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Associations of body mass index and hospital-acquired disability with post-discharge mortality in older patients with acute heart failure

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ABSTRACT

OBJECTIVES To investigate the effect of hospital-acquired disability (HAD) on all-cause mortality after discharge according to the body mass index (BMI) in older patients with acute decompensated heart failure.

METHODS We included 408 patients aged ≥ 65 years who were hospitalized for acute decompensated heart failure and had undergone an acute phase of cardiac rehabilitation at the Sakakibara Heart Institute between April 2013 and September 2015 (median age: 82 years, interquartile range (IQR): 76–86; 52% male). Patients were divided into three groups based on BMI at hospital admission: underweight (< 18.5 kg/m^2), normal weight (18.5 to 25 kg/m^2), and overweight (≥ 25 kg/m^2). HAD was defined as a decrease of at least five points at discharge compared to before hospitalization according to the Barthel Index.

RESULTS The median follow-up period was 475 (IQR: 292–730) days, and all-cause mortality during the follow-up period was 84 deaths (21%). According to multivariate Cox regression analysis, being underweight (HR: 1.941, 95% CI: 1.134–3.321, P = 0.016) or overweight (HR: 0.371, 95% CI: 0.171–0.803, P = 0.012), with normal BMI as the reference, and HAD (HR: 1.857, 95% CI: 1.062–3.250, P = 0.030) were independently associated with all-cause mortality. Patients with HAD exhibited a significantly lower cumulative survival rate in the underweight group (P = 0.001) and tended to have a lower cumulative survival rate in the normal weight group (P = 0.072). HAD was not significantly associated with cumulative survival in the overweight group (P = 0.392).

CONCLUSIONS BMI and HAD independently predicted all-cause mortality after discharge in older patients with acute decompensated heart failure. Furthermore, HAD was significantly associated with higher all-cause mortality after discharge, especially in the underweight group.

In recent years, the prevalence of patients with heart failure has increased rapidly.[1] As the population ages in Japan, there is a growing concern that the prevalence of heart failure will continue to increase.[2] Therefore, there is an urgent need to treat and manage older patients with heart failure by determining the risk factors associated with poor prognoses.

Being overweight and obese are associated with all-cause and cardiovascular mortality.[3,4] Moreover, individuals who are overweight or obese reportedly have a higher risk of developing heart failure than those with normal body weight.[5] Conversely, the "obesity paradox" shows that being underweight, rather than being overweight or obese, is associated with a poorer prognosis in patients with heart failure.[6,7]

A decline in physical function during hospitalization is called hospital-acquired disability (HAD), and has a reported incidence rate of approximately 35% in older patients.[8] HAD is a poor prognostic factor in older patients with heart disease.[9] In a previous study, underweight patients with heart failure had low scores for activities of daily living measured at admission, and the decline tended to continue even at discharge.[10] However, it remains unclear whether HAD influences patient prognosis according to the body mass index (BMI) after discharge. This study aimed to investigate the association of HAD with all-cause mortality after discharge according to BMI categories in patients with acute decompensated heart failure.

METHODS

Study Population

This retrospective study was conducted at a single center. Data from 555 consecutive patients aged ≥ 65 years, who were hospitalized for acute decompensated heart failure and underwent rehabilitation at the Sakakibara Heart Institute between April 2013 and September 2015 were collected. Patients were excluded from analysis based on the following criteria: in-hospital death (n = 22), surgery performed during hospitalization (n = 32), incomplete data on BMI (n = 36), missing data on the Barthel Index (BI) before hospitalization (n = 2), BI < 60 points before hospitalization (n = 27), and no follow-up examination after discharge (n = 23). As our aim was to evaluate the disability that occurred during hospitalization, patients with BI < 60 points before hospitalization, which was defined as a prominent disability in previous studies,[11–13] were excluded. The study was approved by the ethics committee of the Sakakibara Heart Institute (ID: 17-018), and all patients provided written informed consent prior to participation. The study protocol conformed with the Declaration of Helsinki. All information was retrospectively obtained from the patients' medical records or the hospital's database.

BMI

Patients were divided into three groups based on their BMI measured upon hospital admission:[14,15] underweight (< 18.5 kg/m^2), normal weight (18.5 to 25 kg/m^2), and overweight (≥ 25 kg/m^2).

HAD

The functional status of the patients was evaluated using the BI. The BI is widely used to evaluate activities of daily living by assessing the following 10 items: feeding, bathing, grooming, dressing, controlling bowels, controlling the bladder, toilet use, transfers from bed to chair and back, mobility on level surfaces, and climbing stairs.[16] The BI score ranges from 0 (total dependence) to 100 points (total independence) in 5-point intervals. Cases of HAD were defined as those exhibiting a decrease of at least 5 points on the BI score at discharge compared with that before hospitalization.[13,17] The BI score before hospitalization was assessed from a functional status approximately one month before hospitalization by interviewing the patient or/and patient's family during hospitalization.[13,17]

Clinical Endpoint

The endpoint of this study was all-cause mortality after hospital discharge. Follow-up data were obtained from medical records or the hospital's database. The maximum follow-up period was two years.

Statistical Analysis

Continuous data are presented as medians (interquartile range (IQR)), and categorical data are presented as percentages. Comparisons among BMI categories were performed using the Kruskal–Wallis test for continuous data and the chi-square test for categorical data. Cox regression analysis was used to examine the predictors of all-cause mortality after hospital discharge. In the multivariate Cox regression analysis, variables with P-values < 0.15 in the univariate Cox regression analysis were included. The Kaplan–Meier curve and log-rank test were performed to test the power of BMI categories, HAD, and HAD according to each BMI category for estimating the cumulative survival rate. A P-value < 0.05 was considered significant. All analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA) and JMP Pro version 16 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Patient Characteristics and HAD

We analyzed data from 408 patients who met the selection criteria. The patients' characteristics are presented in Table 1. The median age was 82 (76–

Table 1 Patients' baseline characteristics.

Characteristics	Total (n = 408)	Underweight (n = 56)	Normal weight (n = 245)	Overweight (n = 107)	P-value
Age, yrs	82 (76–86)	82 (76–87)	83 (76–87)	81 (74–85)	0.027
Male, %	52	30	53	59	0.002
BMI, kg/m^2	22.6 (20.0–25.3)	17.3 (16.4–18.0)	22.0 (20.6–23.5)	26.8 (25.9–28.2)	< 0.001
NYHA class III or IV on admission, %	63	61	65	60	0.564
HFrEF, %	34	17	38	36	0.019
Main etiology					
Ischemic, %	36	27	35	42	0.146
Valvular, %	32	48	32	24	0.008
Myopathy, %	13	5	14	13	0.215
Hypertensive, %	3	4	2	6	0.212
Others, %	16	16	17	15	0.875
History of heart failure hospitalization, %	47	61	47	39	0.028
Comorbidity					
Myocardial infarction, %	24	21	22	32	0.108
Angina pectoris, %	17	13	17	20	0.511
Hypertension, %	64	59	64	69	0.397
Dyslipidemia, %	35	34	33	41	0.338
Diabetes mellitus, %	32	25	29	42	0.026
Respiratory disease, %	13	14	14	10	0.622
Stroke, %	12	9	15	7	0.072
Orthopedic disease, %	15	13	13	20	0.245
Laboratory data					
Hemoglobin, g/dL	11.6 (10.3–12.9)	11.3 (10.0–12.3)	11.6 (10.3–13.0)	11.7 (10.3–13.1)	0.272
Albumin, g/dL	3.7 (3.4–3.9)	3.7 (3.2–3.9)	3.7 (3.4–3.9)	3.7 (3.4–3.9)	0.783
eGFR, mL/min per 1.73 m^2	44.5 (33.3–58.2)	49.6 (32.8–62.1)	46.0 (33.5–58.6)	40.7 (33.1–54.6)	0.203
Creatinine, mg/dL	1.06 (0.83–1.42)	1.06 (0.71–1.60)	1.03 (0.83–1.35)	1.16 (0.91–1.54)	0.070
Blood urea nitrogen, mg/dL	23.8 (17.6–31.1)	24.5 (18.0–35.3)	23.4 (17.6–30.1)	24.1 (17.3–32.2)	0.364
C-reactive protein, mg/dL	0.57 (0.15–2.69)	0.68 (0.12–2.30)	0.47 (0.15–2.57)	0.65 (0.19–3.02)	0.667
NT-proBNP, pg/dL	3754 (2204–7651)	3412 (1754–9472)	3993 (2480–8796)	3274 (1662–5999)	0.100

Values are presented as medians (interquartile ranges) or percentages. BMI: body mass index; eGFR: estimated glomerular filtration rate; HFrEF: heart failure with reduced ejection fraction; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-brain natriuretic peptide; NYHA: New York Heart Association.

86) years, and 52% of the patients were male. The median BMI was 22.6 (20.0–25.3) kg/m^2. In total, 56 (14%), 245 (60%), and 107 (26%) patients were included in the underweight, normal weight, and overweight groups, respectively. The median age was significantly different among the BMI categories. There were significant differences between the BMI categories in the percentage of male patients, the prevalence of heart failure with reduced ejection fraction (HFrEF, left ventricular ejection fraction < 40%), valvular involvement in the main etiology, history of heart failure hospitalization, and the prevalence of diabetes mellitus. A lower percentage of male patients, a lower prevalence of HFrEF, a higher prevalence of valvular involvement in the main etiology, and a higher prevalence of heart failure hospitalization history were observed in the underweight group compared to those in the normal and overweight groups. A higher prevalence of diabetes mellitus was observed in the over-

weight group compared to those in the underweight and normal-weight groups.

The incidence of HAD is described in Table 2. The BI score before hospitalization and at discharge and the prevalence of HAD were not significantly different among BMI categories. There were no significant differences in hospitalization duration and proportion of patients discharged among the BMI categories.

Association of BMI Categories and HAD with All-cause Mortality

The median follow-up period was 475 (292−730) days. There were 84 (21%) all-cause deaths during the follow-up period. After univariate Cox regression analysis, age, BMI categories, history of heart failure hospitalization, HAD, as well as the hemoglobin, albumin, blood urea nitrogen, and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, were entered into the multivariate Cox regression analysis (Table 3). In the multivariate analysis, being underweight (HR: 1.941, 95% CI: 1.134−3.321, P = 0.016) and overweight (HR: 0.371, 95% CI: 0.171−0.803, P = 0.012) with normal weight as the reference for BMI categories, hemoglobin (HR: 0.881, 95% CI: 0.776−1.000, P = 0.049), and HAD (HR: 1.857, 95% CI: 1.062−3.250, P = 0.030) were independently associated with all-cause mortality after adjusting for the above-mentioned covariates.

The Kaplan–Meier survival curves for all-cause mortality according to BMI categories and HAD are presented in Figure 1. The patients in the underweight group had a significantly lower cumulative survival rate than those of the normal weight and overweight groups (P = 0.001 and P < 0.001, respectively) (Figure 1A). Additionally, the patients in the overweight group had a significantly higher cumulative survival rate than those of the normal weight group (P = 0.002) (Figure 1A). In the Kaplan–Meier survival curves, HAD was significantly associated with a decrease in the cumulative survival rate (P < 0.001) (Figure 1B). Patients with HAD had significantly lower cumulative survival rates in the underweight group (P = 0.001) (Figure 2A) and tended to have a decreased cumulative survival rate in the normal weight group (P = 0.072) (Figure 2B). HAD was not significantly associated with cumulative survival in the overweight group (P = 0.392) (Figure 2C).

Cox regression analysis results for all-cause mortality according to HAD and BMI category are presented in Figure 3. In the underweight group, patients with HAD had a significantly higher risk than those in the non-HAD group for all-cause mortality (HR: 3.797; 95% CI: 1.646−8.758; P = 0.002). In the normal weight and overweight groups, the risk of all-cause mortality was not significantly different between the HAD and non-HAD groups (normal weight, HR: 1.864, 95% CI: 0.936−3.711, P = 0.077; overweight, HR: 1.984, 95% CI: 0.400−9.834, P = 0.401).

DISCUSSION

Herein, we investigated the effects of HAD on all-cause mortality after discharge in patients with acute decompensated heart failure according to differences in BMI. Our results revealed that BMI and HAD were independent predictors of all-cause mortality after discharge. As a result of the novel examination according to the BMI categories, our study was the first to report that HAD was significantly associated with an increase in all-cause mortality after discharge, especially in underweight patients.

The results of this study were similar to those of previous studies. For example, in a study of pa-

Table 2 Hospital-acquired disability.

	Total (n = 408)	Underweight (n = 56)	Normal weight (n = 245)	Overweight (n = 107)	P-value
Barthel Index score before hospitalization, points	100 (95−100)	100 (96−100)	100 (100−100)	100 (95−100)	0.666
Barthel Index score at discharge, points	100 (90−100)	100 (90−100)	100 (93−100)	100 (90−100)	0.162
Hospital-acquired disability, %	15	25	13	15	0.080
Length of hospital stay, days	16 (12−24)	19 (14−27)	16 (12−24)	16 (11−25)	0.310
Discharge to home, %	93	88	93	95	0.179

Values are presented as medians (interquartile ranges) or percentages.

Table 3 Predictors of all-cause mortality in univariate and multivariate Cox regression analysis.

	Univariate		Multivariate	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age (every 1-year increase)	1.041 (1.010–1.072)	0.009	1.026 (0.993–1.061)	0.128
Male	0.988 (0.644–1.517)	0.958		
BMI categories (reference normal weight)				
Underweight	2.247 (1.377–3.666)	0.001	1.941 (1.134–3.321)	0.016
Normal weight	Reference		Reference	
Overweight	0.328 (0.156–0.689)	0.003	0.371 (0.171–0.803)	0.012
NYHA class III or IV on admission	1.300 (0.825–2.047)	0.258		
HFrEF	1.276 (0.811–2.009)	0.292		
History of heart failure hospitalization	1.664 (1.075–2.578)	0.022	1.441 (0.865–2.400)	0.160
Myocardial infarction	1.268 (0.795–2.025)	0.319		
Angina pectoris	1.106 (0.641–1.907)	0.718		
Hypertension	0.947 (0.608–1.475)	0.809		
Dyslipidemia	1.189 (0.767–1.843)	0.438		
Diabetes mellitus	0.967 (0.609–1.536)	0.887		
Respiratory disease	1.376 (0.775–2.443)	0.276		
Stroke	0.914 (0.472–1.769)	0.789		
Orthopedic disease	1.331 (0.772–2.295)	0.303		
Hemoglobin (every 1 g/dL increase)	0.832 (0.743–0.931)	0.001	0.881 (0.776–1.000)	0.049
Albumin (every 1 g/dL increase)	0.495 (0.289–0.846)	0.010	0.557 (0.309–1.004)	0.052
eGFR, mL/min per 1.73 m^2	0.995 (0.983–1.007)	0.374		
Creatinine (every 1 mg/dL increase)	1.151 (0.906–1.463)	0.250		
Blood urea nitrogen (every 1 mg/dL increase)	1.018 (1.005–1.031)	0.006	1.008 (0.990–1.026)	0.402
C-reactive protein (every 1 mg/dL increase)	0.996 (0.936–1.060)	0.911		
NT-proBNP (every 1 pg/dL increase)	1.000 (1.000–1.000)	0.085	1.000 (1.000–1.000)	0.396
Hospital-acquired disability	2.424 (1.490–3.945)	< 0.001	1.857 (1.062–3.250)	0.030

BMI: body mass index; CI: confidence interval; eGFR: estimated glomerular filtration rate; HFrEF: heart failure with reduced ejection fraction; HR: hazard ratio; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-brain natriuretic peptide; NYHA: New York Heart Association.

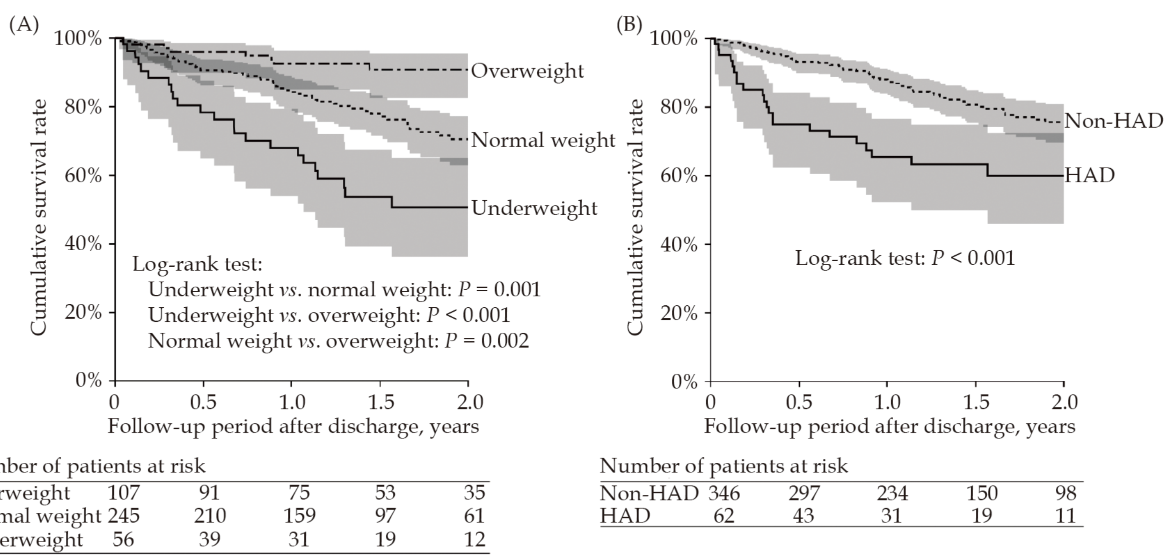

Figure 1 Kaplan–Meier curves with 95% CI for all-cause mortality according to the (A) BMI category and (B) hospital-acquired disability. BMI: body mass index; HAD: hospital-acquired disability

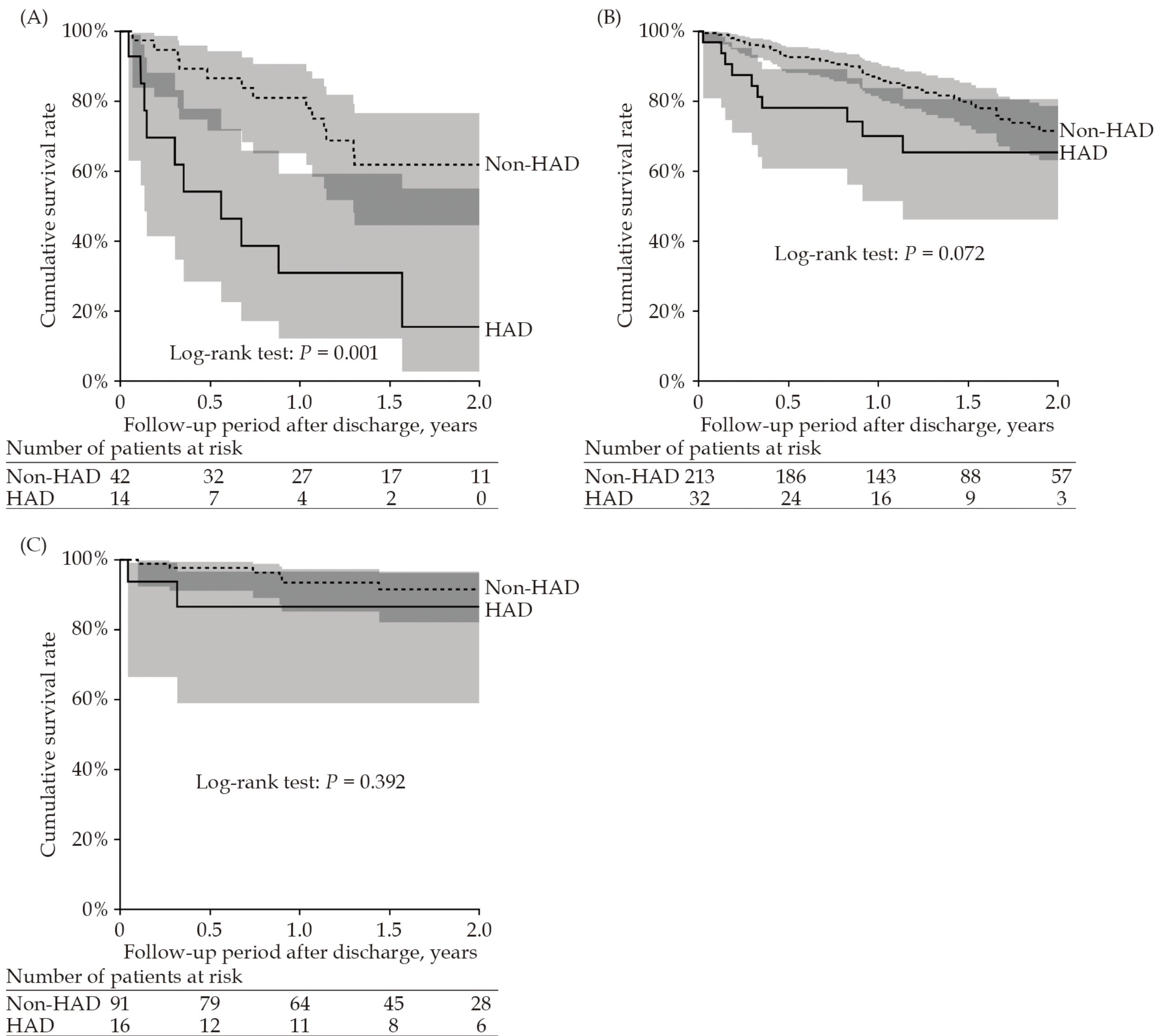

Figure 2 Kaplan–Meier curves with 95% CI for all-cause mortality according to hospital-acquired disability in the (A) underweight, (B) normal weight, and (C) overweight groups. BMI: body mass index; HAD: hospital-acquired disability.

tients with heart failure, a lower BMI was associated with a higher risk of all-cause mortality after discharge.[18] Furthermore, all-cause mortality significantly increased in underweight patients and significantly decreased in overweight patients, compared to those with normal weight.[18] Similarly, underweight and severely underweight individuals had significantly increased all-cause mortality rates compared to those of the normal weight patients with heart failure.[19]

HAD has been identified as a poor prognostic factor in several studies. In a report assessing HAD due to gait impairment in patients with heart failure, disability significantly increased all-cause mortality after discharge.[20] Similar to the present study, an evaluation of HAD using the BI scores in patients with heart failure revealed that a decrease of at least five points significantly increased the risk of all-cause mortality or readmission due to heart failure.[13] In patients with chronic heart failure, a greater degree of disability based on the assessment of activities of daily living was found to be associated with a lower peak oxygen uptake.[21] Since peak oxygen uptake is a prognostic factor,[22] HAD may reduce reserve capacity and increase all-cause mortality after discharge.

In this study, HAD significantly increased the risk of all-cause mortality after discharge in the underweight group. In patients with heart failure, being underweight was associated with a higher pre-

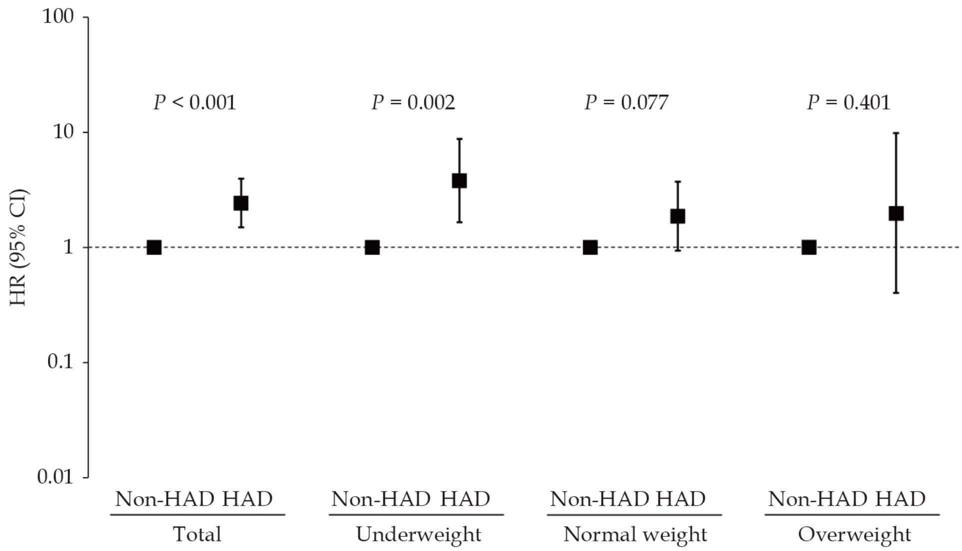

Figure 3 Cox regression analysis for all-cause mortality according to hospital-acquired disability in each BMI category. HAD: hospital-acquired disability.

valence of muscle wasting.[23] There have been previous reports stating that muscle wasting was associated with decreased physical function and exercise tolerance,[24] and with an increase in all-cause mortality.[25] Moreover, in patients with heart failure, underweight patients tend to have a higher rate of poor nutritional status compared to the corresponding of normal weight and overweight patients.[26] Poor nutritional status was found to be associated with decreased physical function and activities of daily living[27] as well as poor prognosis.[28] Underweight patients with heart failure are at increased risk of muscle wasting and poor nutritional status, and HAD may further reduce their already low reserve capacity, leading to worsening of their prognosis.

In patients with heart failure, activities of daily living at admission are reportedly lower in underweight patients compared to those in normal weight and overweight patients, and the decline tends to be prolonged even at discharge.[10] In the present study, there was no significant difference in the prevalence of HAD according to the BMI, but the prevalence tended to be higher in the underweight than in the normal weight or overweight group. Early inpatient rehabilitation for patients with acute heart failure is reported to significantly reduce the rate of physical dysfunction.[29,30] All patients in this study underwent rehabilitation during hospitalization, performed according to the rehabilitation guidelines of the Japanese Circulation Society.[31] Additionally, evidence suggests that, in patients with acute heart failure, nutritional interventions for undernourished patients reduce all-cause mortality and rehospitalization for heart failure after discharge.[32,33] Appropriate nutritional assessment and intervention as early as possible during hospitalization may be helpful, in addition to rehabilitation, especially in underweight patients with heart failure. Further, continued rehabilitation at home after discharge reportedly improves activities of daily living and walking speed in older patients with heart failure.[34] Therefore, at-home rehabilitation after discharge should be considered for individuals who experience a decline in activities of daily living during hospitalization.

This study had several limitations. First, we only evaluated the patients' physique in terms of their BMI, which excludes body composition-related factors, such as muscle and fat mass. Second, the nutritional status could not be evaluated as no corresponding assessment, such as the Mini Nutritional Assessment-Short Form,[35] was conducted upon hospitalization. Third, we could not investigate the changes in physical function after discharge due to a lack of follow-up data. Therefore, it was unclear whether HAD persisted after discharge.

In conclusion, our results revealed that BMI and HAD independently predicted all-cause mortality after discharge in older patients with acute decompensated heart failure. Moreover, HAD was significantly associated with an increase in all-cause mortality after discharge, especially in underweight patients.

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