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ORIGINAL ARTICLE

Predictors of Activities of Daily Living in Intensive Care Unit Survivors: A Propensity Score Matching Analysis

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Objectives: Increased long-term impairment is common among intensive care unit (ICU) survivors. However, predictors of activities of daily living (ADL) in ICU survivors are poorly understood. We aimed to focus on the trajectory of physical function and explore the clinical variables that affect ADL at hospital discharge. **Methods:** We enrolled 411 patients admitted to the ICU from April 2018 to October 2020. Physical function was evaluated at ICU admission, ICU discharge, and hospital discharge. We assessed physical function (grip strength, arm and calf circumference, quadriceps thickness, and Barthel index). Patients were assigned to the high or low ADL group based on their Barthel index at discharge. Propensity score matching analysis was performed to minimize selection biases and differences in clinical characteristics. **Results:** After matching propensity scores, 114 of the 411 patients (aged 65±15 years) were evaluated. The high ADL group showed better physical function at ICU discharge and hospital discharge than the low ADL group. An overall decreasing trend in muscle mass was observed over time; the rates of decline were lower in the high ADL group than in the low ADL group. The cutoff values for relative changes in calf circumference and quadriceps thickness to predict high ADL were −7.89% (sensitivity: 77.8%, specificity: 55.6%) and −28.1% (sensitivity: 81.0%, specificity: 58.8%), respectively. **Conclusions:** The relative decreases in calf circumference and quadriceps thickness during hospitalization were lower in patients who maintained their ADL. Assessment of the trajectory of physical function can predict ADL status at hospital discharge among ICU survivors.

Key Words: calf circumference; critical care unit; grip strength; physical function; quadriceps thickness

INTRODUCTION

Despite an increased number of patients receiving intensive care, improved quality of care has led to decreased mortality and an increased survival rate.[1)] However, intensive care survivors often experience physical dysfunction after hospital discharge.[2)] Intensive care unit (ICU) patients frequently have muscle atrophy and weakness because of their need for bed rest, mechanical ventilation, and various medications. Critically ill patients often acquire neuropathy and/or myopathy, and the resultant condition is referred to as ICU-acquired weakness.[3)] Decline in the activities of daily living (ADL) in post-intensive care survivors poses a problem for their rehabilitation, and one-third of survivors of severe sepsis cannot live independently.[2)]

Generally, ADL status is considered to show some correlation with associated with physical examination parameters. For example, grip strength has a positive correlation with ADL,[4)] and a decrease in calf circumference is associated with a decrease in ADL.[5)] However, few studies have as-

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sessed the relationship between physical examination and the ADL status of ICU patients at hospital discharge. Schandl et al.[6] reported impaired core stability, low educational level, fractures, and a stay in the ICU for more than 2 days as independent predictors of new-onset physical disability. However, to the best of our knowledge, there are no studies on the relationship between the ADL of patients in the ICU at hospital discharge and their physical examination during hospitalization.

In this study, we aimed to evaluate the grip strength of ICU patients, arm circumference, calf circumference, and quadriceps thickness during hospitalization, focusing on the trajectory of physical function and to explore the clinical variables affecting ADL at hospital discharge. Owing to varying backgrounds, we analyzed the entire dataset and matched it using propensity scores.

MATERIALS AND METHODS

Ethics

The current study was conducted in accordance with the ethical recommendations outlined in the Declaration of Helsinki. The ethics committee of Kobe University Hospital approved this study (No. B200102), and informed consent was obtained from patients or their legal guardians.

Study Design and Patients

This retrospective observational study was conducted between April 2018 and October 2020. Patients aged 20 years or older who required urgent admission to the ICU at Kobe University Hospital, Hyogo, Japan, were recruited for this study. Patients with paresis caused by cerebrovascular disease or spinal disease and those who died before leaving the hospital were excluded. Patients who missed serial measurements were also excluded.

Patient Background

As patients' background information, we recorded their age, sex, and degree of care required[7] before admission to the ICU.

Evaluated Factors

We evaluated patients within 48 h following admission to the ICU, after discharge from the ICU, and before discharge from the hospital. We evaluated factors including the acute physiology and chronic health evaluation II (APACHE II) score,[8] sequential organ failure assessment (SOFA) score,[9] physical examinations (Medical Research Council scale [MRC] score,[10] grip strength, arm circumference, calf circumference, and quadriceps thickness), ICU mobility scale (IMS),[11] Barthel index (BI), mechanical ventilation duration, length of stay in the ICU, and length of hospital stay. In addition, we evaluated APACHE II score as the severity of the disease classification system at ICU admission; SOFA score at ICU admission and ICU discharge; and physical examination at ICU admission, ICU discharge, and hospital discharge. Furthermore, we evaluated IMS as an indicator of ADL at ICU admission and ICU discharge, and we evaluated BI as an indicator of ADL at ICU discharge and hospital discharge.

Long-Term Care Insurance System

We collected data on the degree of care required according to the Long-Term Care Insurance System[7] in Japan. The Japanese government implemented the Long-Term Care Insurance System to address the increasing rate of population aging and the increasing need for care of older adults. This system focuses on long-term care and prevention. Its main objective is to enable older adults to live independently in their communities for as long as possible.[12] Citizens aged 65 years and older or those aged 40–64 years with specific diseases can apply for this system. The system involves a two-stage process that categorizes individuals into seven levels: support 1 and 2 and long-term care 1 to 5. Individuals who qualify for long-term care can receive appropriate benefits.[13] We graded support requirement 1 (lowest degree of care required) as 1, and we graded long-term care requirement 5 (highest degree of care required) as 7. Individuals who did not qualify for support or long-term care were scored as 0. In this study, all the patients with score 0 using Long-Term Care Insurance System did not require any care. We did not find any patients who had refused care or had received certified inappropriate care using this system.

Grip Strength Measurement

Grip strength was measured using a JAMAR Plus Digital Hand Dynamometer 5632-13 (Sammons Preston, Rolyon, Bolingbrook, IL, USA). Grip strength was measured in the supine or sitting position. We used the grip strength of the stronger side.

In cases of patients being supported on invasive mechanical ventilation, we measured their grip strength during the spontaneous awakening trials by anesthesiologists. The grip strength values of the patients with disturbance of consciousness or dementia were treated as missing values.

Arm and Calf Circumference Measurements

Patients were encouraged to relax in the supine or sitting position. Arm circumference was measured at the midpoint between the acromion and the head of the elbow with a measuring tape. Patients were asked to stretch their arms. We measured both arms and took into consideration the circumference of the larger side.[14)]

The circumference of the calf was measured at the thickest part of the calf. Patients were asked to stretch their calves. We measured both calves and took into consideration the larger value.[15)]

Quadriceps Thickness

The thickness of the quadriceps was measured at the midpoint between the anterior superior iliac spine and the upper edge of the patella using a Vscan Dual Probe (GE Healthcare, Milwaukee, WI, USA).[16)] The patients stretched their hips and knees and were encouraged to relax in the supine position. We measured the thickness of the quadriceps of both legs and considered the value of the thicker side.

Calculation of Relative Change in Grip Strength, Arm Circumference, Calf Circumference, and Quadriceps Thickness

The changes in grip strength, arm circumference, calf circumference, and quadriceps thickness were calculated as the relative change in strength, circumference, or quadriceps thickness from ICU admission to ICU discharge. We also calculated the relative change from ICU admission to hospital discharge and from ICU discharge to hospital discharge. The relative change was expressed as a percentage.

Definitions of High ADL Group and Low ADL Group

The endpoint was defined as the ADL of patients in the ICU at hospital discharge. We used BI as a measure of ADL of ICU patients at hospital discharge. As performed in the previous study,[17)] patients with BI of 70 or higher at hospital discharge were classified as part of the high ADL group and those with BI of less than 70 at hospital discharge were classified as part of the low ADL group.

Statistical Analysis

A propensity score was calculated to balance the groups on several variables, including age, sex, degree of care required, APACHE II, SOFA, IMS, MRC, grip strength, arm circumference, calf circumference, quadriceps thickness, and duration of mechanical ventilation as independent variables. Two balanced groups were created using a 1:1 match. The Mann–Whitney U test was used for the comparison of continuous variables, and the chi-squared test was used for the comparison of categorical variables. The Friedman test and Bonferroni post hoc test were used to compare the trajectory of the physical examination. Receiver operating characteristic (ROC) curve analysis was used to determine the cutoff point for predicting outcomes. In all analyses, $P<0.05$ indicated statistical significance. Statistical analysis was performed using SPSS (version 19.0; IBM, Armonk, NY, USA).

RESULTS

Of the 411 patients admitted to the ICU emergency department, 105 were excluded from the study population for the following reasons: 40 died during ICU stay, 26 died after ICU discharge during the hospital stay, and 10 had a cerebrovascular disease or spinal disease with paresis. In addition, we missed the evaluation of 29 patients, and these patients were excluded after hospital discharge. Therefore, 306 patients (189 men and 117 women) were enrolled in the study (**Fig. 1**). The types of disease resulting in ICU admission were cardiovascular (159 patients, 52%), cerebrovascular (34 patients, 11%), respiratory (28 patients, 9.2%), sepsis (20 patients, 6.5%), cancer (13 patients 4.2%), musculoskeletal (11 patients, 3.6%), and others (41 patients, 13%).

Patient Backgrounds and Physical Examinations at ICU Admission before and after Propensity Score Matching

Table 1 (left side) shows comparisons of the factors of the ICU patients at ICU admission in the high ADL group and the low ADL group, before matching the propensity score. Age, care required, and APACHE II were significantly lower in the high ADL group than in the low ADL group ($P<0.01$). Grip strength, arm circumference, calf circumference, quadriceps thickness, and IMS were significantly higher in the high ADL group than in the low ADL group ($P<0.01$).

Table 1 (right side) shows the comparison of the factors of the ICU patients at ICU admission after matching the propensity score. One-to-one propensity score matching generated 57 pairs. After matching the propensity score, the length of ICU stay in the high ADL group was significantly shorter than that in the low ADL group ($P=0.037$). The differences in the duration of hospital stay (not ICU) and total hospital stay between the high and low ADL groups were not significant. No significant difference was found in patients' backgrounds

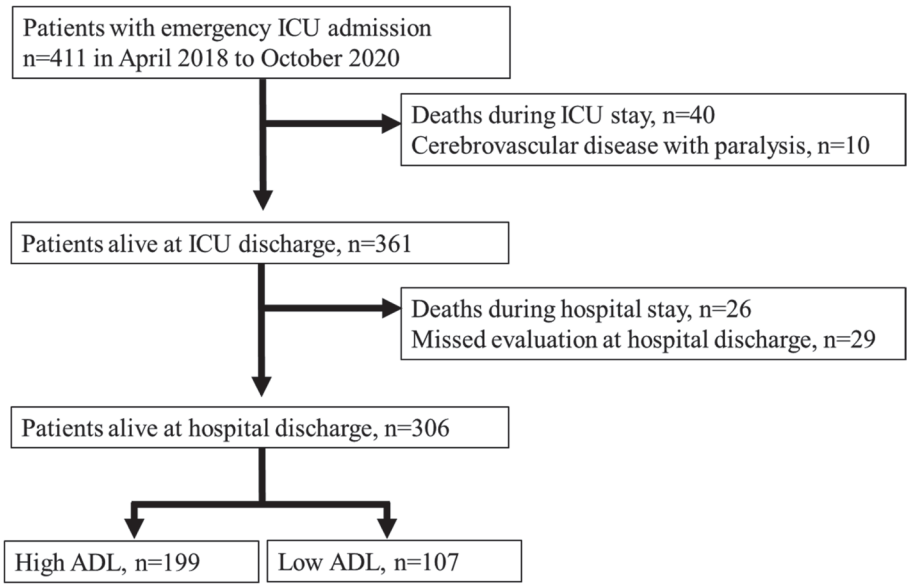

Fig. 1. Selection of patients for the study.

Table 1. Comparison of factors at ICU admission before and after propensity score matching

	Before propensity score matching			After propensity score matching		
	High ADL (n=199)	Low ADL (n=107)	P value	High ADL (n=57)	Low ADL (n=57)	P value
Age (years)	64±14	75±14	<0.01**	69±14	70±16	0.20
Sex (M/F)	129/70	60/47	0.14	35/22	35/22	1.00
Care required (0–7)	0.14±0.58	1.2±1.8	<0.01**	0.43±0.99	0.42±0.937	0.75
APACHE II	18±6.4	22±6.5	<0.01**	20±7.0	20±5.1	0.57
SOFA	6.1±3.2	6.5±3.7	0.60	7.0±3.7	6.6±3.5	0.63
IMS	0.42±0.76	0.29±0.85	<0.01**	0.17±0.38	0.20±0.52	0.97
MRC	55±14	45±21	<0.01**	45±23	45±22	0.78
Grip strength (kg)	18±9.8	10±7.7	<0.01**	13±7.2	12±8.6	0.35
Arm circumference (cm)	26±4.1	24±4.1	<0.01**	26±3.6	25±4.2	0.61
Calf circumference (cm)	33±3.8	29±4.5	<0.01**	31±3.8	30±4.7	0.21
Quadriceps thickness (cm)	3.2±0.95	2.5±0.95	<0.01**	2.9±0.85	2.8±1.0	0.42
On mechanical ventilation (h)	58.0±146	228±405	<0.01**	110±220	280±460	0.09
ICU stay (days)	7.1±8.4	11±11	<0.01**	9.0±9.3	13±13	0.037*
Hospital stay (not ICU) (days)	30±30	34±29	0.056	39±41	35±27	0.69
Hospital stay (days)	37±32	45±31	<0.01**	48±43	48±28	0.19

Data presented as mean ± standard deviation or number of patients.

and physical examinations in each group.

Trajectory of Physical Examinations in All Patients, Patients in the High ADL Group, and Patients in the Low ADL Group

Of 306 patients in the ICU, 199 patients were classified in the high ADL group and 107 in the low ADL group. **Figure 2** shows the trajectory of the means of physical examinations of the high ADL group and the low ADL group. MRC score at ICU admission was significantly lower in the low ADL group than in the high ADL group. Subsequently, the MRC score had improved in each group at hospital discharge (**Fig. 2a**). Grip strength was significantly higher in the high ADL group than in the low ADL group at each time. Over time,

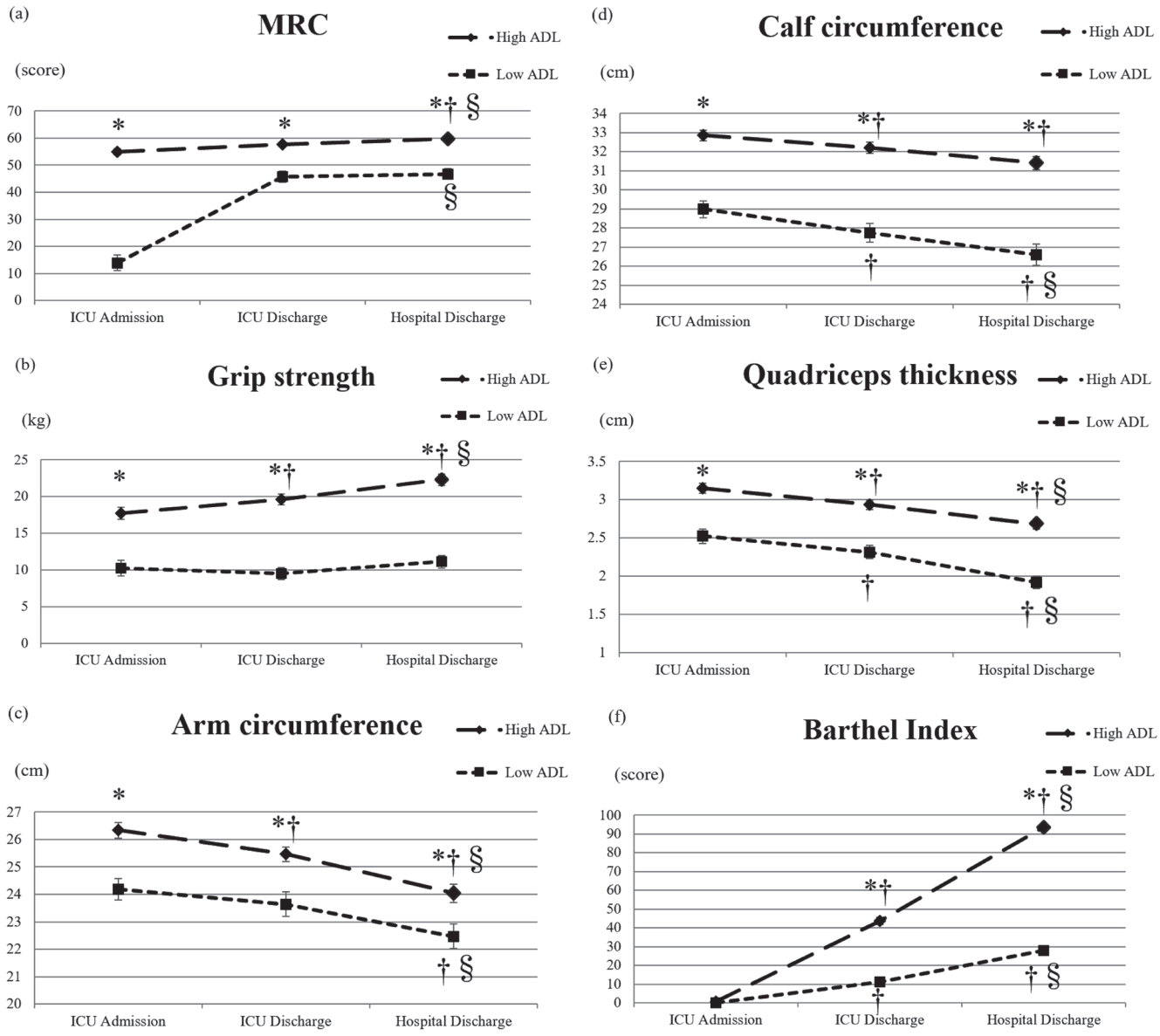

Fig. 2. Trajectories of the means of physical examinations in ICU patients from ICU admission to hospital discharge. (a) MRC, (b) grip strength, (c) arm circumference, (d) calf circumference, (e) quadriceps thickness, (f) BI. * P<0.05 vs. low ADL group; † P<0.05 vs. ICU admission; § P<0.05 vs. ICU discharge.

there was an increasing trend in grip strength in the high ADL group. Grip strength had significantly improved in the high ADL group, but it had not significantly improved in the low ADL group (**Fig. 2b**). Arm circumference, calf circumference, and quadriceps thickness were significantly higher in the high ADL group than in the low ADL group at each time. There were decreasing trends in arm circumference, calf circumference, and quadriceps thickness (**Fig. 2c–e**). At ICU discharge and hospital discharge, the improvement in BI in the high ADL group was greater than that in the low ADL group (**Fig. 2f**).

Trajectory of Physical Examinations after Propensity Score Matching

Figure 3 shows the means of the physical examinations in the high ADL group and in the low ADL group after matching propensity scores. MRC scores at ICU discharge and hospital discharge were significantly higher in the high ADL group than in the low ADL group. In the high ADL group, MRC score at hospital discharge was significantly higher than that at ICU discharge. However, MRC score in the low ADL group had not changed significantly at hospital discharge (**Fig. 3a**).

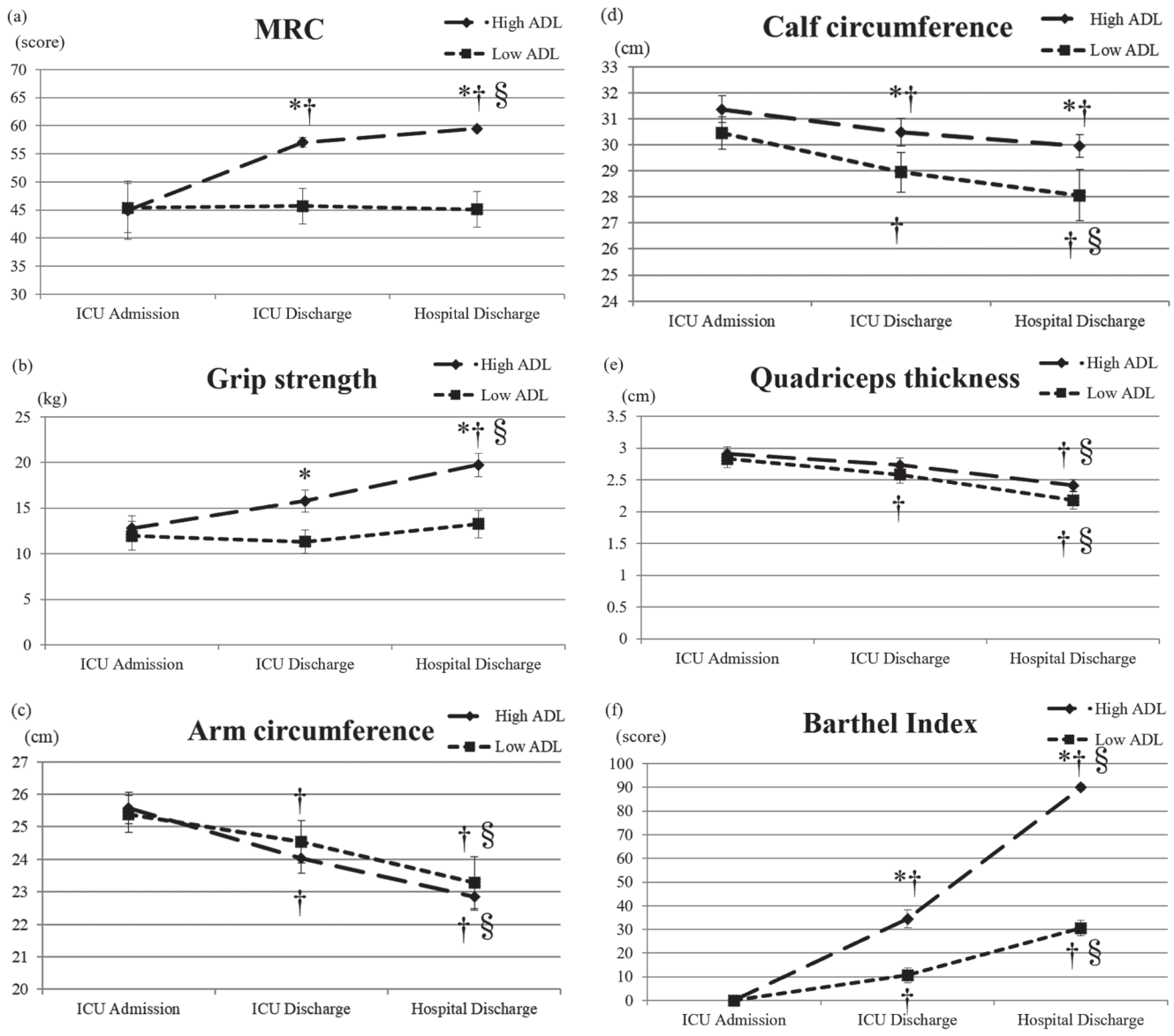

Fig. 3. Trajectories of the means of physical examinations in ICU patients from ICU admission to hospital discharge after matching the propensity scores. (a) MRC, (b) grip strength, (c) arm circumference, (d) calf circumference, (e) quadriceps thickness, (f) BI. * P<0.05 vs. low ADL group; † P<0.05 vs. ICU admission; § P<0.05 vs. ICU discharge.

Grip strength was significantly higher in the high ADL group than in the low ADL group at ICU discharge and at hospital discharge. In the high ADL group, grip strength at hospital discharge was significantly higher than at ICU admission and ICU discharge . However, grip strength in the low ADL group had not significantly changed at hospital discharge (**Fig. 3b**).

Arm circumference had decreased in each group at hospital discharge. There was no significant difference between the high ADL group and the low ADL group (**Fig. 3c**).

Calf circumference had declined in each group at hospital discharge. Calf circumference was significantly higher in the high ADL group than in the low ADL group at discharge from the ICU and at hospital discharge (**Fig. 3d**).

The thickness of the quadriceps had decreased in each group at hospital discharge, but there was no significant difference between the high ADL group and the low ADL group (**Fig. 3e**). BI had improved significantly in each group at ICU discharge and at hospital discharge. BI was significantly higher in the high ADL group than in the low ADL group at ICU discharge and at hospital discharge (**Fig. 3f**).

Table 2 Comparison of relative changes in factors from ICU admission to ICU discharge and from ICU admission to hospital discharge

Factor	Between ICU admission and ICU discharge			Between ICU admission and hospital discharge		
	High ADL (n=57)	Low ADL (n=57)	P value	High ADL (n=57)	Low ADL (n=57)	P value
Grip strength (%)	62±150	18±83	0.66	113±220	16±69	0.10
Arm circumference (%)	−5.7±8.4	−2.9±9.0	0.08	−8.2±8.7	−7.9±13	0.96
Calf circumference (%)	−2.6±11	−3.8±9.9	0.52	−2.4±-12	−8.0±13	<0.01**
Quadriceps thickness (%)	−2.7±30	−6.5±23	0.79	−11±24	−27±23	<0.01**

Data presented as mean ± standard deviation.

Relative Changes in Physical Examinations from ICU Admission to ICU Discharge and from ICU Admission to Hospital Discharge

Table 2 shows the relative changes in physical examinations from ICU admission to ICU discharge and from ICU admission to hospital discharge. From ICU admission to ICU discharge, there was no significant difference in the relative changes between the high ADL group and the low ADL group. However, the relative changes in calf circumference and quadriceps thickness from ICU admission to hospital discharge were significantly higher in the high ADL group than in the low ADL group.

ROC Analysis

Figure 4 shows the ROC curves for the relative changes in calf circumference and quadriceps thickness in the high and low ADL groups. ROC analysis determined −7.89% as the cutoff value of the relative change in calf circumference from ICU admission to hospital discharge with a sensitivity of 77.8%, a specificity of 55.6%, and the area under the curve (AUC) was 0.681 (95% confidence interval [CI]: 0.560–0.803). Furthermore, the ROC analysis determined −28.1% as the cutoff value for the relative change in quadriceps thickness from ICU admission to hospital discharge with a sensitivity of 81.0%, a specificity of 58.8%, and the AUC was 0.693 (95% CI: 0.570–0.815).

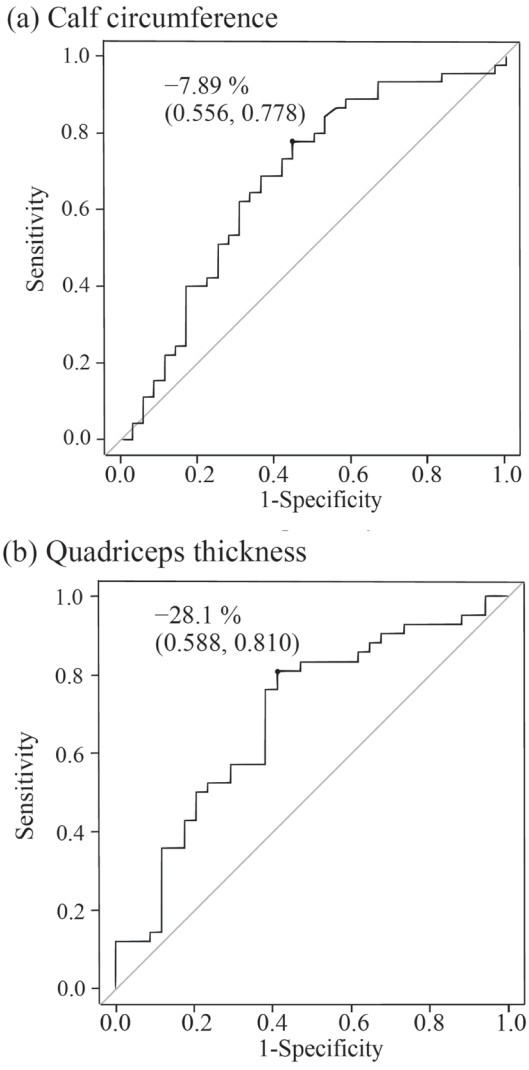

Fig. 4 . ROC analysis for the relative change in (a) calf circumference and (b) quadriceps thickness in the high ADL and low ADL groups.

DISCUSSION

In this study, grip strength, arm circumference, calf circumference, and quadriceps thickness were higher in the high ADL group from ICU admission to hospital discharge. Regarding patient background, ICU patients in the high ADL group were younger, had lower severity, and required less care. Previous reports showed that a decrease in ADL was associated with age,[18] severity of the disease, and physical

function before hospital admission.[19] These findings were similar to those of our study. In this study and in previous studies, better patient background and better physical function at discharge from the ICU were associated with a high ADL at discharge from the hospital. Therefore, for a detailed investigation of the relationship between the trajectory of physical function and ADL at hospital discharge, we aligned their background using the propensity score matching technique.

After matching the propensity score, grip strength, calf circumference, and BI at ICU discharge were higher in the high ADL group than in the low ADL group, and the length of stay in the ICU was shorter in the high ADL group than in the low ADL group. Calf circumference and quadriceps thickness had declined from ICU admission to hospital discharge, and the rates of decline were lower in the high ADL group than in the low ADL group. Although a previous study reported similar results,[20] there was no information on the relationship between calf circumference decline rate and quadriceps thickness and ADL at hospital discharge. In the current study, we found that the cutoff value of the relative change of calf circumference from admission to the ICU to hospital discharge for the high ADL group was −7.89%, and the cutoff value of the relative change of quadriceps thickness from admission to the ICU to hospital discharge for the high ADL group was −28.1%. In addition, each cutoff value had high sensitivity. Therefore, measuring the relative change in calf circumference or quadriceps thickness in ICU patients over time could help predict their ADL at hospital discharge. Given that calf circumference and quadriceps thickness can be measured easily and noninvasively at the bedside, these parameters may be useful predictors of ADL at hospital discharge.

We found that the circumference of the calf in the high ADL group was greater than that in the low ADL group, and its relative decline from ICU admission to hospital discharge in the high ADL group was lower than that in the low ADL group. Furthermore, the degree of improvement in muscle power in the high ADL group was greater than that in the low ADL group. The circumference of the calf is reported to be associated with lower limb muscle mass,[21] total body skeletal muscle mass, and body mass index.[22] Because muscle mass has a positive correlation with muscle strength,[23] the decrease in calf circumference may reflect a decrease in muscle mass, decreased strength of the lower extremities, and decreased mass of whole-body skeletal muscles. In our study, the decline in the quadriceps thickness was similar to that of the calf circumference. Therefore, the results suggested that the mass of the skeletal muscle was associated with the circumference of the calf.

However, in this study, we could not determine the association of MRC score and arm circumference with ADL in ICU patients at hospital discharge. Therefore, the results suggested that a physical examination of the lower limb, which is associated with gait ability, could be useful in predicting ADL of ICU patients at hospital discharge. In addition, we could not determine the association of length of hospital stay after ICU discharge and total hospital stay with ADL in ICU patients at hospital discharge. However, the length of ICU stay in the high ADL group was shorter than that in the low ADL group. Early discharge from the ICU may prevent the decline of ADL in ICU patients at hospital discharge.

Our study has several limitations. First, this was a retrospective observational study. A secondary cohort study is needed to confirm the reliability of the cutoff values. Second, we evaluated the patients during hospitalization. Long-term observation of patients after hospital discharge is necessary. Third, the matching of propensity scores was performed in this retrospective design. Despite careful matching of propensity scores, residual confounding could not be fully excluded.

CONCLUSION

We investigated the factors affecting ADL status at hospital discharge in ICU patients using propensity score matching. We found that ICU patients who had high ADL status at hospital discharge had high muscle strength and a high calf circumference at discharge from the ICU. Furthermore, their rate of decrease in calf circumference and quadriceps thickness from ICU admission to hospital discharge was lower than that of ICU patients with low ADL status at hospital discharge. This study indicates that the evaluation of the calf circumference and quadriceps thickness trajectory can predict ADL status at hospital discharge among ICU survivors.

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CONFLICTS OF INTEREST

The authors have no competing interests to declare.

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