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ORIGINAL ARTICLE
Cardiac Rehabilitation

Barthel Index Score Predicts Mortality in Elderly Heart Failure

— A Goal of Comprehensive Cardiac Rehabilitation —

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Background: A strategy to predict mortality in elderly heart failure (HF) patients has not been established.

Methods and Results: We retrospectively enrolled 413 HF patients aged ≥65 years (mean age 78 years) who had received comprehensive cardiac rehabilitation (CR) during hospitalization. Basic activities of daily life were assessed before discharge using the Barthel index (BI). Of 413 HF patients, 116 (28%) died during a median follow-up period of 1.90 years (interquartile range 1.20–3.23 years). An adjusted dose-dependent association analysis showed that the hazard ratio (HR) of mortality increased in an almost linear manner as the BI score decreased, and that a BI score of 85 corresponded to an HR of 1.0. Kaplan-Meier survival curves showed that the survival rate was lower for patients with a low BI (<85) than for those with a high BI (≥85; 65% vs. 74%, respectively; P=0.007). In multivariate Cox regression analyses, low BI was independently associated with higher mortality after adjusting for predictors, including B-type natriuretic peptide. Inclusion of the BI into the adjusted model improved the accuracy of the prediction of mortality.

Conclusions: A BI score <85 at the time of discharge is associated with increased mortality independent of known prognostic markers, and achieving functional status with a BI score ≥85 by comprehensive CR during hospitalization may contribute to favorable outcomes in elderly HF patients.

Key Words: Activities of daily living; Barthel Index; Elderly; Heart failure; Mortality

Heart failure (HF) is a major public health problem, with a prevalence of over 23 million worldwide, and is a leading cause of morbidity, mortality, and rehospitalization.[1,2] The prevalence of HF increases with aging: more than 80% of patients diagnosed with HF are >65 years of age.[3–5] In addition to establishing preventive and diagnostic protocols, accurate prediction of prognosis is a critical issue for an appropriate decisions regarding treatment strategies in elderly HF patients. Previously, the Seattle Heart Failure model was developed using prognostic markers from clinical trials in which the effects of drug therapies on clinical outcomes were examined.[6] That model

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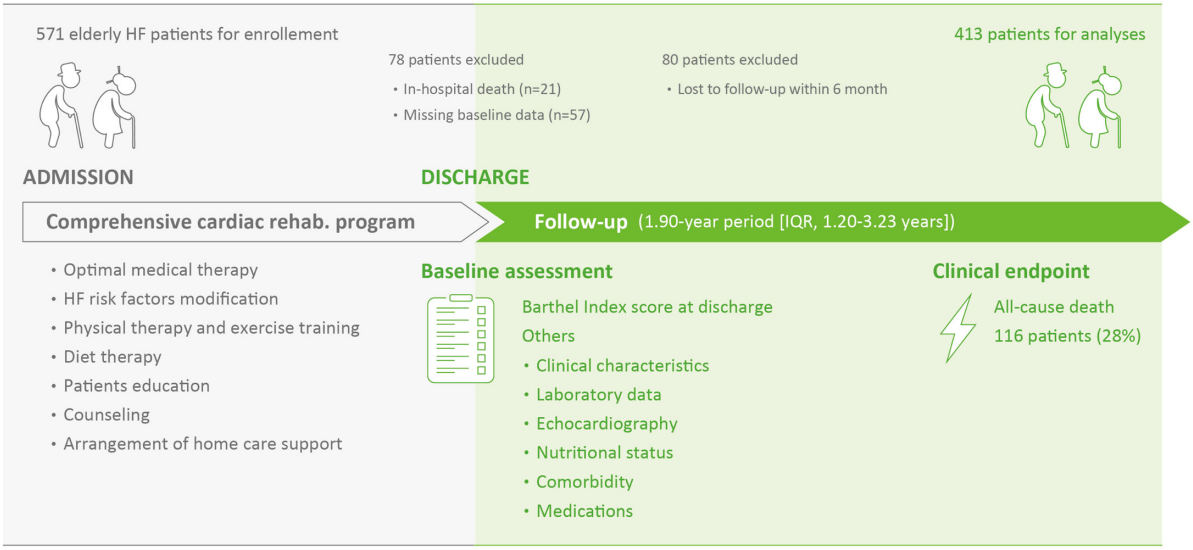

Figure 1. Flow chart showing inclusion of study subjects. HF, heart failure.

has been shown to have acceptable accuracy for the prediction of mortality in HF patients, but a limitation of the model is the overestimation of life expectancy in elderly HF patients.[7] Although other models for the prediction of mortality in elderly HF patients have been developed, a strategy to predict mortality in elderly HF patients has not been established.[3,8–11] A major problem in the prediction of mortality in elderly HF patients is the frequent presence of comorbidities that affect clinical outcomes.[3,12,13]

Basic activities of daily living (ADL) are defined as the ability to perform activities required for independent living, such as grooming, transferring, and toilet use, within one's own residence. A decline in basic ADL leads to functional dependence, a condition in which a person is unable to perform basic ADL without assistance, which is thought to be a convergence point of untoward effects of comorbidities in elderly HF patients on physical function. The Barthel index (BI) is the most widely used tool for the assessment of basic ADL.[14,15] BI scores of 0 and 100 indicate complete dependence and complete independence, respectively, and a BI score of <60 indicates severe functional dependence.[16] Several studies have revealed that the presence of severe functional dependence at the time of hospital discharge in patients treated for acute decompensated HF is associated with an increased risk of rehospitalization and death after discharge.[17–19] However, there is no evidence to indicate that the BI score can be used as a predictor of mortality in elderly HF patients, although favorable effects of comprehensive cardiac rehabilitation (CR) on clinical outcomes and functional status in HF patients have been demonstrated.[20,21]

The aim of this study was to investigate the effects of BI scores on predictions of all-cause death in elderly HF patients. In this study, we analyzed the dose-dependent association between BI scores and all-cause death to determine an optimal cut-off value for prediction of mortality after discharge in elderly HF patients. Considering the heterogeneity of elderly HF patients, HF patients were matched using the inverse probability of treatment weighting (IPTW) method.

Methods

Study Design and Study Subjects

This study was a single-center retrospective observational study. We retrospectively enrolled consecutive patients aged ≥65 years who were admitted to Sapporo Medical University Hospital for the management of HF during the period from August 1, 2010 to August 31, 2019 (**Figure 1**). HF was diagnosed by cardiologists according to the Framingham criteria.[22] The period from August 1, 2010 to August 31, 2019 was selected for the enrollment of study subjects because routine assessment of BI was commenced and comprehensive CR was routinely introduced on August 1, 2010. Exclusion criteria were in-hospital death, missing baseline data, and loss to follow-up with 6 months after discharge. All patients included in the present study received comprehensive CR during hospitalization and multidisciplinary intervention, including education of self-monitoring and medications, as well as nutritional guidance by a heart failure team consisting of cardiologists, nurses, physical therapists, pharmacists, dietitians, and social workers. The CR program was performed as described previously.[23]

This study was conducted in strict adherence with the principles of the Declaration of Helsinki and was approved by the Clinical Investigation Ethics Committee of Sapporo Medical University Hospital (No. 302-243).

Data Collection and Assessment of Clinical Parameters

Functional status for performing basic ADL was assessed using the BI by physical therapists over 3 consecutive days before discharge, as described previously.[23] The BI consists of 10 questions about feeding, transfers, grooming, toilet use, bathing, ambulation, stair climbing, dressing, and bowel and bladder care, with scores ranging from 0 to 100

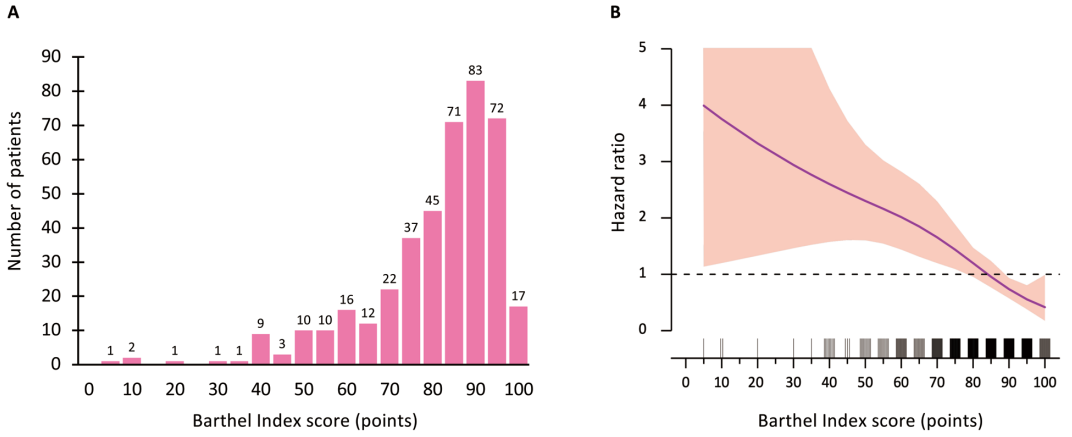

Figure 2. (**A**) Distribution of Barthel Index (BI) scores in heart failure (HF) patients. (**B**) Adjusted dose-dependent association between BI score and all-cause mortality in elderly HF patients. The dotted line represents a hazard ratio (HR) of 1.0, the purple line represents HRs, and the shaded area represents 95% confidence intervals. Rug plots are shown along the x-axes of the graphs to depict the distributions of BI scores. All analyses were adjusted for age, sex, history of HF hospitalization, cachexia, log B-type natriuretic peptide concentration, creatinine-based estimated glomerular filtration rate, hemoglobin, Charlson Comorbidity Index, and the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and β-blockers.

(0=complete dependence; 100=complete independence).

Nutritional status was assessed using the Mini Nutritional Assessment-Short Form (MNA-SF) within 3 days before discharge, as described previously.[23,24] The MNA-SF consists of 6 questions about reductions in food intake over the past 3 months, weight loss during the past 3 months, mobility, psychological stress or acute disease in the past 3 months, neuropsychological problems, and body mass index (BMI) and it is scored from 0 to 14.

Laboratory data were obtained within 7 days of assessment of the BI. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2.[24] Transthoracic echocardiography was performed by the standard protocol, and the left ventricular ejection fraction (LVEF) was measured by the modified Simpson method. HF with reduced ejection fraction (HFrEF) was defined as LVEF <40%.

Comorbidities were examined on the basis of medical information, including the patient's history, data for parameters in clinical examinations, and prescribed drugs. Cachexia was diagnosed by the criteria proposed by Fearon et al: a >5% loss of stable body weight over the past 6 months, a BMI <20 kg/m^2 and ongoing weight loss of >2% or sarcopenia and ongoing weight loss of >2%.[25] Comorbidities were assessed using the Charlson Comorbidity Index (CCI), as described previously.[24,26]

Clinical Endpoint

The clinical endpoint was all-cause death during the follow-up period from the day of discharge until August 31, 2020. Data for the clinical endpoint for enrolled patients were collected from medical records.

Sample Size Calculation

Sample size calculations were performed for this observational study using the Cox proportional hazards model, as reported previously.[27] The prevalence of HF patients with a BI score <85, 1-year mortality rate, and the hazard ratio (HR) for mortality in subjects with a BI score <85 were estimated according to the results of previous studies.[17,23] The required sample size was 283 patients.

Statistical Analysis

Data are presented as the mean±SD or as then median with interquartile range (IQR) depending on the results of the Shapiro-Wilk test for normality of data distribution. Baseline characteristics were compared using Welch's t-test, the Mann-Whitney U test, or the Chi-squared test as appropriate. The dose-dependent association of BI scores with mortality risk was examined using a Cox proportional hazard model with a restricted cubic spline function with 4 knots. Considering the results of an adjusted dose-dependent association analysis between BI score and mortality (**Figure 2**), a multivariate logistic regression model was fit to calculate the propensity scores (PS) for the BI score being <85 based on the following baseline variables: age, sex, BMI, New York Heart Association (NYHA) functional class III or IV, LVEF, prior HF hospitalization, etiology of HF, hypertension, dyslipidemia, diabetes, atrial fibrillation, peripheral artery disease, cancer, chronic lung disease, orthopedic disorder, prior stroke, cachexia, the log of the B-type natriuretic peptide (BNP) concentration, creatinine-based eGFR, hemoglobin, the use of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), β-blockers, a mineralocorticoid receptor antagonist (MRA), and loop diuretics, MNA-SF score, and length of hospital stay. The area under the receiver operating characteristic (ROC) curve to evaluate the discrimination capability of the PS model was 0.845 (95% confidential interval [CI] 0.804–0.879; **Supplementary Figure 1**). To minimize differences in potential confounding factors between patients with a low BI (<85) and those with a high BI (≥85), the IPTW was calculated using PS.[28] The group with a BI score <85 was weighted by 1/PS, and the group with BI score of ≥85 was weighted by 1/(1−PS). Covariates for the IPTW were selected on the basis of their associations with all-cause

Table 1. Baseline Characteristics

Variables	All (n=413)	Before IPTW			After IPTW		
		BI score <85 (n=170)	BI score ≥85 (n=243)	P value	BI score <85 (n=395)	BI score ≥85 (n=402)	P value
Age (years)	78±7	80±7	76±7	<0.001	78±11	78±9	0.397
Female sex	205 (50)	94 (55)	111 (46)	0.054	187 (47)	199 (50)	0.513
Height (cm)	156±9	155±8	158±9	0.006	156±12	157±12	0.189
Body weight (kg)	52.6±10.9	50.7±11.2	53.9±10.5	0.004	51.8±16.5	52.9±13.5	0.331
BMI (kg/m^2)	21.4±3.7	21.1±4.0	21.6±3.4	0.116	21.4±5.7	21.5±4.4	0.777
Heart rate (beats/min)	69±11	71±13	68±10	0.025	70±18	69±13	0.373
Systolic blood pressure (mmHg)	117±19	118±19	117±18	0.627	119±31	118±23	0.595
NYHA functional class III–IV	147 (36)	97 (57)	50 (21)	<0.001	151 (38)	137 (34)	0.220
LVEF (%)	48.3±16.1	49.6±16.2	47.3±16.0	0.149	49.8±25.9	49.1±20.5	0.661
LVEF <40%	136 (33)	51 (30)	85 (35)	0.289	134 (34)	126 (31)	0.435
Smoking history	170 (41)	65 (38)	105 (43)	0.312	162 (41)	161 (40)	0.775
Length of hospital stay (days)	24 [16–37]	27 [18–38]	23 [15–34]	0.007	26 [18–37]	24 [16–41]	0.935
BI score (points)	85 [75–90]	70 [60–80]	90 [85–95]	<0.001	75 [65–80]	90 [85–95]	<0.001
Prior HF hospitalization	193 (47)	94 (55)	99 (41)	0.004	193 (49)	181 (45)	0.272
Etiology				0.050			0.575
Valvular heart disease	145 (35)	65 (38)	80 (33)		159 (40)	144 (36)	
Cardiomyopathy	112 (27)	34 (20)	78 (32)		106 (27)	112 (28)	
Ischemic	79 (19)	34 (20)	45 (19)		65 (17)	69 (17)	
Comorbidity							
Hypertension	295 (71)	122 (72)	173 (71)	20.899	277 (70)	288 (72)	0.662
Dyslipidemia	225 (54)	88 (52)	137 (56)	0.354	211 (53)	215 (53)	0.971
Diabetes mellitus	180 (44)	84 (49)	96 (40)	0.046	157 (40)	162 (40)	0.857
Atrial fibrillation	179 (43)	70 (44)	95 (42)	0.671	155 (39)	161 (40)	0.790
Arterial disease	135 (33)	63 (37)	72 (30)	0.113	143 (36)	131 (33)	0.284
Chronic lung disease	95 (23)	45 (26)	50 (21)	0.161	98 (25)	93 (23)	0.598
Cancer	104 (25)	46 (27)	58 (24)	0.462	109 (28)	114 (28)	0.870
Orthopedic disorder	103 (25)	60 (35)	43 (18)	<0.001	104 (26)	91 (23)	0.232
Prior stroke	99 (24)	42 (25)	57 (23)	0.770	85 (22)	100 (25)	0.284
Cachexia	42 (10)	25 (15)	17 (7)	0.011	41 (10)	34 (8)	0.371
Charlson Comorbidity Index	5 [4–6]	5 [4–7]	5 [3–6]	<0.001	5 [4–7]	5 [3–7]	0.506
Laboratory data							
BNP (pg/mL)	250 [108–501]	314 [134–625]	216 [96–423]	0.001	208 [127–478]	260 [103–422]	0.935
Hemoglobin (g/dL)	11.6±1.7	11.1±1.6	11.9±1.7	<0.001	11.3±2.6	11.5±2.2	0.159
eGFRcre (mL/min/1.73 m^2)	48.5±18.9	47.0±20.2	49.5±18.0	0.207	47.0±20.2	49.5±18.0	0.207
Uric acid (mg/dL)	6.2±1.8	6.2±2.0	6.1±1.6	0.594	6.1±2.8	6.1±2.0	0.962
Medication							
β-blocker	293 (71)	114 (67)	179 (74)	0.146	266 (67)	275 (68)	0.750
ACEI or ARB	205 (50)	73 (43)	132 (54)	0.023	188 (48)	196 (49)	0.726
MRA	211 (51)	87 (51)	124 (51)	0.976	210 (53)	197 (49)	0.233
Loop diuretics	289 (70)	123 (72)	166 (68)	0.378	285 (72)	277 (69)	0.281
Statin	205 (50)	79 (46)	126 (52)	0.282	189 (48)	196 (49)	0.833
XO inhibitor	235 (30)	55 (32)	69 (28)	0.378	138 (35)	124 (31)	0.203
MNA-SF score (points)	8±3	7±3	8±2	<0.001	8±4	8±3	0.439

Data are presented as the mean±SD, median [interquartile range], or n (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BI, Barthel Index; BMI, body mass index; BNP, B-type natriuretic peptide; eGFRcre, creatinine-based estimated glomerular filtration rate; HF, heart failure; IPTW, inverse probability of treatment weighting; LVEF, left ventricular ejection fraction; MNA-SF, Mini Nutritional Assessment-Short Form; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; XO, xanthine oxidase.

mortality. Whether covariates were balanced by the IPTW was confirmed by comparing distributions of covariates before and after IPTW using the standardized mean difference (SMD). An SMD of >0.1 was defined as a meaningful difference.

ROC curves were drawn to calculate the area under the curve and the optimal cut-off value of the BI score to predict all-cause death. The optimal cut-off value was determined on the basis of the Youden Index. Survival curves were calculated by the Kaplan-Meier method, and the

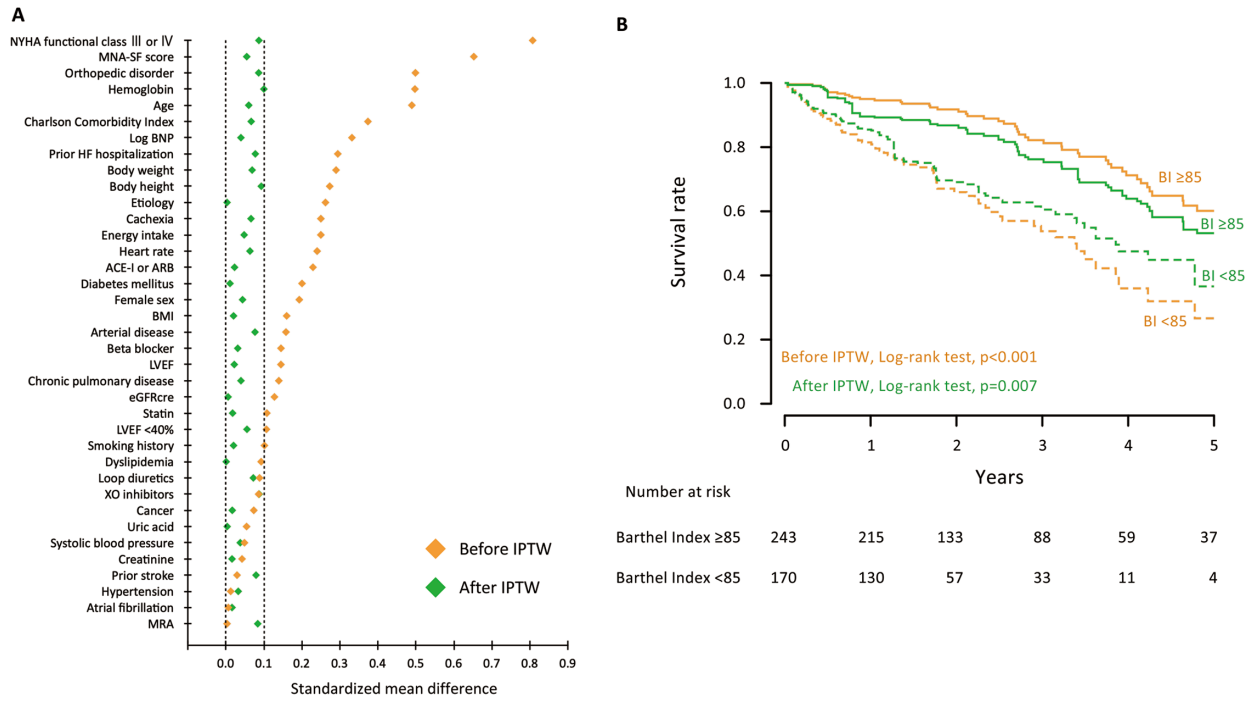

Figure 3. (**A**) Distribution of the standardized mean difference before and after inverse probability of treatment weighting (IPTW). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BI, Barthel Index; BMI, body mass index; BNP, B-type natriuretic peptide; eGFRcre, creatinine-based estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MNA-SF, Mini Nutritional Assessment-Short Form; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; XO, xanthine oxidase. (**B**) Kaplan-Meier survival curves showing the impact of the BI score on all-cause mortality in elderly HF patients before and after IPWT.

statistical significance of differences between curves was assessed using log-rank statistics. Univariate and multivariate Cox proportional hazards analyses were used to evaluate prognostic predictive ability.

Logistic models for all-cause death were constructed using Cox regression models after adjustment for different variables. Harrell's C-index was calculated and compared between the base model and the model with the addition of the BI score.[24] Furthermore, to examine the significance of the incremental discriminative value added by the BI score, the log-likelihood ratio (LLR), continuous net reclassification improvement (cNRI), and integrated discrimination improvement (IDI) were calculated.[24]

Two-tailed P<0.05 was considered statistically significant. Statistical analyses were performed using JMP Pro version 15.2.1 (SAS Institute, Cary, NC, USA) and R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Of 571 HF patients initially screened, 158 patients were excluded based on the exclusion criteria, and data for 413 patients were used for analyses, as shown in **Figure 1**.

Baseline Characteristics

As shown in **Table 1**, the mean age of the patients was 78±7 years and 50% were female. At the time of discharge, 36% of patients were in NYHA functional class III or IV. The mean LVEF was 48.3±16.1%, and 33% of patients had HFrEF; 47% of patients had a prior history of hospitalization for HF. The most frequent etiology of HF was valvular heart disease (35%), followed by cardiomyopathy (27%) and ischemic heart disease (19%).

Relationship Between BI Scores and All-Cause Mortality

During a median follow-up period of 1.90 years (IQR 1.20–3.23 years), 116 patients (28%) died (HF-related causes, n=48; infection, n=21; cancer, n=12). The spline dose-response curve for the BI score-all-cause mortality relationship with adjustment for age, sex, history of HF hospitalization, cachexia, log[BNP], eGFR, hemoglobin, CCI, and the use of ACEI or ARB and β-blockers was almost linear, with an increase in the HR of mortality as the BI score decreased (**Figure 2**). A BI score of 85 corresponded to HR of 1.0, which was similar to the cut-off value of the BI score for all-cause death calculated from the ROC curve (**Supplementary Figure 2**). Therefore, we divided HF patients into 2 groups using a BI score of 85 as the cut-off value.

Patients with a low BI score (<85) were older than those with high BI score (≥85; **Table 1**). Patients with a low BI score had higher heart rate and a higher prevalence of NYHA Class III–IV symptoms than in patients with a high BI score. The proportion of patients with orthopedic disorders and cachexia was higher and the proportion of patients using an ACEI or ARB was lower among those with a low than high BI score. Plasma BNP concentrations were higher and hemoglobin concentrations and MNA-SF scores were lower in patients with a low than high BI score.

Table 2. Impact of BI Score <85 on All-Cause Mortality in Elderly HF Patients

	BI score <85 (vs. ≥85)	
	HR (95% CI)	P value
Univariate model	3.26 (2.23, 4.76)	<0.001
Model 1	3.40 (2.31, 5.00)	<0.001
Model 2	3.11 (2.10, 4.60)	<0.001
Model 3	2.61 (1.74, 3.92)	<0.001
IPTW model	1.83 (1.09, 3.05)	0.021
Model 1	1.84 (1.10, 3.06)	0.019
Model 2	1.80 (1.07, 3.03)	0.027
Model 3	1.75 (1.03, 2.98)	0.039
IPTW model (truncating large weights [IPTW >10])	2.23 (1.39, 3.57)	<0.001
Model 1	2.24 (1.40, 3.60)	<0.001
Model 2	2.12 (1.30, 3.45)	0.002
Model 3	1.99 (1.20, 3.32)	0.008
Propensity score-adjusted model	1.82 (1.15, 2.87)	0.011
Model 1	1.79 (1.13, 2.82)	0.013
Model 2	1.74 (1.09, 2.78)	0.019
Model 3	1.81 (1.14, 2.87)	0.011

Model 1 was adjusted for age and sex, Model 2 was further adjusted for log[BNP], and Model 3 was adjusted for all factors in Model 2 plus prior HF hospitalization, cachexia, Charlson Comorbidity Index, eGFRcre, hemoglobin, and the use of ACEI or ARB and β-blockers . CI, confidence interval; HR, hazard ratio. Other abbreviations as in Table 1.

Table 3. Impact of BI Score on Prediction of All-Cause Mortality in HF Patients

	C-index (95% CI)	LLR improvement from base model	P value	cNRI (95% CI)	P value	IDI (95% CI)	P value
Model 1	0.670 (0.612, 0.724)	–	Ref.	–	Ref.	–	Ref.
+ BI score (continuous)	0.710 (0.653, 0.761)	−2.467	0.026	0.297 (0.088, 0.506)	0.007	0.040 (0.017, 0.063)	<0.001
+ BI score <60	0.680 (0.621, 0.733)	−0.393	0.375	0.146 (−0.004, 0.296)	0.183	0.013 (−0.0002, 0.026)	0.054
+ BI score <85	0.711 (0.654, 0.762)	−1.936	0.049	0.486 (0.276, 0.695)	<0.001	0.043 (0.022, 0.063)	<0.001
Model 2	0.742 (0.685, 0.792)	–	Ref.	–	Ref.	–	Ref.
+ BI score (continuous)	0.755 (0.699, 0.804)	−0.825	0.199	0.292 (0.081, 0.503)	0.008	0.017 (0.003, 0.032)	0.022
+ BI score <60	0.744 (0.687, 0.793)	−0.057	0.735	0.005 (−0.182, 0.193)	0.960	0.004 (−0.003, 0.011)	0.225
+ BI score <85	0.762 (0.706, 0.809)	−1.306	0.106	0.452 (0.242, 0.662)	<0.001	0.020 (0.005, 0.035)	0.010

Model 1 was adjusted for age, sex, and log[BNP]; Model 2 was further adjusted for prior HF hospitalization, cachexia, Charlson Comorbidity Index, eGFRcre, hemoglobin, ACEI or ARB use, and β-blocker use. cNRI, continuous net reclassification improvement; IDI, integrated discrimination improvement; LLR, log-likelihood ratio. Other abbreviations as in Tables 1,2.

After IPTW, the SMDs of all covariates were <0.1, indicating that baseline differences in the covariates incorporated, including nutritional status, were substantially improved (**Table 1**; **Figure 3A**; **Supplementary Figure 3**).

Impact of BI Score on All-Cause Mortality in HF Patients

Kaplan-Meier survival curves showed that patients with a low BI score had a lower survival rate than did patients with a high BI score (60% vs. 80%; P<0.001; **Figure 3B**). A similar result was obtained in the Kaplan-Meier survival curve analyses incorporating IPTW (65% vs. 74% for low vs. high BI scores, respectively; P=0.007, **Figure 3B**). There were no significant differences in modes of death after discharge between patients with a low and high BI score (**Supplementary Table 1**).

Multivariate Cox proportional hazard analyses showed that a low BI score was associated with increased all-cause mortality after adjustment in Models 1, 2, and 3 in both the crude HF patient group and in HF patients with IPTW (**Table 2**). Because the presence of an extremely large IPTW has a profound effect on the results of statistical analyses, multivariate Cox proportional hazard analyses were performed in which patients with an IPTW of >10 were truncated. The independent association of low BI with all-cause mortality remained in this analyses (**Table 2**). Furthermore, an independent association of a low BI score with all-cause mortality was preserved after adjusting for PS as a covariate (**Table 2**).

The impact of the BI score on all-cause mortality in the subgroups of interest was examined (**Supplementary Figure 4**). There were no significant differences in HRs for all-cause mortality among the subgroups including sex (**Supplementary Figure 4**). Although the results of post hoc analyses indicated differences in modes of death between patients with an LVEF of <40% and patients with an LVEF of ≥40% (the prevalence of death due to causes other than HF-related death was higher among patients with an LVEF of ≥40%; **Supplementary Table 2**), there were no significant differences in the HRs for all-cause mortality between these 2 groups (**Supplementary Figure 4**).

Impact of BI Score on the Prediction of All-Cause Mortality in HF Patients

The addition of BI score <85 to each baseline model significantly improved both cNRI and IDI (**Table 3**). Such improvements in cNRI and IDI were not found after the addition of BI score <60, a score indicating severe functional dependence,[16] to each baseline model (**Table 3**).

Discussion

In the present study, there was an almost linear relationship between BI scores at the time of discharge and mortality rates after discharge in an adjusted dose-dependent association analysis in elderly HF patients who received comprehensive CR during hospitalization. This finding is consistent with the result of a recent study by Ryg et al in 74,859 people aged ≥65 years who were registered in a nationwide population-based cohort study.[29] A BI score <85, a higher value than reported previously, was an independent predictor of all-cause mortality after discharge in elderly HF patients after adjusting for known prognostic markers. The addition of BI score <85, but not BI score <60, to established predictors of the prognosis of HF improves the risk stratification of elderly HF patients. Thus, assessment of the BI score is important in risk stratification for mortality and in planning comprehensive CR for elderly HF patients.

Although the prediction of mortality in HF patients is crucial for decision making regarding HF therapies, it is difficult in elderly patients. Elderly HF patients have a higher prevalence of HF with preserved ejection fraction (HFpEF) and atrial fibrillation than younger HF patients.[3,13,30] Noncardiac comorbidities, such as CKD, anemia, sarcopenia, and cognitive impairment, are also more frequent in elderly than younger HF patients.[3,13,30] These distinct characteristics of elderly HF patients are likely to have effects on the accuracy of prognosis prediction. Importantly, the risk prediction models for prognosis of HF were derived from a dataset that included many HF patients aged <70 years and many patients with HFrEF, contributing to a limited predictive accuracy of life expectancy of elderly HF patients by the risk prediction models.[3,6,7,13,30] Furthermore, the results of an earlier study showed that the utility of the established prognostic markers, such as NYHA functional class, history of HF hospitalization, and systolic blood pressure, was lost in elderly patients.[8]

A risk prediction equation for elderly HF patients using variables associated with all-cause mortality or cardiovascular hospitalization was reported by Manzano et al.[8] The application of the equation, which requires biochemical and echocardiographic data, to 926 patients registered in a prospective multicenter observational registry of elderly patients admitted for acute decompensated HF yielded modest accuracy for predicting all-cause mortality.[31] Considering the peculiarity of elderly HF, Pilotto et al examined whether short-term mortality in elderly HF patients can be predicted using a multidimensional prognostic index based on a standardized comprehensive geriatric assessment including comorbidities, medications, and social network status in addition to physical, nutritional, and cognitive status.[9] The results of Pilotto et al indicated that the multidimensional prognostic index is more useful for estimating the risk of 1-month mortality in elderly HF patients than models based on clinical variables that are associated with poor clinical outcomes in cohorts of elderly HF patients (i.e., the Enhanced Feedback for Effective Cardiac Treatment [EFFECT] and the Acute Decompensated Heart Failure National Registry [ADHERE] models).[9–11] Thus, a multidimensional prognostic model appears to be the best tool for predicting clinical outcomes in elderly HF patients. However, it is a time-consuming tool that is not suitable for use in a daily clinical setting. Conversely, the BI is an easy-to-use, inexpensive, repeatable, and semi-quantitative tool for assessing basic ADL and monitoring changes in functional status over time.[14–16] In addition, the BI was shown to have high inter-rater reliability and test-retest reliability.[31] The findings of earlier studies[14–16,32] and the predictive values of the BI score shown in the present study (**Table 3**) support the notion that assessing the BI at the time of discharge is useful for identifying high-risk patients and for decision making regarding further treatment strategies in elderly HF patients.

In the present study, the mechanism of the close association between a decline in ADL and increased mortality was not analyzed. A reduction in ADL has been shown to be associated with a higher risk of HF rehospitalization.[33,34] A plausible explanation for the close association between a decline in ADL and increased mortality is that repeated rehospitalization events because of reduced ADL contribute to further declines in cardiac and physical function, leading to death (i.e., a trajectory of illness for HF).[35] Importantly, changes in body composition, such as muscle/fat mass, novel prognostic markers in HF, and changes in physical function, such as exercise tolerance and muscle strength, were not analyzed in the present study,[36–40] although low BI was an independent predictor of mortality even after adjustment for cachexia (**Table 2**). Furthermore, although the number of comorbidities, including dementia (i.e., CCI), was similar in the 2 groups after IPTW (**Table 1**; **Figure 3A**), the severity of each comorbidity, such as cognitive impairment and respiratory diseases, was not analyzed in the present study. Therefore, further analyses are needed to demonstrate the complex relationship between the decline in basic ADL and increased mortality in elderly HF patients.

Multidimensional impairment is a hallmark of elderly HF, leading to reduced basic ADL. Basic ADL is improved by comprehensive CR even in elderly HF patients with malnutrition.[23] Furthermore, comprehensive CR during the hospital stay administered by a heart failure team was shown to be associated with a lower risk of all-cause mortality and HF hospitalization even when the execution of comprehensive CR was limited during the hospital stay.[21] Favorable effects of CR on all-cause mortality and HF hospitalization are not limited to an inpatient setting: the results of a multicenter retrospective cohort study by Kamiya et al showed that participation in multidisciplinary outpa-

tient CR is associated with long-term survival and a lower rehospitalization rate in HF patients regardless of age.[20] Notably, a favorable effect of comprehensive CR was found in patients with HFpEF and frailty, characteristics of elderly HF.[20] Thus, achieving functional status with a BI score >85 before discharge by comprehensive CR may improve not only quality of life, but also survival rate. However, this possibility needs to be examined by prospective studies in the future.

The present study has some limitations. First, there may have been selection bias in the study subjects even after IPTW. Although there were no obvious differences in mortality rates compared with HF patients in earlier studies,[17,19] the results of the present study should be confirmed in prospective large cohort studies. Second, differences in the effects of BI score on mortality between HF patients with different etiologies (e.g., HFrEF vs. HFpEF) were not analyzed because of insufficient statistical power, although there were no differences in the impact of BI score for the prediction of all-cause mortality between patients with an LVEF of ≥40% and those with an LVEF of <40%. Third, the length of hospital stay in the present study was longer than in previous studies (**Table 1**).[41–43] Thus, the results of the present study should be confirmed in studies including patients with different severities of HF. Fourth, a major limitation is the lack of incorporation of changes in treatments, such as medication and device implantation, into the mortality analysis. Fifth, the reliability of BI for assessing functional status has been demonstrated, but uncertainties remain concerning its reliability in patients with cognitive impairment,[32] which would be the case in patients with delirium and depression. Finally, changes in body composition, such as muscle/fat mass, novel prognostic markers in elderly HF, were not analyzed in the present study,[36–38] although low BI was an independent predictor of mortality even after adjustment for cachexia.

Conclusions

The BI score at the time of discharge is an independent predictor of mortality, and achieving a functional status with a BI score ≥85 by comprehensive CR during hospitalization may contribute to a favorable clinical outcome in elderly HF patients.

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Disclosures

The authors have no conflicts of interest to disclose.

IRB Information

This study was approved by the Clinical Investigation Ethics Committee of Sapporo Medical University Hospital (No. 302-243).

Data Availability

The deidentified data of participants will not be shared.

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Supplementary Files

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