Bone 162 (2022) 116474

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Combined effect of lower muscle quality and quantity on incident falls and fall-related fractures in community-dwelling older adults: A 3-year follow-up study

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A R T I C L E I N F O

Keywords:
Muscle quality
Muscle quantity
Fall
Fall-related fracture
Community-dwelling older adults

A B S T R A C T

Objective: Falls and fractures are serious geriatric adverse events worldwide, and skeletal muscle is considered to be a key factor in these incidents. The objective of this study was to investigate the combined effect of lower muscle quality and quantity on the incidence of falls and fall-related fractures in a 3-year follow-up period among community-dwelling older adults.
Methods: We recruited community-dwelling adults aged 65 years and older who were living independently in 2018. A total of 773 older participants were analyzed in this study. The outcomes were incident falls and fall-related fractures during the 3-year follow-up period. At baseline, we assessed muscle quality and quantity using ultrasonography, and we categorized the participants into four groups based on their combination of poor/better muscle quality and poor/better muscle quantity. Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95 % confidence intervals (CIs) of the relationships among items in the four groups and the time to incident falls and fall-related fractures.
Results: During the 3-year follow-up period, 178 participants (23.0 %) had a fall incident and 51 participants (6.6 %) had fall-related fractures. Older adults with lower muscle quality and quantity had significantly elevated risks of incident falls according to multivariate analyses using older adults with better muscle quality and quantity as the reference (adjusted HR: 1.54 [95 % CI 1.06–2.23]). However, there were no significant differences in fall-related fractures among the four groups.
Conclusion: We found that lower muscle quality and quantity led to higher incidents of falls; thus, identifying community-dwelling older adults with lower muscle quality and quantity is necessary to provide them fall preventive measures and maybe to reduce fall-related outcomes.

1. Introduction

Falls and fractures are serious geriatric adverse events worldwide. One in three older adults has a fall each year [1], and approximately 5 % of falls result in fractures [2]. Falls and fractures lead to hospitalization, disability, and mortality; as a result, they incur huge medical and care costs [3–6]. Numerous risk factors for incident falls have already been reported [7,8], and several international guidelines recommend intervention methods for preventing falls and fractures [9–11]. Among them, skeletal muscle is considered a key factor for preventing falls and fractures [12].

Sarcopenia is a disease characterized by age-related loss of skeletal muscle mass and weakness [13,14]. Age-related skeletal muscle disease is currently attracting attention owing to its high prevalence [15] and significant impact on adverse health outcomes, such as falls and fractures [12]. Since 2010, when the famous consensus on the definition of sarcopenia was reported [16], there has been an increase in the number of studies on sarcopenia, and the indicators of skeletal muscle condition have gradually changed with the progress of research. Among these developments is the importance of quality as an indicator of skeletal

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https://doi.org/10.1016/j.bone.2022.116474
Received 25 January 2022; Received in revised form 12 June 2022; Accepted 17 June 2022
Available online 22 June 2022

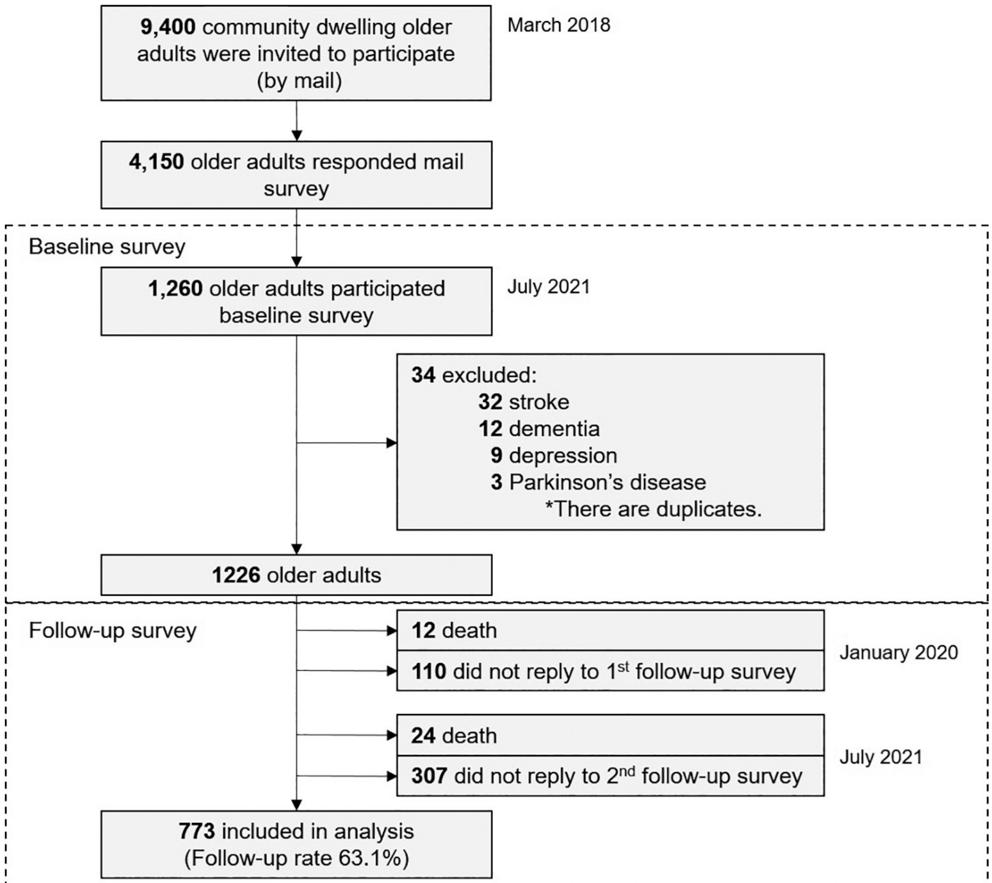

Fig. 1. Flow chart showing the distribution of participants throughout the survey.

muscle, in addition to its quantity and strength [13,17]. Muscle quality can be assessed by several devices such as computed-tomography, magnetic resonance imaging and ultrasound, among which the method of defining muscle quality as the echo intensity of ultrasonography on skeletal muscle is simple and useful for muscle quality estimation [18].

Muscle quality decreases with age, and is a leading cause of falls. Advancing with age, muscle quality decreases due to the increased accumulation of intra- and intermuscular fat, increased muscle fibrosis, and decreased number of fast-twitch fibers [19–23]. Furthermore, previous studies have reported that a higher incidence of falls is associated with lower muscle quality in older adults [24–27]. However, it is not well addressed whether the combined effect of poor muscle quality and quantity on incidents of falls and fall-related fractures is additive or not.

Since 2018, we have been conducting the MUSCLE study, which is a prospective cohort study focused on sarcopenia and frailty in community-dwelling older adults in which we measured muscle quality and quantity along with adverse health outcomes. Therefore, the objective of this study was to investigate the combined effect of lower muscle quality and quantity on incident falls and fall-related fractures in a 3-year follow-up period among community-dwelling older adults. We hypothesized that older adults with lower muscle quality and quantity were at a higher risk of incident falls and fall-related fractures compared with the other older adults. We believe that the current study will provide novel information which will help prevent falls and fractures in older adults.

2. Methods

2.1. Study design and participants

We conducted a prospective cohort study in collaboration with Maibara city in Shiga prefecture, which is located close to the geographical center of Japan. In this study, the source population for the survey was the community-dwelling older adults aged 65 years and older who were living independently. The exclusion criterion was older adults who were already eligible to receive the benefits of the long-term care insurance services. First, a mail survey was conducted in March 2018, and a total of 9400 older adults were sent the survey, and 4150 responded. Second, a physical function survey (baseline survey for this analysis) was conducted in July 2018, and a total of 4150 older adults who responded to the previous mail survey were invited and 1260 participated. Third, 1st and 2nd follow-up mail surveys were conducted in January 2020 and July 2021, respectively. In this study, we excluded 34 older adults with stroke, dementia, depression, and Parkinson's disease after the baseline survey, and 453 older adults who died or did not respond to follow-up survey during the 36-month follow-up period. Finally, 773 older adults were included in this study [Fig. 1]. This study was conducted in accordance with the guidelines proposed by the Declaration of Helsinki, and the study protocol was reviewed and approved by the Ethics Committee of the Faculty of Human Sciences, University of Tsukuba.

2.2. Outcome measure

The outcomes were self-reported falls and fractures incidents over 36 months. Falls were defined as all situations where the participant unintentionally and suddenly came to rest on the ground or at the

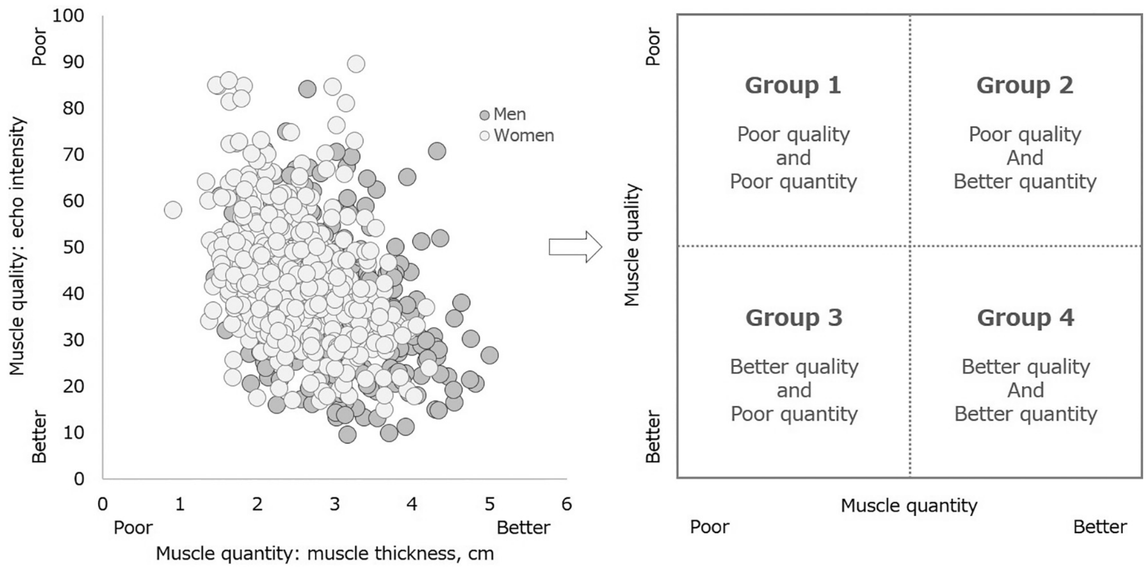

Fig. 2. The relationship between muscle quality and quantity is shown on the left side. We defined the third quintile or above for echo intensity as poor muscle quality, and defined the second quintile or below for muscle thickness as poor muscle quantity in each sex. The participants were categorized into four groups based on their combination of poor/better muscle quality and poor/better muscle quantity in the right side figure: (group 1) poor quality and quantity, (group 2) poor quality and better quantity, (group 3) better quality and poor quantity, or (group 4) better quality and quantity.

surface lower than their original location, but excluded falls due to extraordinary environmental factors, such as traffic accidents or falls while riding a bicycle [28]. Fall-related fractures were defined as any fractures due to falls that were diagnosed by a medical doctor. We assessed the first incidents of fall and fall-related fractures after the baseline survey through a mail survey at 18- and 36-month follow-ups.

2.3. Measurement of muscle quality and quantity

In the baseline survey, we assessed the muscle quality and quantity using ultrasonography. An ultrasound device (ProSound2, Hitachi-Aloka Medical, Tokyo, Japan) with a 7.5-MHz linear-array probe was used to obtain ultrasound images of the rectus femoris and vastus intermedius at the midpoint between the anterior superior iliac spine and the proximal end of the patella, respectively. We also assessed the echo intensity and muscle thickness of the quadriceps femoris, which can accurately indicate sarcopenia [17]. The echo intensity of the quadriceps femoris was calculated as the mean echo intensity of the rectus femoris and vastus intermedius, and can be used to objectively evaluate inter- and intra-muscular fat infiltration as muscle quality indicators [29]. The quadriceps femoris muscle thickness was calculated as the sum of the muscle thickness of the rectus femoris and vastus intermedius; it is widely used as an indicator of muscle quantity. These analyses were performed by a single investigator who was well-trained in the operation technique for ultrasound image analysis and was blinded to the participant information. A detailed description of the assessment and analysis methods has been described previously [17].

The analyzed ultrasonographic data were categorized using the following procedure: we defined the third quintile or above for echo intensity as poor muscle quality in each sex due to higher echo intensity, indicating poor skeletal muscle quality. Similarly, we defined the second quintile or below for muscle thickness as poor muscle quantity in each sex due to lower muscle thickness, indicating poor muscle quantity. Finally, participants were categorized into four groups based on their combination of poor/better muscle quality and poor/better muscle quantity: (group 1) poor quality and quantity, (group 2) poor quality and better quantity, (group 3) better quality and poor quantity, or (group 4) better quality and quantity [Fig. 2].

2.4. Demographic and covariate variables

In the baseline survey, we assessed and measured several types of demographic and covariate variables: age, sex, height, weight, number of medications, cognitive function, frailty status, walking speed, five chair stand test, grip strength, and short physical performance battery (SPPB) [30]. All measurements were recorded and performed by a well-trained therapist who was trained on the correct protocols for all measures included in the study before the start of the study. Body mass index (BMI) was calculated as weight divided by height-squared, and classified into three categories according to the WHO expert consultation: <18.5, 18.5–24.9, ≥25.0, were defined as underweight, normal weight, and overweight, respectively [31]. We defined the use of five or more medications as polypharmacy according to previous studies [32]. Cognitive function was assessed using the Mini Mental State Examination (MMSE), and defined a score of <24 points as low cognitive function [33]. Frailty was defined using the revised Japanese version of the Cardiovascular Health Study criteria [34]. Walking speed, five chair stand time, grip strength, and balance were measured, and poor walking speed, poor chair stand time, poor grip strength, and poor SPPB score were each defined according to the consensus report of the Asian Working Group for Sarcopenia [14].

2.5. Statistical analyses

Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95 % confidence intervals (CIs) of the relationships between items in the four groups and the time to incident falls and fall-related fractures in univariate and multivariate analyses. Multivariate analyses were performed for each covariate and adjusted for age, sex, BMI, cognitive function, and polypharmacy. Survival time was defined as the time between enrollment (the date of the baseline measurements) and incident fall, fall-related fracture, or the end of the follow-up period. Data were analyzed using SPSS software (Statistical Package for the Social Sciences, version 26.0; SPSS, Inc., Chicago, IL, USA). Statistical significance was set at $P < 0.05$.

Table 1
Demographic characteristics of the four groups according to muscle quality and quantity.

	Overall	Group 1	Group 2	Group 3	Group 4
		Poor quality/ Poor quantity	Poor quality/ Better quantity	Better quality/ Poor quantity	Better quality/ Better quantity
	$n = 773$	$n = 167$	$n = 128$	$n = 133$	$n = 345$
Demographic data					
Age [years], mean (SD)	73.8 (6.0)	75.8 (6.0)	73.0 (5.9)	73.7 (6.1)	73.1 (5.8)
Gender [women], n (%)	414 (53.6)	93 (55.7)	75 (58.6)	74 (55.6)	172 (49.9)
Height [cm], mean (SD)	157.2 (9.0)	157.3 (9.0)	157.3 (8.6)	156.2 (8.7)	157.6 (9.3)
Weight [kg], mean (SD)	56.1 (9.9)	53.4 (9.0)	55.6 (9.4)	54.5 (9.1)	58.3 (10.3)
BMI [kg/m^2], mean (SD)	22.6 (3.0)	21.5 (2.7)	22.4 (2.6)	22.3 (3.1)	23.4 (3.1)
Underweight, n (%)	59 (7.6)	21 (12.6)	10 (7.8)	13 (9.8)	15 (4.3)
Normal weight, n (%)	571 (73.9)	130 (77.8)	104 (81.3)	98 (73.7)	239 (69.3)
Overweight, n (%)	143 (18.5)	16 (9.6)	14 (10.9)	22 (16.5)	91 (26.4)
Frailty, n (%)	34 (4.4)	7 (4.2)	4 (3.1)	5 (3.8)	18 (5.2)
Polypharmacy, n (%)	171 (21.9)	44 (26.3)	30 (23.4)	21 (15.8)	76 (22.0)
MMSE score, median (IRQ)	29 (27–30)	29 (27–30)	29 (27–30)	29 (26–30)	29 (27–30)
Poor cognitive function, n (%)	17 (2.2)	2 (1.2)	1 (0.8)	6 (4.5)	8 (2.3)
Physical performance					
Walking speed [m/s], mean (SD)	1.30 (0.24)	1.30 (0.24)	1.33 (0.22)	1.34 (0.23)	1.27 (0.25)
Poor walking speed, n (%)	72 (9.3)	18 (10.8)	4 (3.1)	9 (6.8)	41 (11.9)
Five chair stand [*sec*], mean (SD)	8.2 (2.1)	8.4 (2.0)	8.0 (2.2)	8.1 (1.8)	8.2 (2.1)
Poor chair stand, n (%)	35 (4.5)	9 (5.4)	8 (6.3)	3 (2.3)	15 (4.3)
Grip strength for men, mean (SD)	35.8 (6.5)	34.3 (6.2)	36.7 (6.9)	34.5 (6.4)	36.5 (6.5)
Grip strength for women, mean (SD)	22.1 (4.1)	21.4 (4.0)	22.4 (4.7)	22.4 (4.1)	22.1 (3.9)
Poor grip strength, n (%)	101 (13.1)	29 (17.4)	20 (15.6)	17 (12.8)	35 (10.1)
SPPB score, median (IQR)	12 (12–12)	12 (12–12)	12 (12–12)	12 (12–12)	12 (12–12)
Poor SPPB score, n (%)	27 (3.5)	10 (6.0)	6 (4.7)	0 (0.0)	11 (3.2)

BMI: body mass index, MMSE: mini mental state examination, SPPB: short physical performance battery.
SD: standard deviation, IQR: inter quartile range.

Table 2
Effect of combination of muscle quality and quantity on incident falls/fall-related fracture in 3-year follow-up period.

	Number of cases		Univariate				Multivariate			
			HR	95%CI		*P*-value	HR	95%CI		P-value
	n	%		Min	Max			Min	Max	
Outcome: fall										
Group 1	50/167	29.9 %	1.57	1.09	2.25	0.015	1.54	1.06	2.23	0.025
Group 2	31/128	24.2 %	1.20	0.79	1.84	0.390	1.23	0.80	1.89	0.346
Group 3	26/133	19.5 %	0.95	0.61	1.50	0.838	0.94	0.60	1.48	0.795
Group 4	71/345	20.6 %	1.00	Reference		–	1.00	Reference		–
Outcome: fall-related fracture										
Group 1	16/167	9.6 %	1.90	0.97	3.72	0.062	1.69	0.84	3.38	0.139
Group 2	10/128	7.8 %	1.51	0.70	3.28	0.292	1.42	0.65	3.10	0.379
Group 3	7/133	5.3 %	1.02	0.43	2.44	0.963	0.97	0.40	2.33	0.945
Group 4	18/345	5.2 %	1.00	Reference		–	1.00	Reference		–

Multivariate analysis: adjusted for age, sex, BMI, cognitive function and polypharmacy.
n: number, HR: hazard ratio, Min: minimum, Max: maximum, 95%CI: 95 % confidence interval.

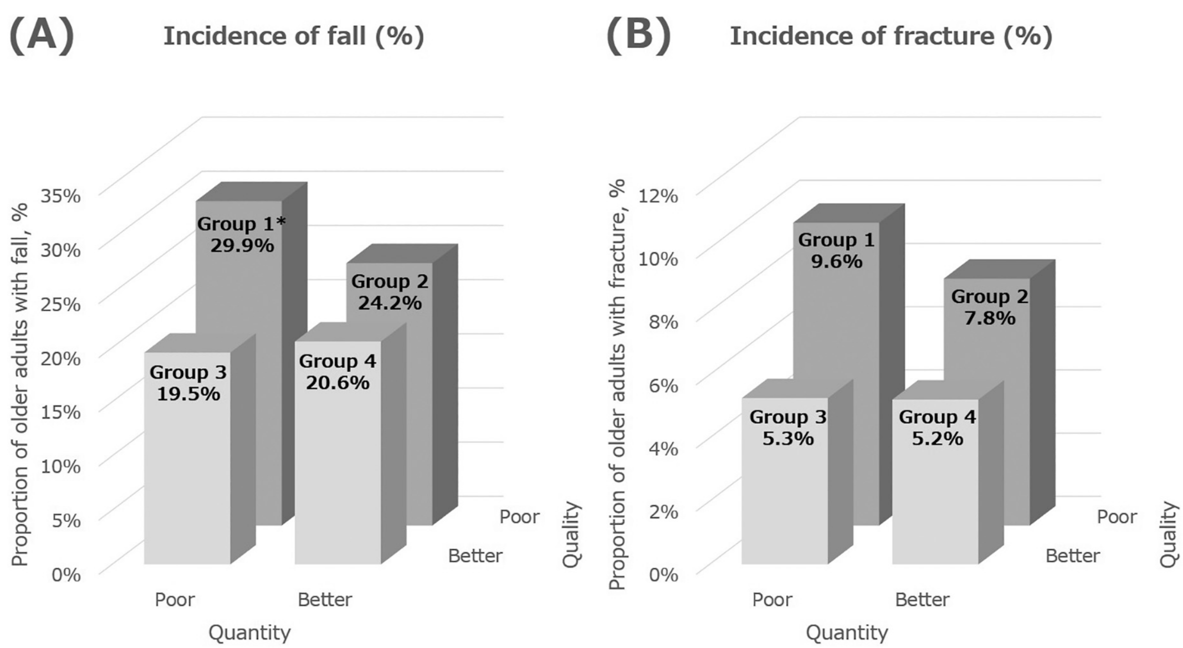

Fig. 3. Association of characteristics of skeletal muscle and incidence of falls (A). Group 1 (lower muscle quality and quantity) had a significantly elevated risk of incident falls according to the results of the multivariate analyses using group 4 (better muscle quality and quantity) values as the reference (adjusted HRs: 1.54 [95 % CIs 1.06–2.23]). Association of characteristics of skeletal muscle and incidence of fall-related fracture (B). There were no significant differences in incident fall-related fractures among four groups according to the results of the univariate and multivariate analyses.

3. Results

Demographic variables are listed in Table 1. The mean age was 73.8 ± 6.0 years, and the proportions of women, underweight, overweight, polypharmacy, and poor cognitive function were 53.6 %, 7.5 %, 18.0 %, 21.9 %, and 2.2 %, respectively. Based on the combination of poor/better muscle quality and poor/better muscle quantity, 167 participants (21.6 %) were classified into group 1, 128 (16.6 %) into group 2, 133 (17.2 %) into group 3, and 345 (44.6 %) into group 4.

During the 36-month follow-up period, 178 participants (23.0 %) experienced falls: 50 participants (29.9 %) in group 1, 31 participants (24.2 %) in group 2, 26 participants (19.5 %) in group 3, and 71 participants (20.6 %) in group 4 [Table 2, Fig. 3]. Group 1 (adjusted HR: 1.54 [95 % CI 1.06–2.23]) had a significantly elevated risk of incident fall according to the results of the multivariate analyses using group 4 as the reference, but not groups 2 or 3 [Table 2].

In terms of fracture, 51 participants (6.6 %) experienced fall-related fracture during the 36-month follow-up period; 16 participants (9.6 %) in group 1, 10 participants (7.8 %) in group 2, 7 participants (5.3 %) in group 3, and 18 participants (5.2 %) in group 4 [Table 2, Fig. 3]. There were no significant differences in fall-related fractures among the four groups according to the results of the univariate and multivariate analyses [Table 2].

4. Discussion

The current prospective cohort study was performed to evaluate the combined effect of lower muscle quality and quantity on incidents of falls and fall-related fractures in a 3-year follow-up period among community-dwelling older adults. We found that group 1 (poor muscle quality and quantity) had an increased risk of incident falls, but not of fall-related fractures. In addition, the risk of incident falls and fractures did not increase if either muscle quality or quantity decreased (groups 2 or 3). These findings suggest that the prevention of falls may be necessary for managing poor muscle quality and quantity in community-dwelling older adults.

Overall, the current study included healthier older adults than in previous studies; thus, the proportion of poor physical function and fallers was also low. The source population of this cohort was 9400 older adults, and this study analyzed 773 older adults who completed all follow-up investigations. Thus, we cannot deny the possibility that only older adults with better health-consciousness participated in the study; they accounted for <10 % of the study population. In fact, the prevalence of frailty among the participants in this study was only 4.4 %, which was significantly lower than the national average of 8.4 % among community-dwelling Japanese older adults [35]. Similarly, the proportion of fallers in this study was 23.0 % during the 3-year follow-up period, which was dramatically lower than the 43.7 % reported in a previous study with the same follow-up period [36]. From these results, it can be concluded that the participants in this study were a population with relatively good health status.

Older adults with poor muscle quality and quantity (group 1) had a significantly higher risk of incident falls than those with better muscle quality and quantity. Previous studies on skeletal muscle in older adults have shown that muscle quality and quantity are independently associated with physical performance and incident falls [12,17,24,25]. The current study expands on these previous studies and clarifies that fall incidents are influenced by both lower muscle quality and quantity. Furthermore, several previous studies have shown that better muscle quality may play a role in compensating for lower muscle quantity [36,37], and the current findings support this tentative theory.

However, there was no significant association between skeletal muscle status and the incidence of fall-related fractures. In a previous study, sarcopenia was shown to have an effect on fall-related fractures and falls in older adults [12]. In this study, there was a trend of higher fall-related fracture incidents in older adults with poor muscle quality and quantity (group 1) in the univariate analysis. The lack of a significant association was thought to be due to the small sample size, which was a limitation for the analysis of fall-related fracture as an outcome.

This prospective cohort study has notable strengths and limitations. Since this cohort study started with a complete survey, we were able to understand the detailed characteristics of the participants of the analysis, which is a strength. Meanwhile, there may have been a selection bias because <10 % of the source population was included in the analysis; thus, some considerations on the generalization of the current results are necessary. Another strength of this study is that we conducted an analysis with a relatively long follow-up period of 3 years for the important outcomes of incident falls and fall-related fractures. However, as mentioned earlier, the sample size was not sufficient to use fall-related fractures as an outcome, which was a limitation. Additionally, we did not investigate the detailed information on medications; therefore, we cannot address the effect of specific medication on the outcomes. Lastly, the condition of other skeletal muscles and the effect of pennation angle were not measured. Although calf muscle and other muscles can play a role for falls, we could not address the role of other muscles in this study.

5. Conclusions

Older adults with poor muscle quality and quantity had a significantly increased risk of incident falls compared to older adults with better muscle quality and quantity. On the other hand, there was no significant association between skeletal muscle status and the incidence of fall-related fractures due to insufficient sample size. These findings suggest that managing muscle quality and quantity may be necessary for fall prevention in community-dwelling older adults.

CRediT authorship contribution statement

As the corresponding author I am responsible for ensuring that the descriptions are accurate and agreed by all authors.

Minoru Yamada and Hidenori Arai: Conceptualization, writing-reviewing and editing.

Yosuke Kimura, Daisuke Ishiyama, Yuhei Otobe, Mizue Suzuki, Shingo Koyama: Data collection and analysis.

Declaration of competing interest

The authors have no potential conflicts of interest to disclose.

Acknowledgments

The authors acknowledge Ms. Sayuri Natsuhara and Mr. Kiyoshi Yomori for their contributions to the data collection. This work was supported by JSPS KAKENHI (Grant Numbers 19K21576 and 21H02834).

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