not equal in the study sample because only 10 of 34 subjects were males. However, one of the strengths of the study was that the participants were recruited on the basis of strict inclusion and exclusion criteria; therefore, the study sample was very homogenous. Second, gold standard assessments, such as DXA or MRI, were used in the study; so the high quality of the data make the results reliable and the skeletal muscle was assessed in many of its components: mass (i.e., ASMMI and CSA), composition (i.e., IMAT), strength (i.e., 1RM leg press test and knee extensors MIS), and function (i.e., gait and balance).

5. Conclusions

Aging is a complex multifactorial process of molecular and cellular decline that affects tissue and function of muscle. Our data might provide new insights to correctly understand and manage elder patients aged between 60 and 80 years. We detected positive correlations between lower limbs muscle mass and strength, and this result underlines that muscle size is an important factor for force expression. A reduced muscle size and strength could affect movement and reduce physical function in older patients. Therefore, it is necessary to adopt strategies to maintain the functional independence and promote a higher quality of movement in elders. In this context, physical exercise represents the most powerful tool to reduce IMAT and increase muscle mass, strength, and function in older people.[53–57]

Author contributions

Conceptualization: J.A.V., G.B., A.L.T.; methodology: J.A.V., M.B., S.B.; data curation: M.B., S.B; writing – original draft preparation: J.A.V., M.B., S.B.; writing - review and editing: J.A.V., G.B, A.L.T., M.B., S.B; funding acquisition: G.B.; project administration: J.A.V.; supervision: J.A.V., G.B, A.L.T. All authors have read and agreed to the published version of the article.

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