

G OPEN ACCESS

Citation: Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Hioka A, et al. (2022) The degree of recovery in swallowing ability in older inpatients with aspiration pneumonia is related to intramuscular adipose tissue of the quadriceps than to muscle mass. PLoS ONE 17(10): e0275810. https://doi.org/10.1371/journal. pone.0275810

Editor: Masaki Mogi, Ehime University Graduate School of Medicine, JAPAN

Received: August 23, 2022

Accepted: September 23, 2022

Published: October 10, 2022

Copyright: © 2022 Akazawa et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its <u>Supporting Information</u> files.

Funding: This work was supported by Japan Society for the Promotion of Science (Grant-in-Aid for Young Scientists B [Grant number JP17K18294] and Grant-in-Aid for Early-Career Scientists [Grant number JP20K19661]). The funders had no role in study design, data collection **RESEARCH ARTICLE**

The degree of recovery in swallowing ability in older inpatients with aspiration pneumonia is related to intramuscular adipose tissue of the quadriceps than to muscle mass

Naoki Akazawa¹*, Masaki Kishi², Toshikazu Hino², Ryota Tsuji², Kimiyuki Tamura², Akemi Hioka¹, Hideki Moriyama³

 Department of Physical Therapy, Faculty of Health and Welfare, Tokushima Bunri University, Tokushima, Tokushima, Japan, 2 Department of Rehabilitation, Kasei Tamura Hospital, Wakayama, Wakayama, Japan,
Life and Medical Sciences Area, Health Sciences Discipline, Kobe University, Kobe, Hyogo, Japan

* akazawa@tks.bunri-u.ac.jp

Abstract

Background & aim

A recent study reported that the increase in intramuscular adipose tissue of the quadriceps in older inpatients is related to a decreasing degree of recovery in swallowing ability compared to the loss of muscle mass. However, whether the association remains true in case of aspiration pneumonia is unclear. Therefore, this study aimed to examine the relationship between the degree of recovery in swallowing ability and intramuscular adipose tissue in the quadriceps of older inpatients with aspiration pneumonia.

Methods

This prospective study included 39 older patients with aspiration pneumonia. Swallowing ability was assessed using the Food Intake Level Scale (FILS). The indicators for the degree of recovery in swallowing ability were FILS at discharge and change in FILS. A greater change in FILS indicates a greater improvement in swallowing ability. Intramuscular adipose tissue and muscle mass of the quadriceps were evaluated at admission using echo intensity and muscle thickness on ultrasound images, respectively. Multiple regression analysis was used to determine whether the echo intensity of the quadriceps was independently and significantly related to FILS at discharge and the change in FILS. Independent variables were age, sex, days from disease onset, echo intensity and muscle thickness of the quadriceps, subcutaneous fat thickness of the thigh, FILS at admission, and number of units of rehabilitation therapy.

Results

Echo intensity of the quadriceps ($\beta = -0.363$, p = 0.012) and FILS at admission ($\beta = 0.556$, p < 0.001) were independently and significantly associated with FILS at discharge ($R^2 = 0.760$, $f^2 = 3.167$, statistical power = 1.000). Similar variables (echo intensity of the

and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

quadriceps [$\beta = -0.498$, p = 0.012] and FILS at admission [$\beta = -0.635$, p < 0.001]) were independently and significantly related to change in FILS (R² = 0.547, f² = 1.208, statistical power = 0.998). Quadriceps muscle thickness was not independently and significantly related to FILS at discharge and change in FILS.

Conclusion

Our results indicate that intramuscular adipose tissue of the quadriceps in older inpatients with aspiration pneumonia is more strongly related to the degree of recovery in swallowing ability (that is, swallowing ability at discharge and change in swallowing ability) than muscle mass, and patients who have high intramuscular adipose tissue of the quadriceps at admission have a lower degree of recovery in swallowing ability.

Introduction

The prevalence of aspiration pneumonia increases with age [1]. In addition, aspiration pneumonia is frequently observed in clinical settings [2, 3] and is related to the mortality of older inpatients [4]. Furthermore, previous studies reported that aspiration pneumonia is associated with dysphagia [5, 6] and sarcopenia [7]. Based on the deep relationship between them [8], which is related to declining activities of daily living (ADL) [9, 10] and increased mortality [11, 12], improving dysphagia and sarcopenia is important for improving the prognosis of older inpatients with aspiration pneumonia.

Recently, swallowing-related muscles as well as appendicular and lower extremity muscles have been shown to be related to swallowing ability [13–15]. Some studies [15, 16] reported that the degree of recovery in swallowing ability in patients with high muscle mass in the appendicular and lower extremities is higher than that for patients with less muscle mass. Furthermore, it has been reported that chair-stand exercises improve swallowing ability [17], and aggressive gait training for patients with nasogastric tube feeding or gastrostomy increases the recovery of oral feeding [18]. Based on these findings, not only swallowing-related muscles but also whole-body muscles, especially the lower extremity muscles, are considered to be important for improving swallowing ability.

The European Working Group on Sarcopenia in Older People proposed the importance of assessing muscle mass as well as muscle quality, including intramuscular adipose tissue, in sarcopenia diagnosis [19]. A recent study [20] reported that intramuscular adipose tissue of the tongue in older persons is related to tongue pressure rather than muscle mass. In addition, because muscle mass of the lower extremity is related to swallowing ability, we examined the relationships between muscle mass and intramuscular adipose tissue of the quadriceps and the degree of recovery of swallowing ability in older inpatients [21]. The results indicated that the increase in intramuscular adipose tissue of the quadriceps in older inpatients was related to the decreasing degree of recovery in swallowing ability compared to the loss of muscle mass [21]. However, whether the intramuscular adipose tissue of the quadriceps in older inpatients with aspiration pneumonia is related to the degree of recovery in swallowing ability compared to examine the relationship between the swallowing ability in these patients. This study aimed to examine the relationship between the degree of recovery in swallowing ability and intramuscular adipose tissue in the quadriceps of older inpatients with aspiration pneumonia site with aspiration pneumonia ability in these patients. This study aimed to examine the relationship between the degree of recovery in swallowing ability and intramuscular adipose tissue in the quadriceps of older inpatients with aspiration pneumonia.

Materials and methods

Study design and participants

This prospective study included older patients with aspiration pneumonia who were referred to the Department of Rehabilitation at Kasei Tamura Hospital. Aspiration pneumonia was diagnosed on the basis of symptoms (fever, phlegm, and cough), inflammatory markers, chest imaging (X-ray and computed tomography), and swallowing status. The exclusion criteria of this study were age < 65 years, lack of data, and hospital admission due to the onset of other diseases. Patients with aspiration pneumonia who died during hospital stay were also excluded. A total of 455 inpatients were included in this study. Of these, patients who were < 65 years of age (n = 33) or lacked the necessary data (n = 18) were excluded. We also excluded 363 patients who were admitted to the hospital because of the onset of other diseases (stroke: 60, fracture: 126, heart disease: 25, spinal cord disease: 15, urinary tract infection: 12, and others: 125). In addition, two patients with aspiration pneumonia were excluded because of death during the hospital stay. Ultimately, 39 patients with aspiration pneumonia were included in the study. Rehabilitation therapy, including physical therapy, occupational therapy, and speech and swallowing therapy, was administered to all the participants during hospitalization. All participants or their guardians provided written informed consent prior to the study, which was approved by the ethics committee of Tokushima Bunri University.

Outcome measures

The main outcome of this study was the degree of recovery in swallowing ability. We also measured the characteristics of the participants at admission, including age, sex, body weight, height, body mass index (BMI), intramuscular adipose tissue and muscle mass of the quadriceps, subcutaneous fat mass of the thigh, nutritional status, inflammation, comorbidities, number of medications, number of units of rehabilitation therapy (1 unit of rehabilitation therapy = 20 min), and ADL. The length of hospital stay (days) and days from disease onset were assessed at discharge. The length of hospital stay was evaluated based on the hospitalization period at Kasei Tamura Hospital. Among the 39 patients, 11 (28.2%) were initially admitted to other hospitals; the days from the onset of disease in these patients were calculated by summing the lengths of both hospital stays.

Assessment of swallowing ability

Swallowing ability was assessed using the Food Intake Level Scale (FILS). The FILS is a 10-point observer-rated scale [22]. Levels 1 to 3 display various degrees of non-oral feeding; levels 4 to 6 relate to various degrees of oral food intake and alternative nutrition, such as enteral and parenteral nutrition; levels 7 to 9 refer to various degrees of oral intake alone; and level 10 displays normal oral food intake [22]. The validity and reliability of the FILS were reported in a previous study [22]. The indicators for the degree of recovery in swallowing ability were FILS at discharge and change in FILS. The change in FILS was calculated by subtracting FILS at admission from FILS at discharge. A greater change in FILS indicates a greater improvement in swallowing ability.

Measurements of intramuscular adipose tissue and muscle mass in the quadriceps and subcutaneous fat mass of the thigh

Transverse ultrasound images were obtained using a B-mode ultrasound system (NanoMaxx; SonoSite Japan, Tokyo, Japan) with a linear array probe (L25n/13–6 MHz; NanoMaxx). The intramuscular adipose tissue and muscle mass of the rectus femoris and vastus intermedius of

all participants were evaluated based on echo intensity and muscle thickness [21, 23–33], respectively. The validity of intramuscular adipose tissue and muscle mass measurements using ultrasound has been confirmed in recent studies using magnetic resonance imaging [34-36]. Images of the rectus femoris and vastus intermedius were obtained at 30% of the distance from the anterior superior iliac spine to the proximal end of the patella [21, 23, 26, 30-33]. The participants laid in a supine position with their lower limbs relaxed while a water-soluble transmission gel was applied to the skin surface of the thigh. The probe was pressed lightly against the skin to prevent muscle deformation. All the ultrasound images were captured by the same investigator. Echo intensity was assessed in the regions of interest to include as much muscle as possible while avoiding the bone and surrounding fascia [21, 23, 26, 30-33]. The thickness of the rectus femoris was determined as the distance between the superficial adipose tissue-muscle interface and the deep muscle-muscle interface [21, 23, 26, 30-33], while that of the vastus intermedius was determined as the distance between the superficial muscle-muscle interface and the bone-muscle interface [21, 23, 26, 30-33]. Fig 1 shows the measurement areas of echo intensity and thickness of the rectus femoris and vastus intermedius. Muscle echo intensity and thickness were measured using the ImageJ 1.49 software (National Institutes of Health, Bethesda, MD, USA) [21, 23, 25–28, 30–33]. Echo intensity was examined by performing a computer-assisted 8-bit gray-scale analysis, and the mean echo intensity of the regions of interest was rated from 0 (black) to 255 (white) [21, 23-33]. A higher echo intensity indicates greater intramuscular adipose tissue [37].

The echo intensity of the quadriceps was calculated as the mean echo intensity of the rectus femoris and vastus intermedius. Mean echo intensities of the right and left quadriceps were used in the analysis. The sum of the thicknesses of the rectus femoris and vastus intermedius

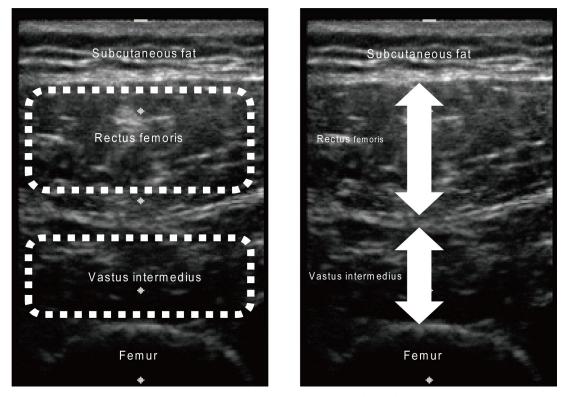


Fig 1. Measurement areas of echo intensity (dashed lines) and muscle thickness (arrows) of the rectus femoris and vastus intermedius.

https://doi.org/10.1371/journal.pone.0275810.g001

was used as quadriceps thickness. The mean quadriceps thickness on the right and left sides was included in the analysis. Measurements of the rectus femoris and vastus intermedius echo intensities and muscle thicknesses have relatively high reliability (intraclass correlation coefficients [1.1], 0.857–0.959) [23]. Subcutaneous fat mass in the thigh was assessed based on the subcutaneous fat thickness, which was defined as the distance between the dermis and adipose tissue interface and the muscle–adipose tissue interface [21, 23, 26, 30–33]. The mean subcutaneous fat thickness of the right and left thighs was used in the analysis.

Measures of other characteristics

Nutritional status was evaluated using the Geriatric Nutritional Risk Index (GNRI) score [38]. The GNRI score was calculated using the following formula: GNRI score = $(14.89 \times \text{serum}$ albumin [g/dL]) + $(41.7 \times \text{body weight [kg]/ideal body weight)}$ [38]. Inflammatory status was assessed using the C-reactive protein (CRP) concentration. Comorbidities were assessed using the updated Charlson Comorbidity Index (UCCI) score [39]. ADL was evaluated using the Barthel Index (BI) [40]. BI is widely used in clinical settings and includes ordinal assessments (0-100 points) [40]. Lower BI scores indicate a poor ability to perform ADL.

Sample size calculation

The effect size (f^2) of the multiple regression analysis in a recent study [21], which reported that an increase in intramuscular adipose tissue of the quadriceps in older inpatients is related to a decreasing degree of recovery in swallowing ability, was 1.512 (number of dependent variables = 13, $R^2 = 0.602$). We speculated that a similar degree of relationship would be observed between intramuscular adipose tissue of the quadriceps and the degree of recovery in the swallowing ability in older patients with aspiration pneumonia. Sample size calculation based on an effect size (f^2) of 1.512, 15 dependent variables, a statistical power of 0.80, and an alpha error of 0.05, indicated that 28 participants were required. The sample size in this study was calculated using G*Power version 3.1.9.2 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany).

Statistical analysis

All statistical analyses were conducted using the SPSS version 28 software (IBM SPSS Japan, Tokyo, Japan). The normality of the variables was assessed using the Shapiro–Wilk test. Parametric data are reported as mean \pm standard deviation, whereas nonparametric data are expressed as median (interquartile range [IQR]).

The FILS at admission and discharge were compared using the Wilcoxon signed-rank test. The associations of echo intensity and muscle thickness of the quadriceps with FILS at admission and discharge and change in FILS were determined using Kendall's τ rank correlation coefficient. Subcutaneous fat thickness affects echo intensity [41]. Therefore, we also examined the associations of echo intensity of the quadriceps with FILS at admission and discharge and change in FILS using partial correlation analysis adjusted for subcutaneous fat thickness of the thigh. Multiple regression analysis (forced entry method) was used to determine whether the echo intensity of the quadriceps was independently and significantly related to FILS at discharge and change in FILS. The independent variables were age, sex (male = 1, female = 2), days from disease onset, echo intensity and muscle thickness of the quadriceps, subcutaneous fat thickness of the thigh, FILS at admission, and number of units of rehabilitation therapy. The variance inflation factor was used to assess multicollinearity; a value > 10 was considered indicative of the presence of multicollinearity. P < 0.05 was considered to express statistical significance. In addition, we calculated the effect size (f²) of the multiple regression analysis for

FILS at discharge and change in FILS using the following equation: $R^2/(1 - R^2)$. The statistical power of the analysis was calculated using G^{*} Power version 3.1.9.2, based on f², an alpha error of 0.05, the total sample size, and a number of predictor variables.

Results

The medians (IQR) of FILS at admission, FILS at discharge, and change in FILS were 7.0 (6.0–7.0), 7.0 (6.0–7.0), and 0.0 (0.0–1.0), respectively. There was no significant difference between FILS at admission and discharge (p = 0.310). Improvement, preservation, and deterioration of FILS were observed in 11 (28.2%), 21 (53.8%), and seven (17.9%) patients, respectively. The median (IQR) of days from disease onset and length of hospital stay were 77.0 (49.0–93.0) and 70.0 (37.0–92.0), respectively. Table 1 presents the characteristics of the participants.

Table 2 presents the results of the correlation analysis. In the correlation analysis, the echo intensity of the quadriceps was significantly related to FILS at discharge and change in FILS, but was not significantly related to FILS at admission. Fig 2 shows the scatter plots between the echo intensity of the quadriceps and FILS at admission and discharge, and the change in FILS. Muscle thickness of the quadriceps was significantly related to FILS at discharge but was not to FILS at admission or change in FILS. In the partial correlation analysis, echo intensity of the quadriceps was significantly related to FILS at admission and discharge and to change in FILS. Tables 3 and 4 present the results of multiple regression analysis. Echo intensity of the quadriceps ($\beta = -0.363$, p = 0.012) and FILS at admission ($\beta = 0.556$, p < 0.001) were independently and significantly associated with FILS at discharge ($R^2 = 0.760$, $f^2 = 3.167$, statistical power = 1.000) (Table 3). Similar variables (echo intensity of the quadriceps [$\beta = -0.498$, p = 0.012] and FILS ($R^2 = 0.547$, $f^2 = 1.208$, statistical power = 0.998) (Table 4). Quadriceps muscle thickness was not independently and significantly related to FILS (R² = 0.547, $f^2 = 1.208$, statistical power = 0.998) (Table 4).

Table 1. Characteristics of p	articipants at admission.
-------------------------------	---------------------------

Characteristics	
Age, years	83.5 ± 7.6
Sex, male/female	26 (66.7)/13 (33.3)
Height, cm	158.0 (149.0–164.0)
Body weight, kg	43.6 (35.2-47.5)
Body mass index, kg/m ²	17.8 ± 3.2
Quadriceps echo intensity (gray-scale range, 0–255)	92.7 ± 19.7
Quadriceps thickness, cm	1.0 ± 0.4
Subcutaneous fat thickness of the thigh, cm	0.3 ± 0.1
C-reactive protein, mg/dL	1.2 (0.4–6.8)
Serum albumin, g/dL	3.0 ± 0.4
Geriatric Nutritional Risk Index score	77.4 ± 9.0
Updated Charlson comorbidity index score	2.0 (2.0-3.0)
Number of medications	5.0 (3.0-8.0)
Number of rehabilitation therapies, units/day	3.0 (2.0-4.0)
Barthel Index score	15.0 (0.0-35.0)

Data are presented as the mean ± standard deviation, n (%), or median (interquartile range).

https://doi.org/10.1371/journal.pone.0275810.t001

Variables	Food Intake Level Scale at admission	p-value	Food Intake Level Scale at discharge	p-value	Change in Food Intake Level Scale	p-value
Quadriceps echo intensity at admission	-0.19^{a}	0.132	-0.42^{a}	< 0.001	-0.36^{a}	0.004
Quadriceps echo intensity at admission	-0.38^{b}	0.019	-0.64^{b}	< 0.001	-0.37 ^b	0.024
Quadriceps thickness at admission	0.22 ^a	0.086	0.29 ^a	0.021	0.12 ^a	0.357

Table 2. Associations of echo intensity and muscle thickness of the quadriceps with Food Intake Level Scale at admission and discharge and with change in Food Intake Level Scale.

^aKendall's τ rank correlation coefficient.

^bpartial correlation coefficient adjusted for subcutaneous fat thickness of the thigh.

https://doi.org/10.1371/journal.pone.0275810.t002

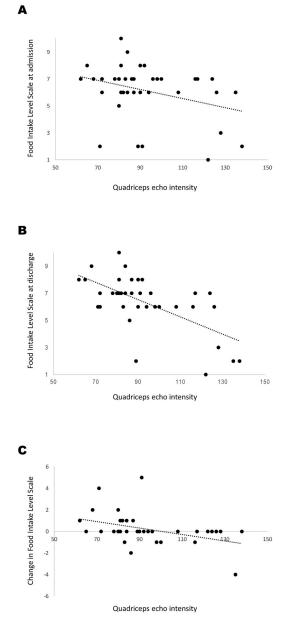
Discussion

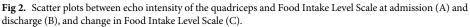
Our results indicate that there is a negative relationship between intramuscular adipose tissue of the quadriceps at admission and the degree of recovery in swallowing ability in older inpatients with aspiration pneumonia. In contrast, there was no relationship between the muscle mass of the quadriceps and the degree of recovery in swallowing ability. Taken together, the intramuscular adipose tissue of the quadriceps in older inpatients with aspiration pneumonia is more strongly related to the degree of recovery in swallowing ability (that is, swallowing ability at discharge and change in swallowing ability) than muscle mass, and patients with high intramuscular adipose tissue of the quadriceps at admission have a lower degree of recovery in swallowing ability.

Based on the results of this study, intramuscular adipose tissue of the quadriceps in older inpatients with aspiration pneumonia is considered a predictor of the degree of recovery in swallowing ability compared to muscle mass. With respect to the background of this result, two points were considered. First, the values might have overestimated the muscle mass because these values include not only actual muscle mass but also the mass of intramuscular adipose tissues [24, 42]. Second, previous studies reported that swallowing ability is related to appendicular skeletal muscle mass [13, 43]. Additionally, appendicular skeletal muscle mass is related to knee extension strength [44, 45], gait ability [46], and ADL [47, 48]. However, intramuscular adipose tissue in the quadriceps shows increased association with knee extension strength [25–27], gait ability [28–30], and ADL [31, 32] as compared to muscle mass. These findings indicate that in contrast to muscle mass, intramuscular adipose tissue of the quadriceps is indirectly related to swallowing ability. These two points were considered the background to our results.

Recently, intervention for lower extremities has been shown to contribute to the recovery of swallowing ability [17, 18]. The degree of recovery in swallowing ability has been reported to be high in stroke patients who perform more chair-stand exercises [17]. Furthermore, aggressive gait training for patients with nasogastric tube feeding or gastrostomy using orthoses that is, knee–ankle–foot orthosis, trunk–hip–bilateral knee–ankle–foot orthoses, and knee orthosis increases the recovery of oral feeding in these patients [18]. Our results, in which intramuscular adipose tissue of the quadriceps is related to the degree of recovery in swallow-ing ability in older patients with aspiration pneumonia, support these recent findings. Considering our results, intervention for intramuscular adipose tissue in the quadriceps may be needed to improve the swallowing ability of older inpatients with aspiration pneumonia.

Physical activity intervention is reported to be effective in improving intramuscular adipose tissue of the thigh in older frail persons [49]. Considering this, physical activity intervention may be an effective approach for improving intramuscular adipose tissue in the quadriceps in older inpatients with aspiration pneumonia. Ishii et al. [50] targeted older patients with low





https://doi.org/10.1371/journal.pone.0275810.g002

ADL and reported that the swallowing ability in older patients who spent 4 or more hours away from the bed in a day was higher than that of older patients who spent less than 4 hours away from the bed. The results of this study indicate that there is a relationship between physical activity and swallowing ability, and thus, support our hypothesis (intervention with physical activity for decreasing intramuscular adipose tissue of the quadriceps is needed to improve swallowing ability in older patients with aspiration pneumonia).

A score below 60 in BI is interpreted as a severe dependency condition [51]. The median BI score at admission of the participants in this study was 15. In other words, the decrease in ADL of the participants was remarkable. The mean BMI of the participants was 17.8 kg/m^2 .

	В	SE	95% confidence interval of B	β	VIF	p-value
Age	-0.02	0.03	-0.07, 0.04	-0.07	1.26	0.519
Sex	0.66	0.43	-0.21, 1.54	0.16	1.34	0.132
Days from onset of disease	-0.01	0.01	-0.02, 0.00	-0.19	1.46	0.092
Quadriceps thickness at admission	0.36	0.81	-1.30, 2.02	0.07	3.39	0.660
Quadriceps echo intensity at admission	-0.04	0.01	-0.06, -0.01	-0.36	2.32	0.012
Subcutaneous fat thickness of the thigh at admission	-0.18	2.28	-4.82, 4.47	-0.01	2.30	0.939
Food Intake Level Scale at admission	0.55	0.10	0.33, 0.76	0.56	1.39	< 0.001
Number of rehabilitation therapy	0.06	0.16	-0.26, 0.38	0.04	1.53	0.700

Table 3. Multiple regression analysis for Food Intake Level Scale at discharge.

B, partial regression coefficient; SE, standard error; β, standardized partial regression coefficient; VIF, variance inflation factor.

https://doi.org/10.1371/journal.pone.0275810.t003

This value was the same as the cut-off value (17.8 kg/m²) for severely low BMI in Asians in the Global Leadership Initiative on Malnutrition criteria [33, 52]. Furthermore, the mean GNRI score of the participants was 77.4. This value was lower than the cut-off value (GNRI score of 82) for major malnutrition risk [38]. Although some studies [53, 54] have reported that resistance training improves intramuscular adipose tissue of the quadriceps, conducting resistance training is difficult for older inpatients with aspiration pneumonia who have low ADL and BMI and major malnutrition risk. Physical activity intervention may be realistic for improving intramuscular adipose tissue in the quadriceps of older inpatients with aspiration pneumonia.

The results of this study showed no statistically significant difference between FILS at admission and discharge, and the FILS of many participants indicated preservation (53.8%) or deterioration (17.9%) during hospitalization. Old age [55, 56], malnutrition risk [57], low weight [56], and low ADL [55] have been known to negatively affect the recovery of swallowing ability. Considering that older patients with aspiration pneumonia in this study had malnutrition risk, low weight, and low ADL, confirming no difference between FILS at admission and discharge might be a valid result. In addition, swallowing ability is closely related to ADL [55, 58–60]. A previous study [61] targeting older patients with aspiration pneumonia who received rehabilitation indicated that the changes in BI score during hospitalization in almost all participants (71.1%) was < 0, and ADL was less likely to improve. Considering the results of the previous study [61] and our study, swallowing ability in older patients with aspiration pneumonia may be difficult to improve, similar to ADL.

The Special Interest Group on Sarcopenia in the International Society of Physical and Rehabilitation Medicine has recommended using quadriceps thickness obtained from ultrasound

Table 4. M	Iultip	le regression ana	lysis for o	change in Food	l Inta	ke Level Scale.	

	В	SE	95% confidence interval of B	β	VIF	p-value
Age	-0.02	0.03	-0.07, 0.04	-0.09	1.26	0.519
Sex	0.66	0.43	-0.21, 1.54	0.22	1.34	0.132
Days from onset of disease	-0.01	0.01	-0.02, 0.00	-0.26	1.46	0.092
Quadriceps thickness at admission	0.36	0.81	-1.30, 2.02	0.10	3.39	0.660
Quadriceps echo intensity at admission	-0.04	0.01	-0.06, -0.01	-0.50	2.32	0.012
Subcutaneous fat thickness of the thigh at admission	-0.18	2.28	-4.82, 4.47	-0.01	2.30	0.939
Food Intake Level Scale at admission	-0.45	0.10	-0.67, -0.24	-0.64	1.39	< 0.001
Number of rehabilitation therapy	0.06	0.16	-0.26, 0.38	0.06	1.53	0.700

B, partial regression coefficient; SE, standard error; β, standardized partial regression coefficient; VIF, variance inflation factor.

https://doi.org/10.1371/journal.pone.0275810.t004

images to assess muscle mass in sarcopenia diagnosis [62]. In addition, the effects of aging and disuse are remarkably observed in the quadriceps of the upper and lower extremity muscles [63, 64]. Furthermore, intramuscular adipose tissue in the quadriceps of older inpatients has been reported to be related to gait ability [28–30], ADL [31, 32], and the onset of hospital-associated complications [65]. Based on these findings, targeting the quadriceps was considered valid in this study.

This study had three limitations. First, it was a prospective study. Therefore, the causal relationship between swallowing ability and intramuscular adipose tissue in the quadriceps of older inpatients with aspiration pneumonia remains unclear. A randomized controlled trial is needed to reveal this relationship. Second, the sample size of the study was small. However, in the post-hoc analysis, the statistical powers of the multiple regression analysis for FILS at discharge and change in FILS were 1.000 and 0.998, respectively. In other words, there were no type 2 errors in the statistical analyses in this study. Finally, smoking history has been shown to negatively affect the recovery of swallowing function [66]. However, this study did not examine the smoking history of participants. Therefore, we were unable to treat smoking history as a confounding factor in the statistical analysis.

Conclusions

Our results indicate that the degree of recovery in swallowing ability in older inpatients with aspiration pneumonia is more strongly associated to intramuscular adipose tissue of the quadriceps than to muscle mass, and patients who have higher intramuscular adipose tissue of the quadquadriceps at admission have a lower degree of recovery in swallowing ability. Intervention for intramuscular adipose tissue of the quadriceps may be needed to improve the swallowing ability of older inpatients with aspiration pneumonia.

Supporting information

S1 Dataset. (XLSX)

Acknowledgments

We thank the participants and staff who helped with this study.

Author Contributions

Conceptualization: Naoki Akazawa, Masaki Kishi, Toshikazu Hino, Ryota Tsuji, Kimiyuki Tamura, Akemi Hioka, Hideki Moriyama.

- **Data curation:** Naoki Akazawa, Masaki Kishi, Toshikazu Hino, Ryota Tsuji, Kimiyuki Tamura.
- Formal analysis: Naoki Akazawa.

Funding acquisition: Naoki Akazawa, Hideki Moriyama.

- **Investigation:** Naoki Akazawa, Toshikazu Hino, Ryota Tsuji, Kimiyuki Tamura, Akemi Hioka, Hideki Moriyama.
- Methodology: Naoki Akazawa, Masaki Kishi, Toshikazu Hino, Ryota Tsuji, Kimiyuki Tamura, Akemi Hioka, Hideki Moriyama.

Project administration: Naoki Akazawa.

Resources: Naoki Akazawa, Akemi Hioka, Hideki Moriyama.

Software: Naoki Akazawa, Akemi Hioka.

Supervision: Naoki Akazawa, Masaki Kishi, Toshikazu Hino, Ryota Tsuji, Kimiyuki Tamura, Akemi Hioka, Hideki Moriyama.

Validation: Naoki Akazawa, Akemi Hioka, Hideki Moriyama.

Visualization: Naoki Akazawa.

Writing – original draft: Naoki Akazawa, Hideki Moriyama.

References

- Teramoto S, Fukuchi Y, Sasaki H, Sato K, Sekizawa K, Matsuse T. High incidence of aspiration pneumonia in community- and hospital-acquired pneumonia in hospitalized patients: a multicenter, prospective study in Japan. J Am Geriatr Soc. 2008; 56: 577–579. https://doi.org/10.1111/j.1532-5415.2008. 01597.x PMID: 18315680
- Baine WB, Yu W, Summe JP. Epidemiologic trends in the hospitalization of elderly Medicare patients for pneumonia, 1991–1998. Am J Public Health. 2001; 91: 1121–1123. <u>https://doi.org/10.2105/ajph.91.</u> 7.1121 PMID: 11441742
- Imamura Y, Miyazaki T, Watanabe A, Tsukada H, Nagai H, Hasegawa Y, et al. Prospective multicenter survey for Nursing and Healthcare-associated Pneumonia in Japan [published online ahead of print, 2022 Apr 9]. J Infect Chemother. 2022; S1341-321X(22)00111-8. https://doi.org/10.1016/j.jiac.2022.03. 030 PMID: 35414437
- Langmore SE, Terpenning MS, Schork A, Chen Y, Murray JT, Lopatin D, et al. Predictors of aspiration pneumonia: how important is dysphagia? Dysphagia. 1998; 13: 69–81. https://doi.org/10.1007/ PL00009559 PMID: 9513300
- van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Meta-analysis of dysphagia and aspiration pneumonia in frail elders. J Dent Res. 2011; 90: 1398–1404. https://doi.org/ 10.1177/0022034511422909 PMID: 21940518
- van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. J Am Med Dir Assoc. 2011; 12: 344–354. https://doi.org/10.1016/j.jamda.2010.12.099 PMID: 21450240
- Okazaki T, Ebihara S, Mori T, Izumi S, Ebihara T. Association between sarcopenia and pneumonia in older people. Geriatr Gerontol Int. 2020; 20: 7–13. https://doi.org/10.1111/ggi.13839 PMID: 31808265
- Wakabayashi H, Kishima M, Itoda M, Fujishima I, Kunieda K, Ohno T, et al. Diagnosis and Treatment of Sarcopenic Dysphagia: A Scoping Review. Dysphagia. 2021; 36: 523–531. https://doi.org/10.1007/ s00455-021-10266-8 PMID: 33620563
- Eglseer D, Halfens RJG, Schols JMGA, Lohrmann C. Dysphagia in Hospitalized Older Patients: Associated Factors and Nutritional Interventions. J Nutr Health Aging. 2018; 22: 103–110. <u>https://doi.org/10.1007/s12603-017-0928-x PMID: 29300429</u>
- Xu W, Chen T, Cai Y, Hu Y, Fan L, Wu C. Sarcopenia in Community-Dwelling Oldest Old Is Associated with Disability and Poor Physical Function. J Nutr Health Aging. 2020; 24: 339–345. https://doi.org/10. 1007/s12603-020-1325-4 PMID: 32115617
- Banda KJ, Chu H, Chen R, Kang XL, Jen HJ, Liu D, et al. Prevalence of Oropharyngeal Dysphagia and Risk of Pneumonia, Malnutrition, and Mortality in Adults Aged 60 Years and Older: A Meta-Analysis [published online ahead of print, 2021 Dec 13]. Gerontology. 2021; 1–13.
- Xu J, Reijnierse EM, Pacifico J, Wan CS, Maier AB. Sarcopenia is associated with 3-month and 1-year mortality in geriatric rehabilitation inpatients: RESORT. Age Ageing. 2021; 50: 2147–2156. https://doi. org/10.1093/ageing/afab134 PMID: 34260683
- Maeda K, Takaki M, Akagi J. Decreased Skeletal Muscle Mass and Risk Factors of Sarcopenic Dysphagia: A Prospective Observational Cohort Study. J Gerontol A Biol Sci Med Sci. 2017; 72: 1290–1294. https://doi.org/10.1093/gerona/glw190 PMID: 27707804
- Matsuo H, Yoshimura Y. Calf circumference is associated with dysphagia in acute-care inpatients. Geriatr Nurs. 2018; 39: 186–190. https://doi.org/10.1016/j.gerinurse.2017.08.003 PMID: 28939287
- Kimura M, Naganuma A, Ogawa Y, Inagawa M, Nishioka S, Momosaki R, et al. Calf circumference and stroke are independent predictors for an improvement in the food intake level scale in the Japanese sarcopenic dysphagia database. Eur Geriatr Med. 2022 May 25. <u>https://doi.org/10.1007/s41999-022-00651-3 PMID: 35612760</u>

- Nishioka S, Yamasaki K, Ogawa K, Oishi K, Yano Y, Okazaki Y, et al. Impact of nutritional status, muscle mass and oral status on recovery of full oral intake among stroke patients receiving enteral nutrition: A retrospective cohort study. Nutr Diet. 2020; 77: 456–466. https://doi.org/10.1111/1747-0080.12579 PMID: 31499583
- Yoshimura Y, Wakabayashi H, Nagano F, Bise T, Shimazu S, Shiraishi A. Chair-stand exercise improves post-stroke dysphagia. Geriatr Gerontol Int. 2020; 20: 885–891. <u>https://doi.org/10.1111/ggi.</u> 13998 PMID: 32772455
- Arai H, Takeuchi J, Nozoe M, Fukuoka T, Matsumoto S, Morimoto T. Association Between Active Gait Training for Severely Disabled Patients with Nasogastric Tube Feeding or Gastrostoma and Recovery of Oral Feeding: A Retrospective Cohort Study. Clin Interv Aging. 2020; 15: 1963–1970. <u>https://doi.org/ 10.2147/CIA.S270277 PMID: 33116450</u>
- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019; 48: 16–31. <u>https://doi.org/10.1093/ageing/afy169 PMID: 30312372</u>
- Nakao Y, Yamashita T, Honda K, Katsuura T, Hama Y, Nakamura Y, et al. Association Among Age-Related Tongue Muscle Abnormality, Tongue Pressure, and Presbyphagia: A 3D MRI Study. Dysphagia. 2021; 36: 483–491. https://doi.org/10.1007/s00455-020-10165-4 PMID: 32743742
- Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Hioka A, et al. Intramuscular adipose tissue of the quadriceps is more strongly related to recovery of swallowing ability than is muscle mass in older inpatients: A prospective study. Nutrition. 2021; 91–92: 111364. https://doi.org/10.1016/j.nut.2021.111364 PMID: 34246889
- 22. Kunieda K, Ohno T, Fujishima I, Hojo K, Morita T. Reliability and validity of a tool to measure the severity of dysphagia: the Food Intake LEVEL Scale. J Pain Symptom Manage. 2013; 46: 201–206. https://doi.org/10.1016/j.jpainsymman.2012.07.020 PMID: 23159683
- Akazawa N, Harada K, Okawa N, Tamura K, Hayase A, Moriyama H. Relationships between muscle mass, intramuscular adipose and fibrous tissues of the quadriceps, and gait independence in chronic stroke survivors: a cross-sectional study. Physiotherapy. 2018; 104: 438–445. https://doi.org/10.1016/ j.physio.2017.08.009 PMID: 29290379
- 24. Fukumoto Y, Ikezoe T, Yamada Y, Tsukagoshi R, Nakamura M, Takagi Y, et al. Age-related ultrasound changes in muscle quantity and quality in women. Ultrasound Med Biol. 2015; 41: 3013-3017. <u>https://doi.org/10.1016/j.ultrasmedbio.2015.06.017</u> PMID: 26278633
- Wilhelm EN, Rech A, Minozzo F, Radaelli R, Botton CE, Pinto RS. Relationship between quadriceps femoris echo intensity, muscle power, and functional capacity of older men. Age. 2014; 36: 9625. https://doi.org/10.1007/s11357-014-9625-4 PMID: 24515898
- Akazawa N, Okawa N, Tamura K, Moriyama H. Relationships between intramuscular fat, muscle strength, and gait independence in older women: a cross-sectional study. Geriatr Gerontol Int. 2017; 17: 1683–1688. https://doi.org/10.1111/ggi.12869 PMID: 27506895
- Mayer KP, Thompson Bastin ML, Montgomery-Yates AA, Pastva AM, Dupont-Versteegden EE, Parry SM, et al. Acute skeletal muscle wasting and dysfunction predict physical disability at hospital discharge in patients with critical illness. Crit Care. 2020; 24: 637. <u>https://doi.org/10.1186/s13054-020-03355-x</u> PMID: 33148301
- Lopez P, Wilhelm EN, Rech A, Minozzo F, Radaelli R, Pinto RS. Echo intensity independently predicts functionality in sedentary older men. Muscle Nerve. 2017; 55: 9–15. <u>https://doi.org/10.1002/mus.25168</u> PMID: 27145419
- Osawa Y, Arai Y, Oguma Y, Hirata T, Abe Y, Azuma K, et al. Relationships of muscle echo intensity with walking ability and physical activity in the very old population. J Aging Phys Act. 2017; 25: 189– 195. https://doi.org/10.1123/japa.2015-0203 PMID: 27623344
- Akazawa N, Okawa N, Kishi M, Hino T, Tsuji R, Tamura K, et al. Quantitative features of intramuscular adipose tissue of the quadriceps and their association with gait independence in older inpatients: A cross-sectional study. Nutrition. 2020; 71: 110600. https://doi.org/10.1016/j.nut.2019.110600 PMID: 31811998
- Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Hioka A, et al. Longitudinal relationship between intramuscular adipose tissue of the quadriceps and activities of daily living in older inpatients. J Cachexia Sarcopenia Muscle. 2021; 12: 2231–2237. https://doi.org/10.1002/jcsm.12842 PMID: 34704384
- Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Moriyama H. Increased intramuscular adipose tissue of the quadriceps is more strongly related to declines in ADL than is loss of muscle mass in older inpatients. Clin Nutr. 2021; 40: 1381–1387. https://doi.org/10.1016/j.clnu.2020.08.029 PMID: 32917418
- Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Moriyama H. Using GLIM criteria, cutoff value for low BMI in Asian populations discriminates high or low muscle mass: A cross-sectional study. Nutrition. 2021; 81: 110928. https://doi.org/10.1016/j.nut.2020.110928 PMID: 32739660

- Miyatani M, Kanehisa H, Ito M, Kawakami Y, Fukunaga T. The accuracy of volume estimates using ultrasound muscle thickness measurements in different muscle groups. Eur J Appl Physiol. 2004; 91: 264–272. https://doi.org/10.1007/s00421-003-0974-4 PMID: 14569399
- Young HJ, Jenkins NT, Zhao Q, Mccully KK. Measurement of intramuscular fat by muscle echo intensity. Muscle Nerve. 2015; 52: 963–971. https://doi.org/10.1002/mus.24656 PMID: 25787260
- Akima H, Hioki M, Yoshiko A, Koike T, Sakakibara H, Takahashi H, et al. Intramuscular adipose tissue determined by T1-weighted MRI at 3T primarily reflects extramyocellular lipids. Magn Reson Imaging. 2016; 34: 397–403. https://doi.org/10.1016/j.mri.2015.12.038 PMID: 26743430
- Pillen S, van Keimpema, Nievelstein RA, Verrips A, van Kruijsbergen-Raijmann W, Zwarts MJ. Skeletal muscle ultrasonography: visual versus quantitative evaluation. Ultrasound Med Biol. 2006; 32: 1315– 1321. https://doi.org/10.1016/j.ultrasmedbio.2006.05.028 PMID: 16965971
- Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr. 2005; 82: 777e83. https://doi.org/10.1093/ajcn/82.4.777 PMID: 16210706
- Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011; 173: 676–682. https://doi.org/10.1093/aje/kwg433 PMID: 21330339
- 40. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J 1965; 14: 61–65. PMID: 14258950
- Ryan ED, Shea NW, Gerstner GR, Barnette TJ, Tweedell AJ, Kleinberg CR, et al. The influence of subcutaneous fat on the relationship between body composition and ultrasound-derived muscle quality. Appl Physiol Nutr Metab. 2016; 27: 1–4. https://doi.org/10.1139/apnm-2016-0238 PMID: 27690567
- 42. Hamaguchi Y, Kaido T, Okumura S, Ito T, Fujimoto Y, Ogawa K, et al. Preoperative intramuscular adipose tissue content is a novel prognostic predictor after hepatectomy for hepatocellular carcinoma. J Hepatobiliary Pancreat Sci. 2015; 22: 475–485. https://doi.org/10.1002/jhbp.236 PMID: 25755128
- Cha S, Kim WS, Kim KW, Han JW, Jang HC, Lim S, et al. Sarcopenia is an Independent Risk Factor for Dysphagia in Community-Dwelling Older Adults. Dysphagia. 2019; 34: 692–697. <u>https://doi.org/10.1007/s00455-018-09973-6 PMID: 30612233</u>
- Chen L, Nelson DR, Zhao Y, Cui Z, Johnston JA. Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States. BMC Geriatr. 2013; 16; 13: 74. https://doi.org/10.1186/1471-2318-13-74 PMID: 23865675
- **45.** Pisciottano MV, Pinto SS, Szejnfeld VL, Castro CH. The relationship between lean mass, muscle strength and physical ability in independent healthy elderly women from the community. J Nutr Health Aging. 2014; 18: 554–8. https://doi.org/10.1007/s12603-013-0414-z PMID: 24886744
- 46. Tanaka KI, Morisato Y, Nakajima H, Kanasaki K, Sugimoto T, Kanazawa I. Which Is a Better Skeletal Muscle Mass Index for the Evaluation of Physical Abilities: The Present Height or Maximum Height? Intern Med. 2021; 60: 1191–1196. https://doi.org/10.2169/internalmedicine.5792-20 PMID: 33229805
- Malmstrom TK, Miller DK, Herning MM, Morley JE. Low appendicular skeletal muscle mass (ASM) with limited mobility and poor health outcomes in middle-aged African Americans. J Cachexia Sarcopenia Muscle. 2013; 4: 179–86. https://doi.org/10.1007/s13539-013-0106-x PMID: 23532635
- 48. Hirani V, Naganathan V, Blyth F, Le Couteur DG, Seibel MJ, Waite LM, et al. Longitudinal associations between body composition, sarcopenic obesity and outcomes of frailty, disability, institutionalisation and mortality in community-dwelling older men: The Concord Health and Ageing in Men Project. Age Ageing. 2017; 46: 413–420. https://doi.org/10.1093/ageing/afw214 PMID: 27932368
- 49. Englund DA, Kirn DR, Koochek A, Zhu H, Travison TG, Reid KF, et al. Nutritional supplementation with physical activity improves muscle composition in mobility-limited older adults, The VIVE2 Study: A randomized, double-blind, placebo-controlled trial. J Gerontol A Biol Sci Med Sci. 2017; 73: 95-101. https://doi.org/10.1093/gerona/glx141 PMID: 28977347
- Ishii M, Nakagawa K, Yoshimi K, Okumura T, Hasegawa S, Yamaguchi K, et al. Time Spent Away from Bed to Maintain Swallowing Function in Older Adults. Gerontology. 2022; 12: 1–10. <u>https://doi.org/10.1159/000522499</u> PMID: 35413713
- Granger CV, Albrecht GL, Hamilton BB. Outcome of comprehensive medical rehabilitation: measurement by PULSES profile and the Barthel Index. Arch Phys Med Rehabil. 1979; 60: 145–54. PMID: 157729
- Maeda K, Ishida Y, Nonogaki T, Mori N. Reference body mass index values and the prevalence of malnutrition according to the Global Leadership Initiative on Malnutrition criteria. Clin Nutr. 2020; 39: 180– 184. https://doi.org/10.1016/j.clnu.2019.01.011 PMID: 30712782
- Gorgey AS, Mather KJ, Cupp HR, Gater DR. Effects of resistance training on adiposity and metabolism after spinal cord injury. Med Sci Sports Exerc. 2012; 44: 165–74. <u>https://doi.org/10.1249/MSS.</u> 0b013e31822672aa PMID: 21659900

- Yoshiko A, Kaji T, Kozuka T, Sawazaki T, Akima H. Evaluation of rehabilitation exercise effects by using gradation-based skeletal muscle echo intensity in older individuals: a one-group before-and-after trial study. BMC Geriatr. 2021; 21: 485. https://doi.org/10.1186/s12877-021-02423-3 PMID: 34488651
- Nakayama E, Tohara H, Hino T, Sato M, Hiraba H, Abe K, et al. The effects of ADL on recovery of swallowing function in stroke patients after acute phase. J Oral Rehabil. 2014; 41: 904–911. <u>https://doi.org/ 10.1111/joor.12212</u> PMID: 25041090
- 56. Nakadate A, Otaka Y, Kondo K, Yamamoto R, Matsuura D, Honaga K, et al. Age, Body Mass Index, and White Blood Cell Count Predict the Resumption of Oral Intake in Subacute Stroke Patients. J Stroke Cerebrovasc Dis. 2016; 25: 2801–2808. https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.07.038 PMID: 27542695
- 57. Nishioka S, Okamoto T, Takayama M, Urushihara M, Watanabe M, Kiriya Y, et al. Malnutrition risk predicts recovery of full oral intake among older adult stroke patients undergoing enteral nutrition: Secondary analysis of a multicentre survey (the APPLE study). Clin Nutr. 2017; 36: 1089–1096. https://doi.org/ 10.1016/j.clnu.2016.06.028 PMID: 27426415
- Matsuo H, Yoshimura Y, Ishizaki N, Ueno T. Dysphagia is associated with functional decline during acute-care hospitalization of older patients. Geriatr Gerontol Int. 2017; 17: 1610–1616. <u>https://doi.org/ 10.1111/ggi.12941</u> PMID: 27910255
- 59. Waza M, Maeda K, Katsuragawa C, Sugita A, Tanaka R, Ohtsuka A, et al. Comprehensive Tool to Assess Oral Feeding Support for Functional Recovery in Post-acute Rehabilitation. J Am Med Dir Assoc. 2019; 20: 426–431. https://doi.org/10.1016/j.jamda.2018.10.022 PMID: 30528795
- 60. Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Hioka A, et al. Nutritional and swallowing statuses but not intramuscular adipose tissue and muscle mass are related to activities of daily living in older inpatients who are judged as severely low body mass index in the Global Leadership Initiative on Malnutrition criteria. Clin Nutr ESPEN. 2022; 49: 411–416. <u>https://doi.org/10.1016/j.clnesp.2022.03.012</u> PMID: 35623846
- Yagi M, Yasunaga H, Matsui H, Fushimi K, Fujimoto M, Koyama T, et al. Effect of early rehabilitation on activities of daily living in patients with aspiration pneumonia. Geriatr Gerontol Int. 2016; 16: 1181– 1187. https://doi.org/10.1111/ggi.12610 PMID: 26460175
- 62. Kara M, Kaymak B, Frontera W, Ata AM, Ricci V, Ekiz T, et al. Diagnosing sarcopenia: Functional perspectives and a new algorithm from the ISarcoPRM. J Rehabil Med. 2021; 53: jrm00209. <u>https://doi.org/10.2340/16501977-2851 PMID: 34121127</u>
- Ikezoe T, Mori N, Nakamura M, Ichihashi N. Atrophy of the lower limbs in elderly women: is it related to walking ability? Eur J Appl Physiol. 2011; 111: 989–995. <u>https://doi.org/10.1007/s00421-010-1728-8</u> PMID: 21082193
- Abe T, Sakamaki M, Yasuda T, Bemben MG, Kondo M, Kawakami Y, et al. Age-related, site-specific muscle loss in 1507 Japanese men and women aged 20 to 95 years. J Sports Sci Med. 2011; 10: 145– 150. PMID: 24149307
- 65. Nagae M, Umegaki H, Yoshiko A, Fujita K, Komiya H, Watanabe K, et al. Echo intensity is more useful in predicting hospital-associated complications than conventional sarcopenia-related parameters in acute hospitalized older patients. Exp Gerontol. 2021; 150: 111397. https://doi.org/10.1016/j.exger. 2021.111397 PMID: 33965558
- Wang T, Ma L, Yang DL, Wang H, Bai ZL, Zhang LJ, et al. Factors predicting dysphagia after anterior cervical surgery: A multicenter retrospective study for 2 years of follow-up. Medicine (Baltimore). 2017; 96: e7916. https://doi.org/10.1097/MD.00000000007916 PMID: 28834916