Both High and Low Body Mass Indexes are Prognostic Risks in Japanese Patients With Chronic Heart Failure: Implications From the CHART Study

KOTARO NOCHIOKA, MD,[1] NOBUYUKI SHIBA, MD, PhD,[1,2] HARUKA KOHNO, RN,[2] MASANOBU MIURA, MD,[1] AND HIROAKI SHIMOKAWA, MD, PhD[1,2]

Sendai, Japan

ABSTRACT

Background: Prognostic impact of body mass index (BMI) in Japanese patients with chronic heart failure (HF) remains unclear.

Methods and Results: We examined the relationship between BMI and the prognosis of Japanese HF patients in the Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART) study. The study sample was 972 Japanese chronic HF patients (mean age, 68.2 ± 13.5; male 65.2%). We categorized them into 5 groups; BMI <18.5, 18.5 to 22.9, 23.0 to 24.9 (reference), 25.0 to 29.9, and ≥30.0. Using a Cox hazards model, the relationships between BMI and deaths or admission for worsening HF were studied in detail. Mean follow-up period was 3.4 ± 1.7 years. Multivariate analysis showed that, as compared with reference group (BMI 23.0 to 24.9), hazard ratios (HR) for all-cause death showed a U-shaped association with 1.70 (95% confidence interval; 1.04−2.76), 1.23 (0.85−1.78), 1.26 (0.84−1.90), and 2.75 (1.51−5.00) among those with BMI<18.5, 18.5 to 22.9, 25.0 to 29.9, and ≥30.0, respectively. There were significant and suggestive U-shaped associations between BMI and cardiac-cause death or admission for worsening HF.

Conclusions: Both high and low BMIs were associated with increased outcomes, suggesting that extreme obesity is not beneficial in improving the prognosis of Japanese chronic HF patients. (*J Cardiac Fail 2010;16:880−887*)

The prognosis of patients with chronic heart failure (HF) is still poor despite recent development in the treatment of HF.[1] Therefore, management of risk factors is one of the first-line strategies to improve the prognosis and quality of life in chronic HF patients. In patients with chronic HF, body mass index (BMI; kg/m^2) has been used for evaluation and management of the disorder, and low BMI was consistently associated with the increased death.[2,3] Furthermore, increased BMI has been recognized as an important risk factor for the development of HF in general.[4−7] However, in established HF patients, the relationship between higher BMI and the risk of death or morbidity is unclear.[3,8−17] Previous studies suggested that patients with high BMI had lower rate of death,[8−14] as is the case with patients with end-stage renal disease,[18] malignant tumors,[19] and elderly individuals.[20] In contrast, other studies showed that there is no,[15] or no significant[3,16,17] relationships between higher BMI and the risk of death in patients with HF.

Although the prognostic effect of higher BMI in HF patients remains unclear, the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines for management of HF recommend that HF patients with obesity should reduce their weight to improve the prognosis.[21,22]

Therefore, in the present study, we examined the association of BMI and the prognosis of Japanese chronic HF patients to clarify the prognostic significance of BMI and to identify the optimal BMI level in our chronic HF patient cohort, named the Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART).[23]

From the [1]Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan and [2]Department of Evidence-based Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan.

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Reprint requests: Nobuyuki Shiba, MD, PhD, Department of Evidence-based Cardiovascular Medicine and Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aobaku, Sendai 980-8574, Japan. Tel: +81-22-717-7153; Fax: +81-22-717-7156. E-mail: nshiba@cardio.med.tohoku.ac.jp

See page 886 for disclosure information.

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Methods

The CHART Study and the Study Sample

The study design and the major results of our CHART study have been reported previously.[23–25] Briefly, the CHART Study was a multicenter, prospective cohort study conducted between February 2000 and December 2005 that evaluated the clinical characteristics and prognoses in Japanese patients with chronic HF. A total of 1278 patients with stable chronic HF were enrolled who met at least 1 of the following 3 predefined inclusion criteria; (1) left ventricular ejection fraction (LVEF) <50%, (2) left ventricular end-diastolic diameter ≥55 mm, or (3) at least one episode of congestive HF.[23] The diagnosis of HF was based on the criteria of the Framingham study.[26] All information, including medical history, height, weight, laboratory data, and echocardiography data, were compiled into a computer database at the time of enrollment and we then performed a follow-up survey every year. The follow-up period was 3.4 ± 1.7 years. The outcomes of the present study were all-cause death, cardiac-cause death, and admission for worsening HF. Cardiac-cause death was defined as deaths from cardiovascular disease including HF and sudden death. Admission for worsening HF was defined as unexpected admission for treatment of HF. The mode of death and the events of admission for worsening HF were determined by the physicians in attendance. Of the 1278 patients enrolled in our CHART study, 177 patients (13.8%) without a clear history of HF and 129 patients (10.1%) who did not have BMI records were excluded. Therefore, the present study sample was 972 chronic HF patients with sufficient data.

Data and Statistical Analysis

All continuous variables are shown as mean ± standard deviation. BMI was calculated as body weight in kilograms divided by the square of the height in meters (kg/m^2). Estimated glomerular filtration rate was calculated using the simplified modification of diet in renal diseases formula.[27] Chronic kidney disease (CKD) was defined as baseline estimated glomerular filtration rate <60 mL/min/1.73 m^2.[28] Anemia was defined as hemoglobin <12 g/dL in females and <13 g/dL in males, based on the World Health Organization (WHO) definition.[29]

To evaluate the risk of outcomes, we categorized the study sample into 5 groups with different BMI based on the WHO definitions: <18.5, 18.5 to 22.9, 23.0 to 24.9 (reference), 25.0 to 29.9, and ≥30.0.[30] BMI was used as a categorical variable for statistical analyses in the present study. Comparisons of data among the 5 groups were performed by analysis of variance test in continuous variables and by chi-square test in dichotomous variables. Kaplan-Meier curves were plotted to evaluate the association between BMI and outcomes. We also constructed the following 4 Cox proportional hazard regression models: (a) unadjusted, (b) age- and sex- adjusted, (c) age-, sex-, and selected covariates-adjusted, and (d) fully adjusted. In the model (c), we included the following covariates; age, sex, New York Heart Association (NYHA) class, ischemic etiology, history of admission for HF, LVEF, and anemia. In the fully adjusted model (d), in addition to the covariates used in the model (c), we adjusted for treatment (β-blocker, angiotensin-converting enzyme inhibitor, and angiotensin II receptor blocker), hypertension,[31] hyperlipidemia,[32] diabetes mellitus,[33] left ventricular hypertrophy, [34] atrial fibrillation (AF),[35] and CKD[36] that were considered to be in the causal pathway between BMI and outcomes. Continuously, we examined the relationship between BMI and all-cause death stratified by LVEF ≥50% or <50%. We conducted all analyses using IBM SPSS Statistics 18.0. A 2-sided P value of <.05 was considered to be statistically significant.

Results

Baseline Characteristics

Mean age was 68.2 ± 13.5 years and male patients accounted for 65.2% in the study sample (n = 972). Figure 1 shows the distribution of BMI in the present study sample by sex. The mean BMI (median) of the present study was 23.0 ± 3.7 (22.8) kg/m^2 and 87.1% of the study sample had their BMIs between 18.5 and 29.9. The BMI < 18.5 group accounted for 9.1% (n = 88) and the percentage of the BMI ≥30.0 group accounted for 3.8% (n = 37) of the study sample. Table 1 shows the baseline characteristics of the patients. As compared with the BMI 23.0 to 24.9 group (reference), the BMI <18.5 group was characterized by older age (73.0 ± 12.8 years), higher percentage of females (58.0%) and of ischemic etiology (33.0%), more severe symptoms (NYHA III or IV, 36.4%), and lower hemoglobin level. In contrast, the BMI ≥ 30.0 group was characterized by younger age (60.8 ± 17.2 years) and higher prevalence of hypertension (75.7%) and of preserved LVEF (LVEF ≥50%, 59.5%). The prevalence of other important cardiovascular risks, such as hyperlipidemia and diabetes mellitus, tended to be higher in patients with higher BMI. In contrast, there were no significant differences in prevalence of AF and CKD among the 5 groups.

BMI and the Death in Patients With Chronic HF

During the mean follow-up of 3.4 ± 1.7 years, 285 patients (29.3%, 184 males and 101 females) died. Figure 2 shows Kaplan-Meier curves describing the relationships between BMI and outcomes. The BMI ≥ 30.0 group and the BMI <18.5 group showed the higher event rates for all-cause death and cardiac-cause death compared with the BMI 23.0 to 24.9 group (reference) with the lowest event rates (log-rank P < .001).

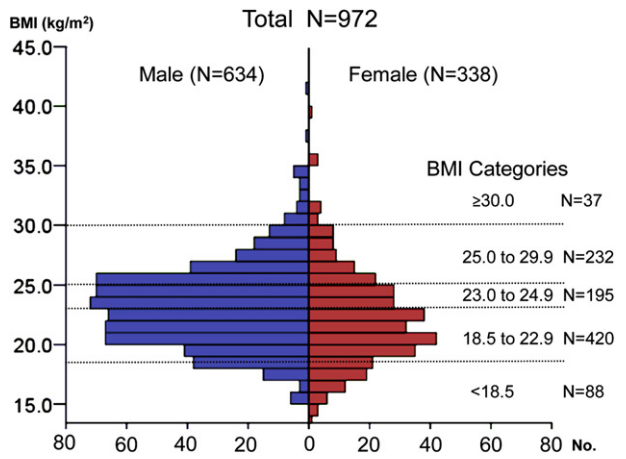

Fig. 1. The distribution of body mass index (BMI) in the study sample stratified by sex.

Table 1. Baseline Characteristics of 972 HF Patients Stratified by BMI Categories

	BMI Categories					
	<18.5 n = 88	18.5 to 22.9 n = 420	23.0 to 24.9 n = 195	25.0 to 29.9 n = 232	≥30.0 n = 37	*P* Value
BMI (kg/m^2)						
Mean (SD)	17.1 (1.2)	20.9 (1.3)	23.9 (0.6)	26.6 (1.3)	32.8 (2.8)	
Median (IQR)	17.4 (1.0)	20.9 (0.9)	23.9 (0.6)	26.2 (0.6)	31.9 (1.3)	
Age (y)	73.0 ± 12.8	69.8 ± 13.1	67.4 ± 12.3	65.6 ± 13.7	60.8 ± 17.2	<.001
Male (%)	42.0	63.1	70.3	73.3	67.6	<.001
Follow-up (y)	2.99 ± 1.74	3.36 ± 1.75	3.75 ± 1.65	3.59 ± 1.77	2.87 ± 1.63	.001
NYHA III or IV (%)	36.4	23.1	12.3	15.1	16.2	<.001
Hypertension (%)	45.5	42.4	48.7	56.0	75.7	<.001
Hyperlipidemia (%)	10.2	14.3	19.0	17.2	24.3	.16
Diabetes mellitus (%)	14.8	17.6	22.1	25.0	27.0	.09
History of admission for HF (%)	29.5	23.8	34.9	29.5	32.4	.02
Atrial fibrillation (%)	37.5	39.8	48.7	42.7	32.4	.16
Etiology						.052
Ischemic (%)	33.0	26.4	23.1	30.6	24.3	
Valvular (%)	26.1	26.0	22.6	13.4	10.8	
LVH (%)	38.6	40.0	39.5	44.8	45.9	.68
Measurement						
LVDD (mm)	55.1 ± 9.1	56.0 ± 9.9	55.6 ± 9.6	56.2 ± 10.1	58.9 ± 11.5	.39
LVDD >55 mm (%)	50.0	51.9	51.0	53.0	62.2	.77
LVEF (%)	49.6 ± 15.7	51.2 ± 16.7	52.1 ± 14.4	52.7 ± 16.0	51.5 ± 17.1	.56
LVEF ≥50% (%)	46.6	47.8	55.7	59.1	59.5	.03
Hemoglobin (g/dL)	11.7 ± 1.9	12.6 ± 2.1	13.5 ± 2.0	13.5 ± 2.1	13.8 ± 2.4	<.001
Anemia or not (%)	65.9	48.2	27.7	29.4	35.1	<.001
Creatinine (mg/dL)	1.1 ± 0.9	1.2 ± 1.3	1.0 ± 0.5	1.0 ± 0.5	0.9 ± 0.3	.03
CKD or not (%)	23.9	27.7	18.5	23.6	21.6	.17
Medical therapy						
ACE-I or ARB (%)	69.3	66.7	76.4	76.3	73.0	.04
β-blocker (%)	34.1	30.0	28.2	28.0	40.5	.49
Loop diuretic (%)	77.8	78.3	68.5	72.9	84.4	.07
Spironolactone (%)	22.2	20.2	21.2	24.8	31.3	.50
Ca blocker (%)	27.1	26.3	35.4	35.4	27.0	.07
Digitalis (%)	50.6	48.9	50.8	42.6	29.7	.08

HF, heart failure; IQR, interquartile range; NYHA, New York Heart Association; LVH, left ventricular hypertrophy; LVDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; CKD, chronic kidney disease; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker. Results are expressed as mean ± standard deviation (SD).

Table 2 shows results of the Cox proportional hazard models for the development of all-cause death and cardiac-cause death. In the unadjusted model (a), as compared with the BMI 23.0 to 24.9 group (reference), the BMI<18.5 group, the BMI 18.5 to 22.9 group, the BMI 25.0 to 29.9 group, and the BMI ≥ 30.0 group showed 147%, 70%, 37%, and 170% increase in the risk for all-cause death, respectively (each *P* value; <.001, <.001, .12, and .001).

In the fully adjusted model (d), as compared with the BMI 23.0 to 24.9 group (reference), the hazard ratios (HR) for all-cause death of the BMI<18.5 group, BMI 18.5 to 22.9 group, BMI 25 to 29.9 group, and the BMI ≥30.0 group were 1.70 (95%CI; 1.04−2.76), 1.23 (0.85−1.78), 1.26 (0.84−1.90), and 2.75 (1.51−5.00), respectively. In the model (d), as compared with the model (c), HR for all-cause death in the BMI <18.5 group was influenced by including the following covariates: hypertension, hyperlipidemia, diabetes mellitus, left ventricular hypertrophy, AF, CKD, and treatment, but the HR for all-cause death in the BMI ≥30.0 group remained robust (Table 2).

We also constructed the Cox models between BMI and all-cause death stratified by LVEF ≥ 50% or <50% (Table 3). In the fully adjusted model (d), a 91% increase in the risk of all-cause death among the BMI <18.5 group with LVEF ≥50% was observed; however, it did not reach statistical significance (Table 3). Otherwise, the BMI ≥ 30.0 group with LVEF ≥ 50% showed significant 187% increase in the risk of all-cause death. Similar trend was also observed in patients with LVEF <50% as shown in the Table 3.

Of 285 deaths, 221 deaths (77.5%) were due to cardiac cause. The HRs (95%CI) for cardiac-cause death in the fully adjusted model (d) were 1.78 (1.02−3.09) and 2.99 (1.56−5.76) in the BMI <18.5 group and the BMI ≥ 30.0 group, as compared with the BMI 23.0 to 24.9 group (reference) (Table 2). Results also showed a U-shaped association between HRs and BMI with the lowest HR in the BMI 23.0 to 24.9 group not only in all-cause death, but also in cardiac-cause death.

BMI and the Risk of Admission for Worsening HF in Patients With Chronic HF

Admission for worsening HF was noted in 309 patients (31.8%) during the study period. Kaplan-Meier curves for admission for worsening HF was plotted in Fig. 2. Patients in the BMI 23.0 to 24.9 group (reference) had the lowest events rate for admission for worsening HF (Fig. 2).

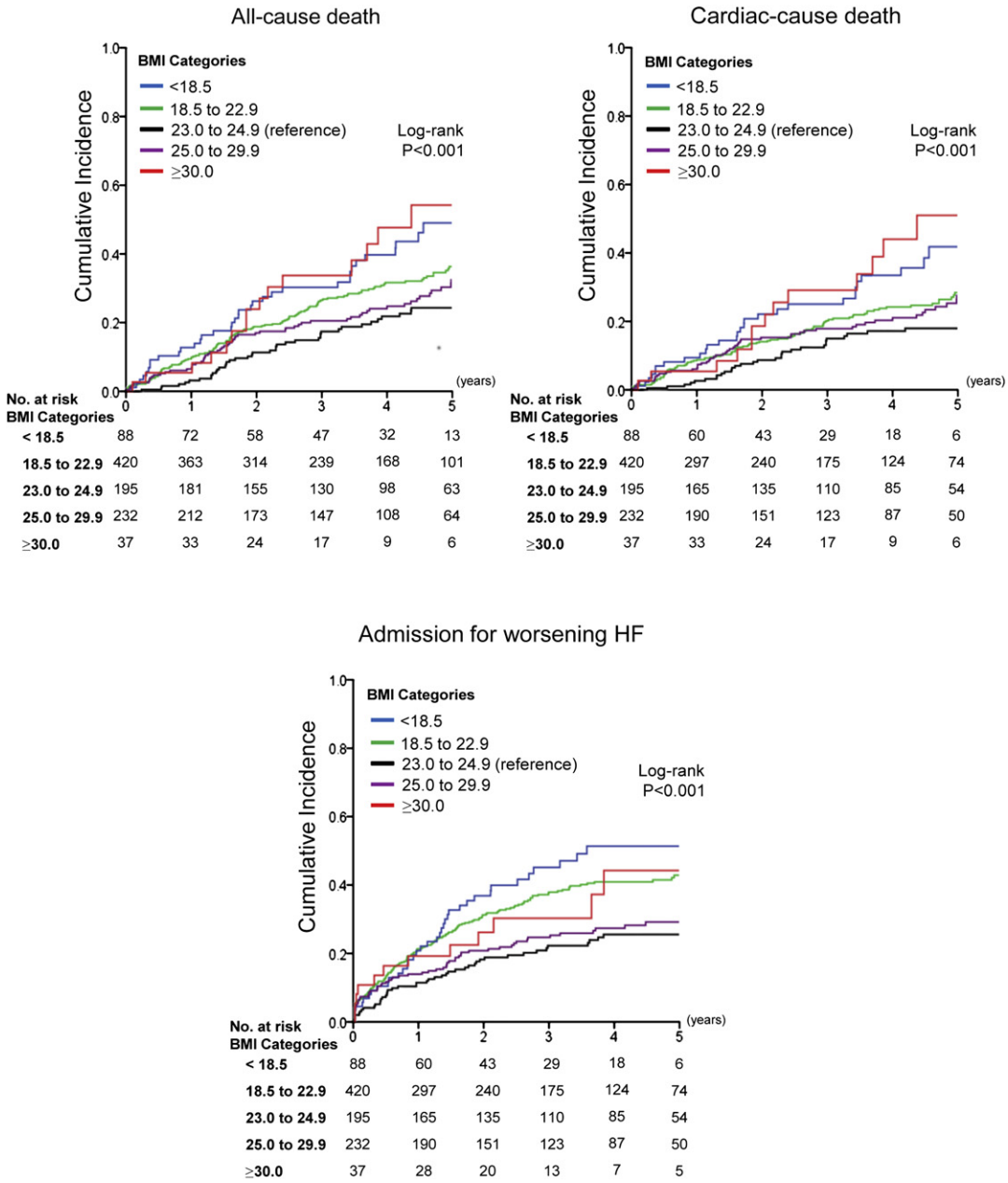

Fig. 2. Kaplan-Meier curves categorized by body mass index (BMI) levels in Japanese patients with chronic heart failure (HF), for all-cause death, cardiac-cause death, and admission for worsening HF.

Results of Cox regression models between BMI and the risk for admission for worsening HF were shown in Table 2. In the unadjusted model (a), as compared with the BMI 23.0 to 24.9 group (reference), the BMI < 18.5 group, the BMI 18.5 to 22.9 group, the BMI 25.0 to 29.9 group, and the BMI ≥ 30.0 group showed 142%, 91%, 19%, and 89% increase in the risk of admission for worsening HF, respectively (each *P* value; < .001, < .001, .38, and .04). This trend was also observed in the age- and sex- adjusted model (b). In the fully adjusted model (d), HRs (95% CI) were 1.44 (0.90−2.29), 1.44 (1.02−2.04), 1.15 (0.77−1.72), and 2.02 (1.07−3.82), suggesting that there was a U-shaped association between BMI and admission for worsening HF.

Discussion

We have shown that Japanese chronic HF patients with BMI 23.0 to 24.9 had the lowest all-cause death, cardiac-cause death, and admission for worsening HF. Both patients with lower or higher BMI had heightened risk of adverse outcomes and the association between BMI and the HRs for outcomes showed a U-shaped profile.

Low BMI and Prognosis of Japanese HF Patients

We showed that lower BMI was associated with increased risk for all-cause death, cardiac-cause death, and admission

Table 2. Cox Proportional Hazard Models for All-cause Death, Cardiac-cause Death, and Admission for Worsening HF

	No. of Events (%)	No. of Events/ 100 Person-year	(a) Unadjusted			(b) Age- and Sex-adjusted			(c) Age-, Sex-, and Covariates-adjusted			(d) Fully Adjusted		
			HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
All-cause death														
BMI categories														
<18.5	36 (40.9)	13.7	2.47	1.57 − 3.88	<.001	1.94	1.22 − 3.08	.005	1.36	0.86 − 2.16	.19	1.70	1.04 − 2.76	.03
18.5 to 22.9	131 (31.2)	9.3	1.70	1.19 − 2.42	<.001	1.53	1.07 − 2.18	.02	1.18	0.84 − 1.67	.34	1.23	0.85 − 1.78	.27
23.0 to 24.9 (reference)	40 (20.5)	5.5	1.00			1.00			1.00			1.00		
25.0 to 29.9	62 (26.7)	7.4	1.37	0.92 − 2.04	.12	1.41	0.94 − 2.09	.94	1.22	0.83 − 1.79	.32	1.26	0.84 − 1.90	.26
≥30.0	16 (43.2)	15.1	2.70	1.51 − 4.83	.001	3.12	1.74 − 5.60	< .001	2.42	1.36 − 4.31	.003	2.75	1.51 − 5.00	.001
Cardiac-cause death														
BMI categories														
<18.5	29 (33.0)	11.0	2.63	1.58 − 4.39	<.001	2.09	1.24 − 3.53	.006	1.35	0.80 − 2.28	.25	1.78	1.02 − 3.09	.04
18.5 to 22.9	97 (23.1)	6.9	1.67	1.11 − 2.52	.01	1.52	1.01 − 2.29	.05	1.13	0.76 − 1.68	.55	1.17	0.76 − 1.80	.47
23.0 to 24.9 (reference)	30 (15.4)	4.1	1.00			1.00			1.00			1.00		
25.0 to 29.9	51 (22.0)	6.1	1.58	0.96 − 2.36	.08	1.54	0.98 − 2.42	.06	1.29	0.84 − 2.00	.25	1.38	0.87 − 2.19	.17
≥30.0	14 (37.8)	13.2	3.12	1.65 − 5.88	<.001	3.42	1.80 − 6.49	<.001	2.60	1.39 − 4.87	.003	2.99	1.56 − 5.76	.001
Admission for worsening HF														
BMI categories														
<18.5	38 (43.2)	14.5	2.42	1.57 − 3.74	<.001	1.99	1.28 − 3.10	.002	1.20	0.77 − 1.86	.42	1.44	0.90 − 2.29	.13
18.5 to 22.9	155 (36.9)	10.7	1.91	1.37 − 2.67	<.001	1.82	1.30 − 2.54	.001	1.31	0.95 − 1.79	.10	1.44	1.02 − 2.04	.04
23.0 to 24.9 (reference)	44 (22.6)	6.1	1.00			1.00			1.00			1.00		
25.0 to 29.9	59 (25.4)	7.0	1.19	0.81 − 1.76	.38	1.23	0.83 − 1.82	.29	1.01	0.70 − 1.86	.95	1.15	0.77 − 1.72	.49
≥30.0	13 (35.1)	12.3	1.89	1.02 − 3.51	.04	2.09	1.12 − 3.90	.02	1.58	0.86 − 2.92	.14	2.02	1.07 − 3.82	.03

BMI, body mass index; HF, heart failure; HR, hazard ratio; CI, confidence interval. In the model (c), we adjusted the model by age, sex, New York Heart Association class, ischemic etiology, history of admission for HF, left ventricular ejection fraction, and anemia. In the fully adjusted model (d), in addition to the covariates used in the model (c), we adjusted for the following covariates; treatment (β-blocker, angiotensin-converting enzyme inhibitor, and angiotensin II receptor blocker), hypertension, hyperlipidemia, diabetes mellitus, left ventricular hypertrophy, atrial fibrillation, and chronic kidney disease.

Table 3. Cox Proportional Hazard Models Stratified by LVEF for All-cause Death

	No. of Events (%)	No. of Events/100 Person-year	(a) Unadjusted			(b) Age-and Sex- adjusted			(c) Age-, Sex-, and Covariates-adjusted			(d) Fully Adjusted		
			HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Patients with LVEF ≥50%														
BMI categories														
<18.5	21 (51.2)	16.9	3.20	1.75 − 5.86	.01	2.38	1.26 − 4.47	.01	1.59	0.83 − 3.06	.16	1.91	0.98 − 3.70	.06
18.5 to 22.9	69 (34.7)	9.9	1.88	1.15 − 3.07	.01	1.63	0.99 − 2.66	.052	1.21	0.74 − 1.97	.44	1.29	0.77 − 2.15	.34
23.0 to 24.9 (reference)	21 (19.4)	5.3	1.00			1.00			1.00			1.00		
25.0 to 29.9	28 (20.6)	5.4	1.03	0.59 − 1.82	.92	1.06	0.60 − 1.87	.83	1.02	0.59 − 1.76	.95	1.13	0.64 − 1.99	.68
≥30.0	10 (45.5)	14.2	2.70	1.27 − 5.73	.01	3.45	1.60 − 7.43	.002	2.94	1.38 − 6.28	.005	2.87	1.31 − 6.29	.01
Patients with LVEF <50%														
BMI categories														
<18.5	15 (31.9)	10.8	1.81	0.92 − 3.57	.09	1.52	0.76 − 3.05	.24	1.08	0.54 − 2.14	.83	1.49	0.71 − 3.13	.29
18.5 to 22.9	59 (27.2)	8.3	1.44	0.86 − 2.41	.17	1.36	0.81 − 2.26	.25	1.04	0.62 − 1.72	.89	1.17	0.68 − 2.04	.57
23.0 to 24.9 (reference)	19 (22.1)	5.8	1.00			1.00			1.00			1.00		
25.0 to 29.9	32 (34.0)	10.2	1.77	1.00 − 3.12	.05	1.87	1.06 − 3.32	.03	1.40	0.80 − 2.45	.25	1.67	0.91 − 3.05	.10
≥30.0	6 (40.0)	16.7	2.73	1.09 − 3.57	.03	3.16	1.24 − 8.02	.02	1.80	0.71 − 4.56	.21	3.00	1.15 − 7.85	.03

BMI, body mass index; LVEF, left ventricular ejection fraction; HR, hazard ratio; CI, confidence interval. In the model (c), we adjusted the model by age, sex, New York Heart Association class, ischemic etiology, history of admission for HF, and anemia. In the fully adjusted model (d), in addition to the covariates used in the model (c), we adjusted for the following covariates; treatment (β-blocker, angiotensin-converting enzyme inhibitor, and angiotensin II receptor blocker), hypertension, hyperlipidemia, diabetes mellitus, left ventricular hypertrophy, atrial fibrillation, and chronic kidney disease.

for worsening HF in Japanese chronic HF patients. Results were consistent with previous studies using Western HF patients.[2,3]

The recent report from the CHARM Study showed that patients with lower BMI had a graded increase in risk of all-cause death as compared with patients with BMI between 30.0 and 34.9, who had the lowest HR for death.[3] Underweight, which is frequently observed in HF patients, has been considered to be associated with malnutrition and wasting that are related to chronically increased inflammatory status.[37] In patients with advanced HF, the release of pro-inflammatory cytokines is increased, leading to the development of protein-energy malnutrition that might be the major mechanism of this reverse relationship between lower BMI and poor prognosis in chronic HF patients.[2,3,37]

High BMI and Prognosis of Japanese HF Patients

In the present study, we showed that higher BMI was associated with the increased risk for all-cause death, cardiac-cause death, and admission for worsening HF, suggesting that extreme obesity was associated with poor prognosis in Japanese patients with chronic HF. Elevated BMI is associated with hemodynamic overload, increased metabolic demand, and increased peripheral resistance, all of which could cause LV remodeling.[12,38] And it was also reported that high BMI was associated with enhanced neurohumoral activation and increased oxidative stress.[39]

Several previous studies have shown inconsistent results with the present study. Oreopoulos et al reported in their meta-analysis of 9 observational studies that both overweight patients (BMI 25.0 to 29.9) and obese patients (BMI ≥30.0) were associated with lower all-cause death, concluding that such obese status might be protective.[14] However, Alla et al observed no significant association between high BMI and the mortality of chronic HF patients,[15] and Kenchaiah et al showed that in the CHARM Study, compared with HF patients with BMI between 30.0 and 34.9, patients with BMI ≥35 had a 17% increased risk of death, but did not reach statistical significance probably because of the small sample size, overadjustment for covariates, or both.[3]

Our result supports the recommendation of the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines for management of HF, which advise for HF patients with obesity to reduce their weight for better prognosis.[21,22]

Optimal BMI Level to Improve Prognosis of Japanese HF Patients

We demonstrated that the association between BMI and all-cause death or cardiac-cause death showed a U-shaped profile with the lowest event rate at between 23.0 and 24.9 in Japanese chronic HF patients. The shape of the association between BMI and admission for worsening HF also suggested a U-shaped profile. We were unable to evaluate the association between BMI and noncardiac death because of the small number of events (event number; 7 in the BMI <18.5 group, 34 in the BMI 18.5 to 22.9 group, 10 in the BMI 23.0 to 24.9

group, 11 in the BMI 25.0 to 29.9 group, and 2 in the BMI ≥30.0 group).

In the present study, optimal BMI level was shifted to the lower levels than previous studies in Western countries. Although the detailed mechanism of this discrepancy is unclear and may be attributed to complex clinical conditions, we speculate that it was due to anthropometrical characteristics of the Japanese population. In general, Asian population has lower BMI compared with Western population and hence the distribution of BMI is shifted toward lower BMI levels.[40] In 2007, the Organization for Economic Co-operation and Development reported that adult individuals with BMI ≥30.0 accounted for about 32% of the US adult population; however, the percentage of adult obese individuals was only 3% in Japan.[41] This lower rate of the population with BMI ≥30.0 may influence the distribution of BMI in our study sample.

Japanese individuals have a high percentage of adipose tissue at a lower BMI[42] and have a higher rate of beta-3 adrenergic receptor gene mutation, which might be associated with more likelihood of weight gain.[43,44] Excessive deposition of adipose tissue causes insulin resistance and prolonged inflammatory responses,[45] which may lead to the development of cardiovascular disease and death at lower BMI levels in Japanese populations. In this sense, Japanese HF patients might be a more "fat-sensitive" population and might be more susceptible to adverse cardiovascular effects caused by obesity compared with Western HF patients.

Limitations of the Study

Several limitations should be mentioned for the present study. First, the sample size of the present study was relatively small, especially in patient with BMI ≥30.0, which could cause possible selection bias. Second, we excluded the patients who did not have BMI data (n = 129). The mean age of patients without BMI data was 72.3 ± 11.1 years and male accounted for 62.0%. When we constructed the unadjusted survival curves using Kaplan-Meier method, the cumulative incidence rates between the group with BMI data and that without BMI data were not statistically significant (data not shown). Therefore, we believe that the exclusion of patients without BMI data did not influence the major findings of the present study. Third, in the Cox hazard models, we did not include other important variables, especially chronic obstructive pulmonary diseases and peripheral edema that were shown to have close interactions with BMI[4,12] because of limited data availability. Fourth, we did not account for changes in BMI during follow-up.

Conclusions

Despite the study limitations, the present results from our CHART study imply that both high and low BMI are associated with increased death and hospitalization for HF in Japanese chronic HF patients. Further studies should be performed to evaluate the optimal BMI level for better prognosis and quality of life in chronic HF patients.

Disclosures

None.

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