

1 **Muscle evaluation and hospital-associated disability in acute hospitalized older**
2 **adults**

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25 **Abstract**

26 **OBJECTIVES:** We aimed to examine the association of muscle evaluation, including muscle
27 ultrasound, with hospital-associated disability (HAD), focusing on ADL categories.

28 **DESIGN:** A prospective observational cohort study.

29 **SETTING AND PARTICIPANTS:** We recruited patients aged 65 years or older who were admitted
30 to the geriatric ward of an acute hospital between October 2019 and September 2021.

31 **MEASUREMENTS:** Handgrip strength, bioimpedance analyzer-determined skeletal muscle mass,
32 bilateral thigh muscle thickness (BATT), and the echo intensity of the rectus femoris on muscle
33 ultrasound were performed as muscle assessments. HAD was evaluated separately for mobility
34 impairments and self-care impairments.

35 **RESULTS:** In total, 256 individuals (mean age, 85.2 years; male sex, 41.8%) were analyzed. HAD in
36 mobility was more common than HAD in self-care (37.5% vs. 30.0%). Only BATT was independently
37 associated with HAD in mobility in multiple logistic regression analysis. There was no significant
38 association between muscle indicators and HAD in self-care.

39 **CONCLUSION:** A lower BATT was associated with a higher prevalence of HAD in mobility,
40 suggesting the need to reconsider muscle assessment methods in hospitalized older adults. In addition,
41 approaches other than physical may be required, such as psychosocial and environmental interventions
42 to improve HAD in self-care.

43

44 **Keywords**

45 Hospital-associated disability, Mobility, Self-care, Muscle thickness, Sarcopenia

46

47 **Introduction**

48 Functional decline is common in older adults, and a strategy for preventing an activity of daily living
49 (ADL) decline is required. In the International Classification of Functioning Disability and Health
50 (ICF) framework established by the World Health Organization (WHO) in 2001, ADLs are also
51 considered a significant part of the “activities and participation” component[1]. The evaluation of
52 ADLs is important for independent daily living in older adults living in the community.

53 An ADL decline due to hospitalization is often referred to as hospital-associated disability
54 (HAD). HAD is commonly defined as the new loss of one or more elements of basic ADLs[2]. A
55 recent meta-analysis reported a 30% prevalence rate for HAD[3], and this rate has not changed in the
56 last three decades[4]. Risk factors for HAD include multiple domains, such as background factors,
57 acute illness, and factors during hospitalization[2,5]. For example, the reported risk factors for HAD
58 include age, mobility, cognitive function, ADL and instrumental ADL (IADL) levels, comorbidities,
59 geriatric syndromes, social factors, depression, malnutrition, polypharmacy, and illness severity. Older
60 hospitalized patients are frailer and share multiple risk factors that would heighten the risk of HAD.

61 HAD is associated with poor prognosis after discharge, including increased mortality, a non-return to
62 pre-illness functional levels[6], an increased readmission rate[7], and institutionalization[8]. Therefore,
63 prevention and early intervention of HAD in hospitalized older adults is an urgent clinical task.

64 In recent years, a relationship between sarcopenia and HAD has also been indicated. Sarcopenia
65 is defined as a progressive skeletal muscle disorder involving decreased muscle mass, muscle strength,
66 and physical function[9]. Low handgrip strength at acute hospitalization is associated with ADL
67 dependency[10] and is a risk factor for newly **developed** ADL disability after discharge[11]. Therefore,
68 evaluation of muscle strength, muscle mass, and physical function in hospitalized older adults **could**
69 be important for preventing HAD. However, it often has some limitations. Muscle strength can be
70 restricted or underestimated by acute illness or comorbidities such as paralysis or cognitive
71 dysfunction. Muscle mass is commonly assessed by dual-energy X-ray absorptiometry (DXA) or
72 bioelectrical impedance analysis (BIA), but these modalities are expensive, involve radiation exposure,
73 and can be affected by hydration status. Moreover, the evaluation of physical function in hospitalized
74 older adults is often restricted to bedridden individuals due to acute illness or comorbidity.

75 Muscle ultrasound of the quadriceps femoris has recently been found useful for evaluating
76 muscle morphology and muscle quality[12]. The muscle thickness of the quadriceps femoris shows
77 strong correlations with muscle mass[13], and echo intensity (EI) is an indicator of skeletal muscle
78 quality[14]. Muscle ultrasound has been performed in clinical practice to diagnose sarcopenia[15] and

79 to predict mortality[16], and worse recovery of ADLs[17]. We have also previously reported that
80 higher corrected EI of the quadriceps femoris was associated with hospital-associated
81 complication[18], and also reported that the thigh muscle thickness tended to be associated with
82 mortality within 3 months after discharge[19].

83 It would be meaningful to explore the relationship between muscle evaluation, including muscle
84 ultrasound and HAD, but in clinical practice, it may be more useful to classify ADLs by category
85 because changes in ADL during hospitalization are not uniform, and management needs to be changed
86 accordingly. In particular, mobility (ICF chapter: d4) and self-care (ICF chapter: d5) are considered to
87 be key points of ADL assessment by WHO[1]. The former comprises four subdomains—changing and
88 maintaining body position; carrying, moving, and handling objects; walking and moving; and moving
89 around using transportation, while the latter comprises seven subdomains—washing oneself; caring
90 for body parts; toileting; dressing; eating; drinking; and looking after one’s health. The classification
91 of ADLs in hospitalized older adults can be used to set goals during hospitalization and to improve
92 quality of daily life after discharge.

93 Therefore, in the present study of acute hospitalized older adults, we examined the association
94 of muscle evaluation, including muscle ultrasound, with ADL categories. The hypothesis was that
95 muscle thickness and EI would both be related to HAD but that the relationship would differ by ADL
96 categories,.

97

98 **Materials and Methods**

99 **1. Setting and participants**

100 We used data from a prospective observational cohort study conducted in a geriatric ward of an
101 acute hospital, **which was very similar to ACE unit[20]**. Written informed consent was obtained from
102 all participants. If participants were unable to provide consent, family members provided consent on
103 their behalf. The study was approved by the Ethics Committee of Nagoya University Graduate School
104 of Medicine (approval number 2019-0260) and conducted in accordance with the provisions of the
105 Declaration of Helsinki and its later amendments.

106 We recruited patients aged 65 years or older who were admitted to the geriatric ward of Nagoya
107 University Hospital between October 2019 and September 2021. Participants were excluded if (1) they
108 were discharged within 48 h; (2) they or their family members did not provide written informed
109 consent; (3) their estimated life expectancy was within 1 month, as determined by their attending
110 physician; (4) they were readmitted within 3 months after discharge and were enrolled at the time of
111 their previous admission; (5) they were transferred from other departments; and (6) there was any
112 other reason for the patient's participation to be reconsidered.

113

114 **2. Data collection**

115 Data were first registered in the medical charts within 48 h and also at discharge.

116

117 **2.1. Data collection at admission**

118 Background data were obtained from clinical records, including age, sex, type of admission
119 (emergency or planned), residence before this hospitalization, height, weight, and body mass index
120 (BMI). The attending geriatrician conducted a comprehensive geriatric assessment to determine the
121 cognitive, functional, and nutritional status of each participant. Cognitive function was assessed using
122 the Mini-Mental State Examination (MMSE), which is scored from 0 to 30, with a lower score
123 indicating poorer cognitive status[21]. The degree of depressive condition was assessed by the
124 Geriatric Depression Scale-15 (GDS-15), which is scored from 0 to 15, with a higher score indicating
125 more depressed[22]. A cutoff value of 6 or higher was considered to indicate depressive symptoms[23].
126 Basic ADLs at baseline (2 weeks before admission) were assessed using the Barthel Index (BI)[24].
127 The BI comprises 10 items (eating, transfers, grooming, toilet use, bathing, walking, stairs, dressing,
128 bowels, and bladder) and is scored from 0 to 100, with a lower score indicating greater dependence.
129 IADLs were assessed using the Lawton and Brody scale, which is scored from 0 to 8, with a lower
130 score indicating greater dependence[25]. Nutritional status was assessed using the Mini-Nutritional
131 Assessment-Short Form (MNA-SF), which is scored from 0 to 14, with a lower score indicating poorer
132 nutritional status[26]. Comorbidity was evaluated using the Charlson Comorbidity Index (CCI)[27].

133 **2.2. Muscle ultrasound**

134 Muscle ultrasound was performed within the first 7 days of admission by the same physician. The
135 procedure was as described previously[18]. A B-mode ultrasound system (GE LOGIQ e; GE
136 Healthcare Japan, Tokyo, Japan) with a 5–10 MHz linear-array probe was used. The ultrasound
137 settings were as follows: frequency, 8 MHz; gain, 70 dB; depth, 4.0–6.0 cm; and focus point 1 (top of
138 the image). The depth was unchanged during the measurements of the same participants. The
139 participants were instructed to lie in the supine position, and a sufficient amount of water-soluble
140 transmission gel was applied to the skin to achieve acoustic coupling. Images of the rectus femoris
141 (RF) and vastus intermedius (VI) were obtained at the midpoint between the greater trochanter and
142 proximal border of the patella on both lower limbs. Three images of the quadriceps in each lower limb
143 were taken perpendicularly to the femur bone in the transverse plane, and the mean muscle thickness
144 and subcutaneous fat thickness were obtained. Bilateral thigh muscle thickness (BATT) was defined
145 as the sum of the muscle thickness (right RF + right VI + left RF + left VI)[28]. The EI of the RF was
146 measured with ImageJ software, version 1.52k (National Institutes of Health, Bethesda, MD). EI was
147 determined by 8-bit gray scale analysis and is expressed as arbitrary units (a.u.) in the range of 0–255.
148 The EI of the RF was measured in the largest possible rectangular region of interest, avoiding the
149 visible fascia. These methods for measuring BATT and the EI of the RF had high reliability (interclass
150 correlation coefficients [1.1] = 0.995 [0.994–0.996] for BATT and 0.989 [0.986–0.991] for the EI of

151 the RF). Because the EI of the RF is attenuated by the subcutaneous fat thickness, the corrected EI of
152 the RF was also calculated by the following formula: corrected EI = EI + 40.5278 × subcutaneous fat
153 thickness (cm)[29].

154

155 **2.3. Other muscle assessments**

156 **Handgrip strength and bioimpedance analyzer-determined skeletal muscle mass were also measured**
157 **for comparison with muscle ultrasound.**

158 Handgrip strength was measured by a Jamar-type hand-held dynamometer (Baseline Hydraulic Hand
159 Dynamometer, Fabrication Enterprises Inc., Elmsford, NY). Two trials were taken with each hand,
160 and the maximum value was recorded. The measurement was taken with the elbows fixed at 90° in
161 the sitting position but, when the participant struggled to achieve the sitting position, it was taken in
162 the supine position. Skeletal muscle mass (SMM) was measured by a portable bioimpedance analyzer
163 (InBody S10; InBody Co., Ltd., Tokyo, Japan), and the skeletal muscle index (SMI) was calculated by
164 dividing SMM by height squared (kg/m²).

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166 **2.4. Data collection at discharge**

167 Discharge destination (including in-hospital death and transfer to another department), length
168 of hospital stay, and the BI were obtained from medical records.

169

170 **2.5. HAD**

171 The BI was bi-classified into mobility and self-care categories through the application of the
172 ICF[30]. BI (mobility) includes transfers, walking, and stairs (total score, 0–40), whereas BI (self-
173 care) includes eating, grooming, toilet use, bathing, dressing, bowels, and bladder (total score, 0–60).
174 In this study, HAD was evaluated separately for mobility impairments (HAD in mobility) and self-
175 care impairments (HAD in self-care). A previous review using the BI determined that the minimal
176 amount of functional decline was 10%[31]. Therefore, in the present study, HAD in mobility and HAD
177 in self-care were defined as a $\geq 10\%$ decrease in the BI score at discharge compared with baseline (2
178 weeks before admission).

179

180 **3. Statistical analysis**

181 All statistical analyses were conducted using SPSS software, version 28 (IBM Corp., Armonk,
182 NY). Continuous variables are reported as the mean \pm standard deviation or the median (interquartile
183 range), whereas categorical variables are reported as absolute numbers and percentages. BI (mobility)
184 and BI (self-care) were compared between admission and discharge and the prevalence of HAD was
185 calculated. Student's *t*-test or Mann–Whitney *U* test was used to compare muscle indicators (handgrip
186 strength, SMI, BATT, EI, and corrected EI) in two groups (with HAD and without HAD). Multiple

187 logistic regression analysis was conducted to clarify muscle indicators that were independently
188 associated with HAD after adjustment for potential confounders. The confounding factors were age
189 and sex in Model 1, age, sex, MMSE, CCI, and MNA-SF in Model 2, and age, sex, MMSE, CCI,
190 MNA-SF, BI at admission, IADLs, and GDS-15 in Model 3. Spearman's correlation coefficient was
191 used to examine the relationships between muscle indicators and other related parameters. It was also
192 used to examine the relationships between these related parameters and HAD by Student's *t*-test or
193 Mann–Whitney U test (for continuous variables) and χ^2 test (for categorical variables). A P-value less
194 than 0.05 was considered statistically significant in all comparisons.

195

196 **Results**

197 The number of participants was 256, after excluding cases of in-hospital death (n=20), transfer
198 to another department (n=6), and a missing value of the BI (n=18). **The median length of hospital stay**
199 **was 17 (11-28).**

200 **Table 1** shows the background characteristics of the participants at admission. The mean age
201 was 85.2 ± 5.9 years, the percentage of men was 41.8%, the median MMSE value was 21 (13–26), the
202 median CCI value was 2 (1–3), the mean MNA-SF was 8.6 ± 3.4 , and the median BI was 85 (51.3–
203 100).

204 **Table 2** shows the changes in the BI score (the difference from baseline to discharge) and the

205 prevalence of HAD. The median BI (mobility) and BI (self-care) at baseline were 35 and 55,
206 respectively, and were lower at discharge. HAD in mobility was more common than HAD in self-care
207 (37.5% vs. 30.0%). **On the other hand, in 19.9% of cases, the BI score at discharge was higher than at**
208 **baseline.**

209 [Table 3](#) shows the values of muscle indicators in the two groups (with and without HAD).
210 Handgrip strength was lower in both the HAD in mobility and HAD in self-care groups than in the
211 groups without HAD. BATT was lower only in the HAD in mobility group. In contrast, SMI, EI, and
212 corrected EI were not significantly different between the two groups.

213 [Table 4](#) illustrates the results of multiple logistic regression analysis conducted to clarify muscle
214 indicators that were independently associated with HAD in mobility. BATT [odds ratio 0.57, 95%
215 confidence interval 0.36–0.89, P=0.013] was independently associated with HAD in mobility in Model
216 3, whereas handgrip strength, SMI, EI, and corrected EI were not.

217 [Table 5](#) shows the results of multiple logistic regression analysis to clarify the muscle indicators
218 that were independently associated with HAD in self-care. No significant associations of HAD in self-
219 care were seen for all muscle indicators, but especially in Models 2 and 3.

220 [Supplementary Table 1](#) details the results of correlations among muscle indicators and related
221 parameters. Handgrip strength was significantly related to age, MMSE, MNA-SF, BI at baseline, and
222 IADLs.

223 **Table 6** shows the values of related parameters compared in groups with and without HAD.

224 Both HAD groups showed a higher age, lower MMSE, and lower IADLs. The prevalence of depressive
225 symptoms was higher in HAD in mobility, whereas the MNA-SF and BI were lower in HAD in self-
226 care.

227

228 **Discussion**

229 In this study, we classified ADL declines during hospitalization into HAD in mobility and HAD
230 in self-care and examined the association with muscle indicators. To our knowledge, this is the first
231 study to classify HAD into mobility and self-care categories and to investigate their association with
232 muscle indicators. Our results indicated that HAD in mobility was more common than HAD in self-
233 care. In addition, a lower BATT was significantly associated with a higher prevalence of HAD in
234 mobility, unlike handgrip strength and EI. Regarding HAD in self-care, no significant associations
235 were found with muscle indicators.

236 With regards to the association between muscle mass and ADLs, a meta-analysis reported that
237 a low muscle mass was associated with worsening ADLs in community-dwelling older adults[32],
238 while the Position Statements of the Sarcopenia Definition and Outcomes Consortium (SDSC)
239 concluded that lean muscle mass measured by DXA was not a good predictor of adverse health-related
240 outcomes, including an ADL decline[33]. A recent longitudinal study evaluating the annual assessment

241 of ADLs in individuals who experienced hospitalization showed that pre-hospital muscle mass on
242 DXA was not associated with new ADL disabilities at follow-up[11]. Moreover, in a recent systematic
243 review including inpatients, most longitudinal studies reported that muscle mass was not associated
244 with ADL scores[34]. In the present study of muscle mass assessment, a BIA-based muscle mass
245 indicator (i.e., SMI) was not associated with HAD in mobility, unlike an ultrasound-based muscle
246 mass indicator (i.e., BATT) (Table 4).

247 The following reasons might explain why the association between muscle mass and HAD in
248 this study differed from that of previous studies. First, there are differences in the evaluation of ADLs.
249 In contrast with the present study, previous studies used the BI as the entire ADL assessment or just a
250 part of the assessment (transferring, bathing, and dressing). In this study, BATT was also associated
251 with HAD in mobility and not associated with HAD in self-care. That may suggest improving muscle
252 mass of lower limbs is essential for prevention of HAD in mobility, which is more closely associated
253 with physical functional decline. BATT could prevent HAD in mobility, which reflects physical
254 function rather than self-care. Second, previous studies targeted community-dwelling individuals or
255 those in rehabilitation hospitals, whereas the participants in the present study were more frail acute
256 inpatients, which may have affected the results by increasing the muscle changes caused by acute
257 inflammation or disuse. Third, muscle mass evaluation using BIA is regarded as one of the standard
258 methods in clinical settings[35], and many studies have used the SMI as an index of muscle mass,

259 which is calculated from both muscles of the upper and lower limbs. Muscle mass evaluation by
260 ultrasound was also reported to be a reliable and valid method for the assessment of muscle size in
261 older adults[36]. The anterior thigh muscles are more prone to muscle loss than other muscles and are
262 more commonly and severely affected in sarcopenia[37]. These muscles are fundamental to mobility
263 skills. Therefore, BATT, which could directly evaluate them, may be more suitable for assessing
264 mobility skills than SMI. In addition, the BIA method can be affected by hydration status[38], which
265 may influence the results in the case of inpatients with dehydration or overhydration. Muscle
266 ultrasound is a relatively simple and less invasive measurement method, and it is commonly available
267 in clinical practice. The results of the present study may indicate the need for a reconsideration of the
268 assessment of muscle mass or interventions in hospitalized older adults. However, BATT could also
269 be temporarily increased by inflammation or vascular permeability[39]. Thus, this method must be
270 used properly and a cutoff value must be established.

271 Regarding the association between muscle strength and ADLs in hospitalized older adults,
272 previous studies reported that a low handgrip strength at admission was associated with ADL
273 dependency[10] and was a risk factor for newly **developed** ADL disability after discharge[11]. In fact,
274 in the present study, handgrip strength was associated with HAD in univariate analysis, but not in
275 multivariate analysis. The participants of this study had a higher rate of undernutrition or cognitive
276 decline that was related to low handgrip strength ([Supplementary Table 1](#)), thereby weakening the

277 association between handgrip strength and HAD in mobility. Furthermore, handgrip strength could be
278 underestimated due to acute illness, and it does not necessarily reflect lower limb muscle strength[40].
279 A recent study showed that knee extension strength was decreased by 11% during hospitalization,
280 while handgrip strength was unchanged[41]. There may be challenges in the use of handgrip strength
281 to assess mobility status in hospitalized older adults.

282 It has been reported that muscle EI is related to muscle strength in older adults[42], therefore,
283 EI may become an important parameter for understanding the physical condition in older adults.
284 Furthermore, in terms of EI, previous studies among subacute and convalescent rehabilitation wards
285 reported that EI of the quadriceps was independently associated with motor Functional Independence
286 Measure scores and was related to the recovery of ADLs[17,43]. In contrast with these results, EI was
287 not associated with HAD in mobility in the present study. This is possibly because muscle quality
288 could not be accurately evaluated by EI in the acute phase. A recent review reported that EI is affected
289 by not only muscle damage, but also water balance or glycogen under acute conditions[14]. It has been
290 suggested that muscle intracellular hydration status is related to functional capacity[44] and that the
291 glycogen level within skeletal muscle is related to exercise durability[45]. It may be thought that
292 factors other than muscle fibers affected EI and its relationship with HAD in the present study.
293 However, in the intensive care unit, a change in EI was associated with intensive care unit-acquired
294 muscle weakness or mortality[46,47]. Further research is required to explore the association between

295 EI and clinical outcomes in various settings, such as home medical care and nursing homes.

296 In contrast to the results of HAD in mobility, no muscle indicators were associated with HAD
297 in self-care. Self-care is commonly defined as the practice of activities that an individual initiates and
298 carries out in order to maintain life, health, and well-being[48], and HAD in self-care has been
299 associated with prolonged functional recovery and increased mortality[6]. A previous study indicated
300 that the risk factors for HAD in self-care were grouped into three main themes: patient factors,
301 healthcare provision, and hospital environment[49]. The authors suggested that a fear of falls and
302 nurses' work overload were barriers to functional self-care, while having a positive mindset and an
303 age-friendly environment were facilitators of functional self-care. Another study reported that patients
304 who received a higher amount of ADL/self-care training through occupational therapy had a lower
305 risk of readmission[50]. In the present study as well, these environmental factors appear to have been
306 more closely associated with HAD in self-care than muscle indicators. However, a lower MMSE,
307 MNA-SF, BI at baseline, and IADLs and a higher age were found in HAD in self-care (Table 6). The
308 prevention of HAD in self-care may be required to identify the above risk factors early in acute
309 hospitalization and to conduct multidisciplinary interventions with the involvement, for example, of
310 physicians, nurses, dietitians, occupational therapists, and family members.

311 This study provides important findings, but some limitations should be considered. First,
312 muscle evaluation by ultrasound was conducted by the seventh day after admission (median interval=

313 second days) because our research was performed after medical treatment. In addition, measurements
314 of handgrip strength and BIA were not always performed on the same day as muscle ultrasound.
315 Muscle changes caused by disuse after hospitalization may thus have affected the results. However,
316 the association between BATT, bioimpedance analyzer-determined skeletal muscle mass and HAD in
317 mobility was not changed when we controlled for the measurement date. Second, rehabilitation during
318 hospitalization might have influenced the results. Rehabilitation exercise to prevent deterioration of
319 physical function may affect HAD, but early rehabilitation is commonly conducted in the acute care
320 setting, and most participants had individually undergone rehabilitation. Third, restrictions on family
321 visits on hospital due to COVID-19 pandemic might affect the results. However, access to
322 physiotherapist and dieticians were not restricted during the hospitalization. Before and after the
323 COVID-19 pandemic, BATT and HAD were unchanged, and not significantly different in this study,
324 The association between BATT and HAD in mobility was also unchanged even after adjusting before
325 and after the COVID-19 pandemic.

326 Fourth, this study was conducted at a single university hospital. Our findings should be verified
327 at other facilities.

328

329 **Conclusion**

330 We found that only a lower BATT, not other muscle indicators, was significantly associated

331 with a higher prevalence of HAD in mobility. The results of this study suggest muscle ultrasound is
332 useful for evaluations of older adults in acute care settings. There are several modalities for muscle
333 evaluations, and each one of them has strong points and weakness, and clinicians should know these
334 characteristics of modalities for appropriate evaluations and interpretations of the results. Muscle
335 ultrasound can be considered for muscle evaluation in acute care, and may be used more widely.
336 Physical rehabilitation and a nutritional intervention aimed at improving muscle mass could be
337 emphasized to prevent HAD in mobility. However, no muscle indicators were related to HAD in self-
338 care. Thus, psychosocial and environmental intervention approaches may be required to prevent HAD
339 in self-care, rather than physical training.

340

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342

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344

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351

352 **Author contributions:** **Masaaki Nagae:** Conceptualization, Methodology, Formal analysis,

353 Investigation, Data curation, Writing-original draft preparation. **Hiroyuki Umegaki:** Writing-review

354 and editing, Supervision, Funding acquisition. **Akito Yoshiko:** Writing-review and editing. **Kosuke**

355 **Fujita:** Validation. **Hitoshi Komiya:** Project administration. **Kazuhisa Watanabe:** Software. **Yosuke**

356 **Yamada:** Visualization. **Tomomichi Sakai:** Resources.

357

358 **References**

359 [1] World Health Organization. *The International Classification of Functioning, Disability and*

360 *Health (ICF)*. Geneva, Switzerland: World Health Organization; 2001.

361 [2] Covinsky KE, Pierluissi E, Johnston CB. Hospitalization-associated disability “She was probably

362 able to ambulate, but i’m not sure.” *JAMA - J Am Med Assoc* 2011;306(16):1782–93. doi:

363 10.1001/jama.2011.1556.

364 [3] Loyd C, Markland AD, Zhang Y, et al. Prevalence of Hospital-Associated Disability in Older

365 Adults: A Meta-analysis. *J Am Med Dir Assoc* 2020;21(4):455-461.e5. doi:

366 10.1016/j.jamda.2019.09.015.

- 367 [4] Brown CJ. After Three Decades of Study, Hospital-Associated Disability Remains a Common
368 Problem. *J Am Geriatr Soc* 2020;68(3):465–6. doi: 10.1111/jgs.16349.
- 369 [5] Zisberg A, Shadmi E, Gur-Yaish N, Tonkikh O, Sinoff G. Hospital-Associated Functional
370 Decline: The Role of Hospitalization Processes Beyond Individual Risk Factors. *J Am Geriatr*
371 *Soc* 2015;63(1):55–62. doi: 10.1111/jgs.13193.
- 372 [6] Boyd CM, Landefeld CS, Counsell SR, et al. Recovery of activities of daily living in older adults
373 after hospitalization for acute medical illness. *J Am Geriatr Soc* 2008;56(12):2171–9. doi:
374 10.1111/j.1532-5415.2008.02023.x.
- 375 [7] Tonkikh O, Shadmi E, Flaks-Manov N, Hoshen M, Balicer RD, Zisberg A. Functional status
376 before and during acute hospitalization and readmission risk identification. *J Hosp Med*
377 2016;11(9):636–41. doi: 10.1002/jhm.2595.
- 378 [8] Portegijs E, Buurman BM, Essink-Bot ML, Zwiderman AH, de Rooij SE. Failure to Regain
379 Function at 3 months After Acute Hospital Admission Predicts Institutionalization Within 12
380 Months in Older Patients. *J Am Med Dir Assoc* 2012;13(6):569.e1-569.e7. doi:
381 10.1016/j.jamda.2012.04.003.
- 382 [9] Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet* 2019;393:2636–46. doi: 10.1016/S0140-
383 6736(19)31138-9.
- 384 [10] Meskers CGM, Reijnierse EM, Numans ST, et al. Association of Handgrip Strength and Muscle

385 Mass with Dependency in (Instrumental) Activities of Daily Living in Hospitalized Older Adults
386 - The Empower Study. *J Nutr Heal Aging* 2019;23:232–8. doi: 10.1007/s12603-019-1170-5.

387 [11] Andrews JS, Gold LS, Reed MJ, et al. Appendicular Lean Mass, Grip Strength, and the
388 Development of Hospital-Associated Activities of Daily Living Disability Among Older Adults
389 in the Health ABC Study. *Journals Gerontol Ser A* 2021;XX:1–7. doi: 10.1093/gerona/qlab332.

390 [12] Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: Revised European consensus on definition
391 and diagnosis. *Age Ageing* 2019;48:16–31. doi: 10.1093/ageing/afy169.

392 [13] Madden KM, Feldman B, Arishenkoff S, Meneilly GS. A rapid point-of-care ultrasound marker
393 for muscle mass and muscle strength in older adults. *Age Ageing* 2021;50:505–10. doi:
394 10.1093/ageing/afaa163.

395 [14] Stock MS, Thompson BJ. Echo intensity as an indicator of skeletal muscle quality: applications,
396 methodology, and future directions. *Eur J Appl Physiol* 2021;121:369–80. doi: 10.1007/s00421-
397 020-04556-6.

398 [15] Fukumoto Y, Ikezoe T, Taniguchi M, et al. Cut-off values for lower limb muscle thickness to
399 detect low muscle mass for sarcopenia in older adults. *Clin Interv Aging* 2021;16:1215–22. doi:
400 10.2147/CIA.S304972.

401 [16] Lee ZY, Ong SP, Ng CC, et al. Association between ultrasound quadriceps muscle status with
402 premorbid functional status and 60-day mortality in mechanically ventilated critically ill patient:

403 A single-center prospective observational study. *Clin Nutr* 2021;40:1338–47. doi:
404 10.1016/j.clnu.2020.08.022.

405 [17] Akazawa N, Kishi M, Hino T, et al. Intramuscular adipose tissue in the quadriceps is more
406 strongly related to recovery of activities of daily living than muscle mass in older inpatients. *J*
407 *Cachexia Sarcopenia Muscle* 2021;12:891–9. doi: 10.1002/jcsm.12713.

408 [18] Nagae M, Umegaki H, Yoshiko A, et al. Echo intensity is more useful in predicting hospital-
409 associated complications than conventional sarcopenia-related parameters in acute hospitalized
410 older patients. *Exp Gerontol* 2021;150:111397. doi: 10.1016/j.exger.2021.111397.

411 [19] Nagae M, Umegaki H, Yoshiko A, et al. Muscle changes on muscle ultrasound and adverse
412 outcomes in acute hospitalized older adults. *Nutrition* 2022 in press.

413 [20] Palmer R, Landefeld C, Kresevic D, et al. A medical unit for the acute care of the elderly. *J Am*
414 *Geriatr Soc* 1994; 42: 545-552. doi: 10.1111/j.1532-5415.1994.tb04978.x.

415 [21] Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the
416 cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98. doi: 10.1016/0022-
417 3956(75)90026-6.

418 [22] Almeida OP, Almeida SA. Short versions of the Geriatric Depression Scale: A study of their
419 validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. *Int J*
420 *Geriatr Psychiatry* 1999;14:858–65. doi: 10.1002/(SICI)1099-1166(199910)14:10<858::AID-

- 421 GPS35>3.0.CO;2-8.
- 422 [23] Dennis M, Kadri A, Coffey J. Depression in older people in the general hospital: A systematic
423 review of screening instruments. *Age Ageing* 2012;41:148–54. doi: 10.1093/ageing/afr169.
- 424 [24] MAHONEY FI, BARTHEL DW. FUNCTIONAL EVALUATION: THE BARTHEL INDEX.
425 *Md State Med J* 1965;14:61–5.
- 426 [25] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities
427 of daily living. *Gerontologist* 1969;9:179–86.
- 428 [26] Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric
429 practice: Developing the Short-Form Mini-Nutritional Assessment (MNA-SF). *Journals Gerontol*
430 - *Ser A Biol Sci Med Sci* 2001;56:366–72. doi: 10.1093/gerona/56.6.M366.
- 431 [27] Medical C. a New Method of Classifying Prognostic in Longitudinal Studies : Development. *J*
432 *Chronic Dis* 1987;40:373–83.
- 433 [28] Wilson D V., Moorey H, Stringer H, et al. Bilateral Anterior Thigh Thickness: A New Diagnostic
434 Tool for the Identification of Low Muscle Mass? *J Am Med Dir Assoc* 2019;20:1247-1253.e2.
435 doi: 10.1016/j.jamda.2019.04.005.
- 436 [29] Young HJ, Jenkins NT, Zhao Q, Mccully KK. Measurement of intramuscular fat by muscle echo
437 intensity. *Muscle and Nerve* 2015;52:963–71. doi: 10.1002/mus.24656.
- 438 [30] Prodinge B, O'Connor RJ, Stucki G, Tennant A. Establishing score equivalence of the functional

439 independence measure motor scale and the barthel index, utilizing the international classification
440 of functioning, disability and health and rasch measurement theory. *J Rehabil Med* 2017;49:416–
441 22. doi: 10.2340/16501977-2225.

442 [31] Buurman BM, Van Munster BC, Korevaar JC, De Haan RJ, De Rooij SE. Variability in
443 measuring (instrumental) activities of daily living functioning and functional decline in
444 hospitalized older medical patients: A systematic review. *J Clin Epidemiol* 2011;64:619–27. doi:
445 10.1016/j.jclinepi.2010.07.005.

446 [32] Wang DXM, Yao J, Zirek Y, Reijnierse EM, Maier AB. Muscle mass, strength, and physical
447 performance predicting activities of daily living: a meta-analysis. *J Cachexia Sarcopenia Muscle*
448 2020;11:3–25. doi: 10.1002/jcsm.12502.

449 [33] Bhasin S, Travison TG, Manini TM, et al. Sarcopenia Definition: The Position Statements of the
450 Sarcopenia Definition and Outcomes Consortium. *J Am Geriatr Soc* 2020;68:1410–8. doi:
451 10.1111/jgs.16372.

452 [34] Lunt E, Ong T, Gordon AL, Greenhaff PL, Gladman JRF. The clinical usefulness of muscle mass
453 and strength measures in older people: A systematic review. *Age Ageing* 2021;50:88–95. doi:
454 10.1093/ageing/afaa123.

455 [35] Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 Consensus
456 Update on Sarcopenia Diagnosis and Treatment. *J Am Med Dir Assoc* 2020;21:300-307.e2. doi:

457 10.1016/j.jamda.2019.12.012.

458 [36] Nijholt W, Scafoglieri A, Jager-Wittenaar H, Hobbelen JSM, van der Schans CP. The reliability
459 and validity of ultrasound to quantify muscles in older adults: a systematic review. *J Cachexia*
460 *Sarcopenia Muscle* 2017;8:702–12. doi: 10.1002/jcsm.12210.

461 [37] Kara M, Kaymak B, Frontera WR, et al. Diagnosing sarcopenia: Functional perspectives and a
462 new algorithm from ISarcoPRM. *J Rehabil Med* 2021;53. doi: 10.2340/16501977-2851.

463 [38] Ceniccola GD, Castro MG, Piovacari SMF, et al. Current technologies in body composition
464 assessment: advantages and disadvantages. *Nutrition* 2019;62:25–31. doi:
465 10.1016/j.nut.2018.11.028.

466 [39] Welch C, Greig CA, Hassan-Smith ZK, Pinkney TD, Lord JM, Jackson TA. A pilot observational
467 study measuring acute sarcopenia in older colorectal surgery patients. *BMC Res Notes*
468 2019;12:1–7. doi: 10.1186/s13104-019-4049-y.

469 [40] Phillipe de Lucena Alves C, Câmara M, Dantas Macêdo GA, et al. Agreement between upper and
470 lower limb measures to identify older adults with low skeletal muscle strength, muscle mass and
471 muscle quality. *PLoS One* 2022;17:e0262732. doi: 10.1371/journal.pone.0262732.

472 [41] Hartley P, Romero-Ortuno R, Wellwood I, Deaton C. Changes in muscle strength and physical
473 function in older patients during and after hospitalisation: A prospective repeated-measures
474 cohort study. *Age Ageing* 2021;50:153–60. doi: 10.1093/ageing/afaa103.

- 475 [42] Fukumoto Y, Ikezoe T, Yamada Y, et al. Skeletal muscle quality assessed from echo intensity is
476 associated with muscle strength of middle-aged and elderly persons. *Eur J Appl Physiol*
477 2012;112:1519–25. doi: 10.1007/s00421-011-2099-5.
- 478 [43] Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Moriyama H. Increased intramuscular adipose
479 tissue of the quadriceps is more strongly related to declines in ADL than is loss of muscle mass in
480 older inpatients. *Clin Nutr* 2021;40:1381–7. doi: 10.1016/j.clnu.2020.08.029.
- 481 [44] Lorenzo I, Serra-Prat M, Carlos Yébenes J. The role of water homeostasis in muscle function and
482 frailty: A review. *Nutrients* 2019;11:1–15. doi: 10.3390/nu11081857.
- 483 [45] Schweitzer GG, Kearney ML, Mittendorfer B. Muscle glycogen: where did you come from,
484 where did you go? *J Physiol* 2017;595:2771–2. doi: 10.1113/JP273536.
- 485 [46] Mayer KP, Thompson Bastin ML, Montgomery-Yates AA, et al. Acute skeletal muscle wasting
486 and dysfunction predict physical disability at hospital discharge in patients with critical illness.
487 *Crit Care* 2020;24:1–12. doi: 10.1186/s13054-020-03355-x.
- 488 [47] Umbrello M, Guglielmetti L, Formenti P, et al. Qualitative and Quantitative Muscle Ultrasound
489 Changes in Covid-19 Related Ards Patients. *Nutrition* 2021;91–92:111449. doi:
490 10.1016/j.nut.2021.111449.
- 491 [48] Orem D, Taylor S, Renpenning K. *Nursing: Concepts of practice*, 6th edn. St. Louis:
492 Mosby, 2001.

- 493 [49] Chan EY, Samsudin SA, Lim YJ. Older patients' perception of engagement in functional self-
494 care during hospitalization: A qualitative study. *Geriatr Nurs (Minneap)* 2020;41:297–304. doi:
495 10.1016/j.gerinurse.2019.11.009.
- 496 [50] Edelstein J, Walker R, Middleton A, Reistetter T, Gary KW, Reynolds S. Higher Frequency of
497 Acute Occupational Therapy Services Is Associated With Reduced Hospital Readmissions. *Am J*
498 *Occup Ther* 2022;76:1–9. doi: 10.5014/ajot.2022.048678.
- 499

Table 1: Background characteristics

Age, years	85.2 ± 5.9
Male sex	107 (41.8%)
Emergency admission	169 (66.0%)
Main diseases	Neurological 59 (23.0%), respiratory 18 (7.0%), cardiovascular 12 (4.7%), gastrointestinal 9 (3.5%), musculoskeletal 9 (3.5%), dermatological 16 (6.3%), endocrinal 21 (8.2%), urinary 26 (10.2%), hematological 20 (7.8%), psychological 3 (1.2%), others 62 (24.2%), unknown 1(0.4%)
Height, cm (n=243)	152.7 ± 9.9
Weight, kg (n=255)	48.3 ± 11.2
BMI, kg/m ² (n=243)	20.7 ± 3.9
MMSE (n=245)	21 (13–26)
CCI	2 (1–3)
MNA-SF (n=237)	8.6 ± 3.4
BI	85 (51.3–100)

IADLs	4 (1–7)
Depressive symptoms (GDS \geq 6) (n=210)	93 (44.3%)
Handgrip strength, kg (n=209)	15.4 \pm 6.9
	(Male 19.7 \pm 6.5, Female 11.8 \pm 4.9)
SMI, kg/m ² (n=178)	6.3 \pm 1.5
	(Male 7.1 \pm 1.2, Female 5.7 \pm 1.3)
Interval from admission to ultrasound, days	2 (1-3)
BATT, cm (n=228)	3.3 \pm 1.0
	(Male 3.5 \pm 1.0, Female 3.1 \pm 0.9)
EI, a.u. (n=228)	94.0 \pm 15.2
	(Male 92.2 \pm 15.2, Female 95.3 \pm 15.1)
Corrected EI, a.u. (n=225)	113.2 \pm 13.5
	(Male 109.2 \pm 13.4, Female 116.1 \pm 12.8)

Data are presented as mean \pm standard deviation, median (interquartile range), or number (percentage).

a.u., arbitrary units; BATT, bilateral anterior thigh thickness; BI, Barthel Index; BMI, body mass index;

CCI, Charlson Comorbidity Index; EI, echo intensity; GDS, Geriatric Depression Scale; IADLs,

instrumental ADLs; MMSE, Mini-Mental State Examination; MNA-SF, Mini-Nutritional

Assessment-Short Form; SMI, skeletal muscle index.

Table 2: Changes in the BI score and the prevalence of HAD

	BI score at admission	Change in BI score	HAD
BI (mobility)	35 (20–40)	-2.8 ± 9.8	93 (37.5%) (n=248)
BI (self-care)	55 (30–60)	-3.2 ± 13.4	73 (30.0%) (n=243)

Data are presented as mean \pm standard deviation, median (interquartile range), or number (percentage).

BI, Barthel Index; HAD, hospital-associated disability.

Change in BI score means the difference from admission to discharge.

HAD means that the BI score at discharge was 10% lower or more than at admission, except for cases

where the score at admission was 0.

Table 3: The values of muscle indicators compared in groups with and without HAD

	Mobility			Self-care		
	Without HAD (n=155)	With HAD (n=93)	P-value	Without HAD (n=170)	With HAD (n=73)	P-value
Handgrip strength, kg	16.7 ± 7.1 (n=132)	13.3 ± 5.9 (n=74)	<0.01	16.2 ± 6.9 (n=155)	13.8 ± 6.4 (n=50)	0.035
SMI, kg/m ²	6.4 ± 1.4 (n=105)	6.2 ± 1.5 (n=69)	0.18	6.5 ± 1.3 (n=123)	6.1 ± 1.6 (n=49)	0.08
BATT, cm	3.4 ± 1.0 (n=141)	3.1 ± 1.0 (n=83)	0.024	3.4 ± 1.0 (n=158)	3.2 ± 1.0 (n=62)	0.20
EI, a.u.	92.9 ± 13.8 (n=140)	95.7 ± 17.3 (n=83)	0.22	93.1 ± 14.7 (n=157)	95.2 ± 16.5 (n=63)	0.35
Corrected EI, a.u.	111.8 ± 12.8 (n=139)	115.2 ± 13.9 (n=82)	0.07	112.4 ± 13.0 (n=156)	114.7 ± 14.2 (n=61)	0.25

Data are presented as mean ± standard deviation. a.u., arbitrary units; BATT, bilateral anterior thigh thickness; EI, echo intensity; HAD, hospital-associated disability; SMI, skeletal muscle index.

Table 4: Association of muscle indicators with HAD in mobility in multiple logistic regression analysis

	Model 1		Model 2		Model 3	
	Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Handgrip strength	0.92 (0.87–0.98)	<0.01	0.95 (0.89–1.01)	0.09	0.94 (0.88–1.01)	0.11
SMI	0.93 (0.72–1.19)	0.54	0.94 (0.71–1.24)	0.65	0.96 (0.70–1.33)	0.81
BATT	0.81 (0.59–1.10)	0.18	0.71 (0.49–1.04)	0.08	0.57 (0.36–0.89)	0.013
EI	1.01 (0.99–1.03)	0.49	1.01 (0.99–1.03)	0.48	1.00 (0.98–1.03)	0.71
Corrected EI	1.01 (0.99–1.04)	0.25	1.02 (0.99–1.04)	0.17	1.01 (0.99–1.04)	0.38

Model 1 was adjusted by age and sex. Model 2 was adjusted by age, sex, MMSE, CCI, and MNA-SF. Model 3 was adjusted by age, sex, MMSE, CCI, MNA-SF, BI (at baseline), IADLs, and depressive symptoms. BATT, bilateral anterior thigh thickness; BI, Barthel Index; CCI, Charlson Comorbidity Index; EI, echo intensity; IADL, instrumental ADLs; MMSE, Mini-Mental State Examination; MNA-SF, Mini-Nutritional Assessment-Short Form; SMI, skeletal muscle index.

Table 5: Association of muscle indicators with HAD in self-care in multiple logistic regression analysis

	Model 1		Model 2		Model 3	
	Odds ratio	P	Odds ratio	P	Odds ratio	P
Handgrip strength	0.93 (0.87–0.99)	0.021	0.99 (0.91–1.07)	0.74	0.97 (0.88–1.06)	0.51
SMI	0.73 (0.55–0.99)	0.040	0.81 (0.56–1.16)	0.25	0.84 (0.55–1.28)	0.42
BATT	0.95 (0.68–1.32)	0.75	0.77 (0.48–1.24)	0.28	0.73 (0.42–1.28)	0.27
EI	1.00 (0.98–1.02)	0.75	1.00 (0.98–1.03)	0.88	1.00 (0.97–1.03)	0.86
Corrected EI	1.01 (0.98–1.03)	0.52	1.01 (0.98–1.04)	0.70	1.00 (0.97–1.04)	0.81

Model 1 was adjusted by age and sex. Model 2 was adjusted by age, sex, MMSE, CCI, and MNA-SF. Model 3 was adjusted by age, sex, MMSE, CCI, MNA-SF, BI (at baseline), IADLs, and depressive symptoms. BATT, bilateral anterior thigh thickness; BI, Barthel Index; CCI, Charlson Comorbidity Index; EI, echo intensity; IADLs, instrumental ADLs; MMSE, Mini-Mental State Examination; MNA-SF, Mini-Nutritional Assessment-Short Form; SMI, skeletal muscle index.

Table 6: The values of related parameters compared in groups with and without HAD

	Mobility			Self-care		
	Without HAD (n=155)	With HAD (n=93)	P-value	Without HAD (n=170)	With HAD (n=73)	P-value
Age, years	84.5 ± 5.6	86.5 ± 6.2	0.010	84.4 ± 5.5	87.2 ± 6.1	<0.01
Female sex	86 (55.5%)	57 (61.3%)	0.37	95 (55.9%)	42 (57.5%)	0.81
MMSE	23 (17–28) (n=148)	19 (10.5–23) (n=89)	<0.01	24 (18–28) (n=168)	15 (3.5–20) (n=65)	<0.01
CCI	2 (1–3)	2 (1–3)	0.68	2 (1–3)	2 (1–3)	0.053
MNA-SF	8.6 ± 3.5 (n=149)	8.7 ± 3.1 (n=82)	1.00	9.1 ± 3.2 (n=166)	7.8 ± 3.5 (n=60)	<0.01
BI	85 (60–100)	85 (55–95)	0.17	90 (70–100)	70 (50–90)	<0.01
IADLs	5 (1–8)	3 (1–6)	<0.01	6 (2–8)	2 (0–3.5)	<0.01

Depressive symptoms 50 (37.6%) (n=133) 42 (56.8%) (n=74) <0.01 70 (42.7%) (n=164) 22 (51.2%) (n=43) 0.32

(GDS \geq 6)

Data are presented as mean \pm standard deviation, median (interquartile range), or number (percentage). BI, Barthel Index; CCI, Charlson Comorbidity Index;

GDS, Geriatric Depression Scale; HAD, hospital-associated disability; IADLs, instrumental ADLs; MMSE, Mini-Mental State Examination; MNA-SF, Mini-

Nutritional Assessment-Short Form.