



# Hospital-associated disability and hospitalization costs for acute heart failure stratified by body mass index- insight from the JROAD/JROAD-DPC database

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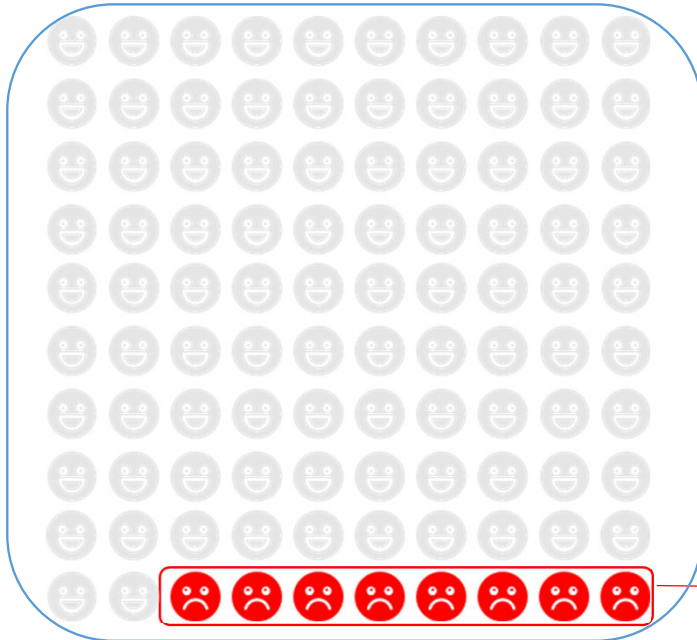
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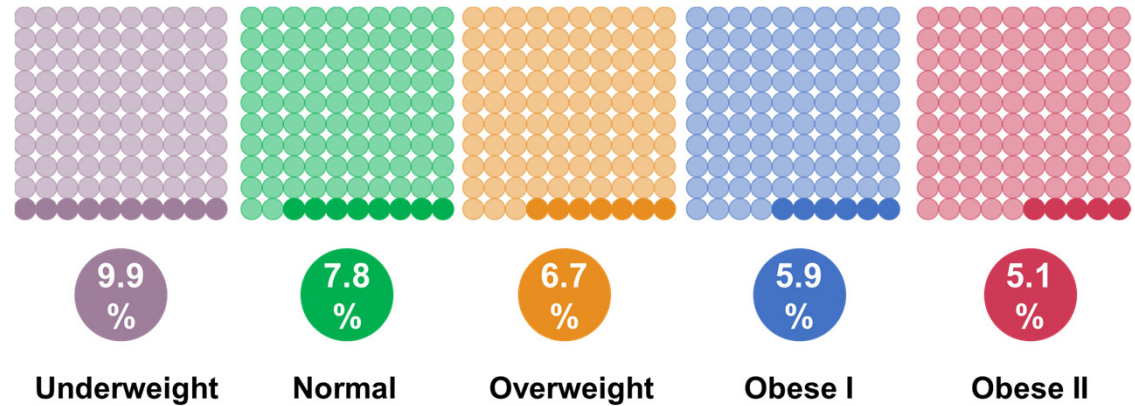


# Hospital-associated disability

AHF patients (n = 238,284)



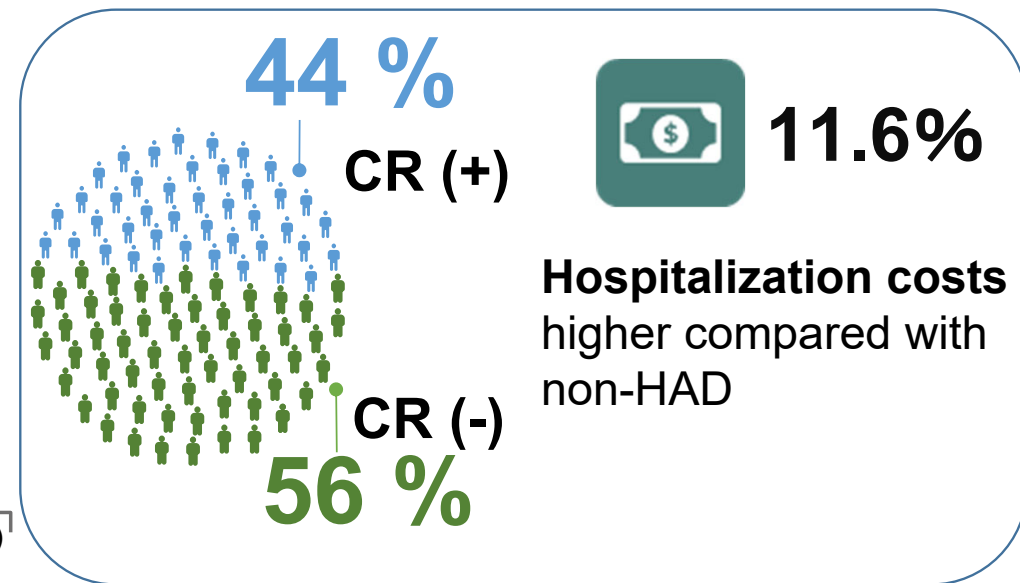
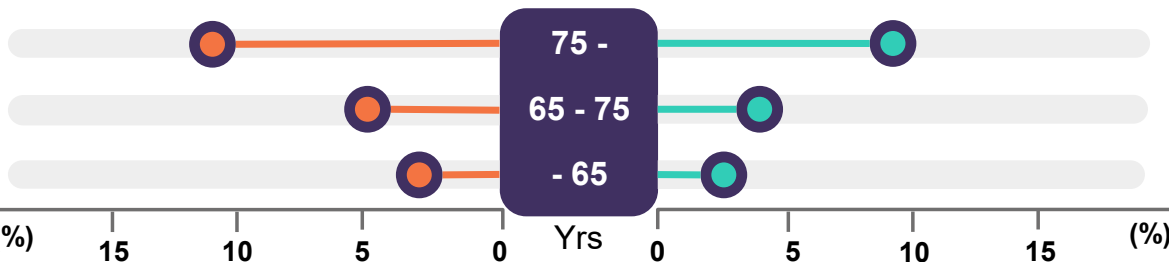
Total AHF patients



Population Chart

Females

Males



***Hospital-associated Disability and Hospitalization Costs for Acute Heart Failure***

***Stratified by Body Mass Index- Insight from the JROAD/JROAD-DPC Database***

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*\*This author takes responsibility for all aspects of the reliability and freedom from bias of the  
data presented and their discussed interpretation.*

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2    ***Conflicts of interest:***..None

3    ***Key words:*** Diagnosis procedure combination, heart failure, Japanese Registry of All Cardiac and

4    Vascular Diseases, body mass index, hospital-associated disability, healthcare costs

5

6

## **Abstract**

## **Background**

The impact of body mass index (BMI) on hospital mortality in patients with acute heart failure has been well documented in Asian populations. However, the relationship between BMI, hospital-associated disability (HAD), and hospitalization costs in patients with heart failure is poorly understood. This study aimed to explore the impact of BMI on HAD and hospitalization costs for acute heart failure in Japan.

## **Methods**

From April 2012 to March 2020, the Japanese Registry of All Cardiac and Vascular Disease Diagnosis Procedure Combination (JROAD-DPC) database was used to identify patients with acute heart failure. All patients were categorized into five groups according to the World Health Organization Asian BMI criteria. The hospitalization costs and HAD were evaluated.

## **Results**

Among the 238,160 eligible patients, 15.7% were underweight, 42.2% were normal, 16.7% were overweight, 19.3% were obese I, and 6.0% were obese II, according to BMI. The prevalence of HAD was 7.43% in the total cohort, and the risk of HAD increased with a lower BMI. Restricted cubic spline analysis showed a U-shaped relationship between BMI and hospitalization costs for all ages. Furthermore, developing HAD was associated with greater costs compared with non-HAD,

1 regardless of BMI category.

## 2 ***Conclusions***

3 We found that the lower the BMI, the higher the incidence of HAD. A U-shaped association was  
4 confirmed between BMI and hospitalization costs, indicating that hospitalization costs increased  
5 for both lower and higher BMI regardless of age. BMI could be an important and informative risk  
6 stratification tool for functional outcomes and economic burdens.

1    *Abbreviations*

2    ADL                      Activities of daily living

3    ANOVA                  Analysis of variance

4    BI                         Barthel index

5    BMI                      Body mass index

6    CI                         Confidence intervals

7    DPC                      Diagnosis Procedure Combination

8    HAD                      Hospital-associated disability

9    IABP                      Intra-aortic balloon pumps

10   IQR                      Interquartile range

11   JCS                       Japanese Circulation Society

12   JROAD                   Japanese Registry of All Cardiac and Vascular Diseases

13   NYHA                    New York Heart Association

14   OR                       Odds ratios

15

16



## 1        **1. Introduction**

2        The incidence of heart failure has rapidly increased worldwide. It is one of the most important  
3        international health issues [1]. Particularly, in Japan, which is a super-aging society, a rapid increase  
4        in the number of patients with heart failure has been recognized as a "heart failure pandemic [2]." As  
5        heart failure is a condition that requires repeated hospitalizations, the high cost of treatment and the  
6        medical costs associated with hospitalization can result in a pressing financial problem [3]. In Japan,  
7        the length of hospitalization for patients with heart failure is longer than that in other countries, and  
8        the cost of hospitalization for heart failure is high [2].

9        Body mass index (BMI) is an important factor in defining mortality during hospitalization in patients  
10       with heart failure [4]. A nationwide inpatient database in Japan demonstrated a reverse J-shaped  
11       association between BMI and in-hospital mortality in patients with heart failure [4]. This association  
12       also implies that cardiac peptides—as exemplified by brain natriuretic peptide—are inversely  
13       associated with BMI, and patients with a higher BMI are more likely to present with symptoms of  
14       heart failure at an earlier stage [5,6]. This explains the importance of BMI for risk stratification in  
15       patients with heart failure.

16       On the other hand, hospital-associated disability (HAD), which is defined as either a new or worsened  
17       disability in activities of daily living (ADL) during hospitalization, is known to be a strong risk factor  
18       for mortality and rehospitalization [7,8]. Generally, ADL depends on BMI, and obesity in midlife is a

1 risk factor for frailty, leading to a decline in late life [9]. Contrastingly, being underweight is often the  
2 result of malnutrition, sarcopenia, and cachexia that contribute to the decline in ADL [10].  
3 Nevertheless, the effect of BMI on HAD in patients with heart failure remains poorly understood.  
4 Moreover, from the perspective of healthcare financial aspects, HAD is an urgent social issue, as it  
5 leads to prolonged hospital stays and additional costs.  
6 This study aimed to investigate the impact of BMI on hospitalization costs and HAD in patients  
7 with acute heart failure in Japan.

## 8 9 **2. Methods**

### 10 **2.1. Data source**

11 The data source for this study was the Japanese Registry of All Cardiac and Vascular Diseases  
12 (JROAD) and the Diagnosis Procedure Combination (DPC) discharge databases, which is a  
13 nationwide registry collected by the Japanese Circulation Society (JCS) [11]. The JROAD  
14 specifically covers all cardiovascular training facilities, as described in the literature [11,12]. The  
15 database includes inpatient information, such as age, sex, diagnosis, comorbidities, treatments,  
16 medications, discharge status, and hospitalization costs. The main diagnoses or comorbidities of  
17 each patient were coded using the International Classification of Disease and Related Health  
18 Problems 10th revision (ICD-10) codes. As no information specifying individuals was included,

the requirement for informed consent was waived. Patient data were anonymized using original DPC data. This study complied with the principles of the Declaration of Helsinki regarding investigations in human subjects and was approved by the Kobe University Institutional Review Board (approval no. B210052).

## *2.2. Study population*

We included patients who were hospitalized between April 2012 and March 2020 with heart failure as defined by ICD-10 codes (I50.0, I50.1, and I50.9) [13] for either a main diagnosis, admission-precipitating diagnosis, or most resource-consuming diagnosis. A flowchart of the study participants' selection is shown in **Figure 1**. To investigate patients with acute decompensated heart failure, we excluded patients who did not have an additional disease code of acute exacerbation of acute or chronic heart failure (30101 or 30102) [13], and those who were admitted not due to an emergency situation. We further excluded patients who died in the hospital, those aged < 20 years, those with New York Heart Association (NYHA) class I or no NYHA data on admission, and those with missing BMI and ADL data at admission and discharge. We also excluded patients who had a hospital stay  $\leq 3$  days because the effect of hospitalization on HAD is questionable in short hospitalization cases. Finally, hospitals with  $\leq 10$  patients admitted for heart failure per year were excluded, which is consistent with a previous study [14].

### ***2.3. Body mass index and categorization***

BMI is defined as body weight divided by the square of body height and is expressed in units of  $\text{kg/m}^2$ . We categorized the patients according to the World Health Organization (WHO) Asian BMI classification [15] as follows: Underweight,  $\text{BMI} < 18.5 \text{ kg/m}^2$ ; Normal range,  $18.5 \text{ kg/m}^2 \leq \text{BMI} < 23 \text{ kg/m}^2$ ; Overweight,  $23 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$ ; obese I,  $25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$ ; and obese II,  $30 \text{ kg/m}^2 \leq \text{BMI}$ .

### ***2.4. Activities of daily living, hospital-associated disability, and hospitalization costs***

We assessed ADL using the Barthel index (BI) score [16]. The BI consists of 10 items (feeding, transfer, grooming, toilet use, bathing, ambulation, stair climbing, dressing, urination, and defecation management) to evaluate ADL on a scale of 0 to 100, with lower scores indicating greater dependency. The BI was used to evaluate ADL at two distinct time points, i.e., on admission and discharge. In this study, HAD was defined as a  $\geq 5$ -point decrease in BI score at discharge compared to that at admission, similar to that of a previous report [17]. Hospitalization costs were calculated as the sum of bundled payments and fee-for-services, excluding the food fee. All charges were converted into US dollars according to the current exchange rate (1 US dollar=120.0 Japanese yen; March 20, 2022).

## 2.5. *Statistical analysis*

Continuous and categorical data were presented as median (interquartile range [IQR]) and number (percentage), respectively. Continuous data were compared using one-way analysis of variance, and chi-square analysis was performed to compare categorical variables by BMI category (five groups). To analyze the factors predicting HAD, a multilevel mixed-effect logistic regression analysis using institution as a random intercept was performed to examine the association between the incidence of HAD and each variable. The independent variables were the BMI category and factors theoretically related to HAD, such as age, sex, Charlson comorbidity index, NYHA class, number of hospital beds, implementation of cardiac rehabilitation, and BI on admission. Odds ratios (OR) and 95% confidence intervals (CI) for HAD were calculated for each BMI category with respect to the reference value for normal BMI. Restricted cubic spline models were used to assess the relationship between BMI and hospitalization costs and the risk of HAD. The relationship between BMI and hospitalization costs or the risk of HAD was stratified into three age subgroups ( $20 \leq \text{age} < 65$  years,  $65 \leq \text{age} < 75$  years, and  $75 \text{ years} \leq \text{age}$ ). Splines were adjusted by age, sex, Charlson comorbidity index, NYHA class, the number of hospital beds, implementation of cardiac rehabilitation, and BI on admission. The splines were restricted to linear below the first knot point and above the last knot point. In this study, we used the four cut-

off points for BMI (18.5, 22.0, 25.0, and 30.0 kg/m<sup>2</sup>) as the knots for non-linear effects of continuous BMI assessment. Statistical analyses were performed using R version 4.2.0 (The R Foundation for Statistical Computing, Vienna, Austria) using the “rms” packages.

### **3. Results**

#### **3.1. Baseline characteristics**

We identified 1,166,567 patients who were diagnosed with heart failure at admission to 1,086 hospitals during the study period. We selected 238,160 eligible patients from 958 hospitals after all exclusions (**Figure 1**). The median age (IQR) was 81.0 (72.0–87.0) years, and 46.2% were women. The median BMI (IQR) was 22.2 (19.6–25.1) kg/m<sup>2</sup>. Patients were divided into five groups according to the WHO Asian BMI classification: 15.7%, underweight; 42.2%, normal; 16.7%, overweight; 19.3%, obese I; and 6.0%, obese II. **Table 1** presents the background characteristics of the study population. Overall, the underweight group tended to be older and more likely to be women. Contrastingly, obese II patients tended to have many comorbidities, such as diabetes, hypertension, and dyslipidemia. Regarding the treatment of heart failure, patients with higher BMI were more frequently treated with respirators and therapeutic devices, such as intra-aortic balloon pumps. Cardiac rehabilitation was implemented in 39.4% of the total cohort, and no major variations were found between BMI and the prevalence of cardiac

rehabilitation. Patients in the low BMI group could not be discharged home directly and tended to be transferred to a hospital or admitted to a nursing facility.

### **3.2. Hospital-associated disability**

The total proportion of patients with HAD was 7.43% (underweight, 9.90%; normal, 7.81%; overweight, 6.72%; obese I, 5.93%; obese II, 5.09%; **Figure S1**). The leaner group was more likely to develop HAD. In each BMI category, the prevalence of HAD resulted in a longer length of hospital stay (**Table S1**). **Figure 2** shows the multilevel mixed-effects multiple logistic regression analysis. Underweight was significantly associated with a higher incidence of HAD (OR, 1.32; 95%CI:1.26–1.37). Contrastingly, the overweight and obese I groups were significantly associated with preserved HAD (overweight OR, 0.88; 95%CI:0.84–0.93, obese I OR, 0.83; 95%CI:0.79–0.87). Older age was also significantly associated with the development of HAD (65 years <age<75 years, OR:1.80; 95%CI:1.64–1.98, age > 75 years, OR:5.04; 95%CI:4.65–5.47). The incidence of HAD markedly increased as the NYHA class worsened (NYHA III OR:1.14; 95%CI:1.10–1.19, NYHA IV OR:1.19; 95%CI:1.14–1.25). Moreover, Charlson comorbidity index (OR:1.09; 95%CI:1.08–1.10), cardiac rehabilitation (OR:1.16; 95%CI:1.11–1.20), and BI at admission > 70 (OR:2.56; 95%CI:2.48–2.65) tended to be associated with the development of HAD. The restricted cubic spline also showed the same trend,

in which HAD increased with decreasing BMI (**Figure S2**). When stratified by age subgroup, the risk of HAD tended to increase with lower BMI in all age groups. Conversely, the risk for HAD only increased with higher BMI in patients aged > 75 years (**Figure 3A**).

### ***3.3. Hospitalization cost***

The median hospitalization cost was US\$ 6,630 (795,628 Japanese yen). In each BMI category, the prevalence of HAD resulted in higher hospitalization costs (**Table S1**). The overweight group showed the lowest hospitalization cost, and hospitalization costs tended to increase if the participants were thin or obese. **Figure 3B** represented the association between BMI and hospitalization costs among the three age subgroups. A U-shaped relationship was observed, suggesting that with the overweight group at the bottom point, the hospitalization costs increased when the patient was underweight or overweight. This relationship was consistent regardless of age, although younger patients had higher costs.

## ***4. Discussion***

This study using the JROAD/DPC database demonstrated that BMI affects hospitalization costs and HAD for acute heart failure in Japan. Our main findings were as follows: 1) the prevalence of HAD was 7.43% in total patients with acute heart failure, and the risk of HAD increased in



1 proportion to thinness; 2) the development of HAD was associated with greater costs compared  
2 with non-HAD regardless of the BMI category; and 3) a U-shaped relationship was found between  
3 BMI and hospitalization costs at all ages (**Graphical Abstract**). These results provide promising  
4 intervention strategies stratified by BMI and risk stratification using BMI. Additionally, it can provide  
5 rehabilitation intervention strategies to prevent HAD. Moreover, since Japan is the front runner of  
6 super-aged societies, these results can be a helpful suggestion for future clinical practice ahead of the  
7 world.

8 To the best of our knowledge, this is the first study to demonstrate the prevalence of HAD  
9 stratified by BMI category in a large national data. The JROAD-DPC database obtained data from  
10 1,231 hospitals using the Japanese DPC/PDPS claim data. In Japan, 1,755 hospitals used the  
11 DPC/PDPS system in 2019 [18]; therefore, the JROAD-DPC database is mainstream in  
12 cardiovascular practice and represents real-world clinical data in Japan. The BMI distribution in  
13 our study was similar to those in other Asian countries [19]. Nevertheless, the BMI and prevalence  
14 of obese patients were substantially lower than those in Western countries [20].

15 The decline in ADL associated with hospitalization is a matter of great concern in Japan and other  
16 developed countries with aging populations. In this study, the prevalence of HAD was 7.43%, and  
17 it increased as BMI decreased. This is an important finding of our study. Although few reports are  
18 available regarding HAD in patients with heart failure, previous studies in Japan demonstrated that

1 the prevalence of HAD was 10.5 to 24.4% [7,21,22], which is a slightly greater percentage than  
2 that in the present study. Multiple regression analysis of our results revealed that the incidence of  
3 HAD tended to increase with the number of beds. High-volume centers were more likely to admit  
4 patients who were critically ill and required more invasive treatment, thus increasing the  
5 likelihood of developing HAD. Previous reports investigating HAD were mostly conducted in  
6 high-volume centers or university hospitals, which may partly explain the difference in prevalence  
7 of HAD in this study from that in previous studies. Hence, our JROAD/DPC data represent both  
8 under- and overestimated real-world data in Japan.

9 Of note, age and BMI are closely related, as people generally lose more weight as they age [23].

10 Our finding suggested that patients with low BMI were more likely to cause HAD, regardless of  
11 age (**Figure 3A**). Patients with low BMI are more likely to have malnutrition, frailty, sarcopenia,  
12 and other geriatric complications [24], which may reduce the effectiveness of rehabilitation,  
13 impair ADL, and make it difficult for them to return to society. Conversely, the prevalence of  
14 HAD in patients with high BMI differed for each age group, with older patients having a higher  
15 risk of developing HAD. Interestingly, patients in the high BMI group tended to receive more  
16 invasive treatment or surgery; thus, the risk of loss of muscle mass and HAD may have been  
17 higher than that of the patients with low BMI. However, it was possible that HAD did not occur  
18 in the younger age group because their base ADL were somewhat preserved. Contrary, the effect

of treatment may have unfolded as HAD in older people with low reserve capacity. Further studies are needed to elucidate the mechanisms underlying the effect of BMI on clinical outcomes.

Although little evidence exists regarding hospitalization costs for heart failure in Japan, this is the first report of a U-shaped association between BMI and hospitalization costs. The relationship between increased costs for both thin and obese individuals, regardless of age, underscores the importance of BMI from a health economic perspective. A recent systematic review concluded that the median hospitalization cost for heart failure was \$13,418 per patient in the United States [25]. This result (median hospitalization cost: US\$ 6,748) was higher than that in our present data.

As the estimated cost of care for heart failure will increase markedly because of aging and new expensive advanced heart failure management every year [26], a similar trend may be observed in Japan in the future. Subsequently, younger individuals tended to have higher hospitalization costs, and the trend was similar for each BMI class after adjusting for other clinical factors. The reason for this trend is unclear; however, it may be because older patients choose to withdraw or withhold invasive treatment. Notably, once HAD occurs in any BMI group, it incurs high hospitalization costs and increases the length of hospital stay. Assessments or interventions to prevent HAD, especially in underweight patients, may help improve prognosis and economic burden.

HAD leads to a prolonged hospital stay, and rehabilitation is considered an effective treatment

strategy to prevent HAD. However, it is surprising that only 44% of the patients in this study underwent rehabilitation even when HAD occurred. Japan has a unique high-cost medical care benefit system that addresses high health-care costs; thus, patients were only required to pay a pre-fixed ceiling amount. Therefore, in most cases, the implementation of rehabilitation does not increase the cost burden on patients, and there are very few cases in which rehabilitation is not prescribed due to patients' financial status. Some recent studies reported that early rehabilitation within 3 days of admission reduced hospital stay and readmissions after discharge [27, 28]. Additionally, another study demonstrated that energy intake during hospital stay was an independent predictor of functional status in older patients with acute heart failure [29]. Therefore, our findings recommend early rehabilitation and nutritional intervention based on BMI at admission, and especially early and intensive intervention for thin patients of any age. Furthermore, only 7.3% patients with heart failure received outpatient rehabilitation after discharge in Japan [30]; thus, the prevention of HAD during hospitalization is very important due to the lack of an established follow-up system in the outpatient setting. Moreover a one-day extension of hospital stay will cost more than \$ 400 in additional medical expenses [25,31]; therefore, the prevention of HAD is a crucial issue for the stability of the health insurance system as well as patients' quality of life. Furthermore, the cost associated with heart failure is higher than that associated with any other acute cardiovascular disease [27]. Considering the rapid

1 increase in total healthcare costs associated with the upcoming heart failure pandemic, the present  
2 data provide a more comprehensive understanding of the true burden of HAD and valuable  
3 information for risk stratification, policy making, and benchmarking in HAD prevention,  
4 especially for underweight patients.

#### 5 *4.1.Limitations*

6 Our study had a few limitations. First, we analyzed only a limited number of facilities included  
7 in the JROAD centers, focusing on hospitals certified by the Japanese Circulation Society. This  
8 may have led to a selection bias and prevented the application of our findings to other non-  
9 certified hospitals. Although DPC data must be confirmed by a physician and be highly reliable,  
10 some of the data are based on medical claims. Therefore, it is possible that these data may contain  
11 certain errors. Second, the database only included information related to the period of  
12 hospitalization; thus, we were unable to analyze long-term outcomes. Furthermore, the patient's  
13 pre-hospitalization status including place of residence and severity of heart failure remain  
14 unknown.

15 Third, we classified heart failure using the ICD-10 codes. The accuracy of this diagnosis has been  
16 documented; nevertheless, these are less validated in the JROAD-DPC database than in  
17 prospective trials. Assessment of BMI was done at hospital admission in this study. Patients with  
18 acute decompensated heart failure often present with weight gain due to edema, which occurs

1 when fluid builds up in the body tissues. Therefore, BMI at admission may not be representative  
2 of a patient's normal weight. Next, we excluded patients who died in the hospital because we used  
3 ADL as the outcome of the present study. Therefore, more severely ill patients may have been  
4 excluded, or there may have been an information bias due to missing data. Therefore, our findings  
5 should be interpreted with caution in clinical practice. Lastly, an age gradient exists across the  
6 BMI categories. We conducted several statistical adjustments on age to minimize the age effects  
7 for HAD and hospitalization costs as much as possible. Nevertheless, the relationship between  
8 age and BMI is not completely inseparable.

## 10 **5. Conclusion**

11 Our results from a nationwide inpatient database showed the prevalence of HAD and  
12 hospitalization costs stratified by BMI. We found that the lower the BMI, the higher the incidence  
13 of HAD. A U-shaped association was confirmed between BMI and hospitalization costs,  
14 indicating that both lower and higher BMI were related to higher hospitalization costs, regardless  
15 of age. This study provides valuable suggestions for the need for future interventions for  
16 underweight patients who are more likely to suffer from HAD.

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## *Data availability statement*

**Deidentified participant data will not be shared.**

## *References*

- [1] A.P. Ambrosy, G.C. Fonarow, J. Butler, O. Chioncel, S.J. Greene, M. Vaduganathan, S. Nodari, C.S.P. Lam, N. Sato, A.N. Shah, M. Gheorghiade, The global health and economic burden of hospitalizations for heart failure: Lessons learned from hospitalized heart failure registries, *J. Am. Coll. Cardiol.* 63 (2014) 1123–1133. <https://doi.org/10.1016/j.jacc.2013.11.053>.
- [2] M. Isobe, The heart failure “pandemic” in Japan: Reconstruction of Health Care System in the Highly Aged Society, *JMA J.* 2 (2019) 103–112. <https://doi.org/10.31662/jmaj.2018-0049>.
- [3] P. Stafylas, D. Farmakis, G. Kourlaba, G. Giamouzis, K. Tsarouhas, N. Maniadakis, J. Parissis, The heart failure pandemic: The clinical and economic burden in Greece, *Int. J. Cardiol.* 227 (2017) 923–929. <https://doi.org/10.1016/j.ijcard.2016.10.042>.

- [4] H. Itoh, H. Kaneko, H. Kiriyama, T. Kamon, K. Fujiu, K. Morita, H. Yotsumoto, N. Michihata, T. Jo, N. Takeda, H. Morita, H. Yasunaga, I. Komuro, Reverse J-shaped relationship between body mass index and in-hospital mortality of patients hospitalized for heart failure in Japan, *Heart Vessels*. 36 (2021) 383–392. <https://doi.org/10.1007/s00380-020-01699-6>.
- [5] M. Koizumi, H. Watanabe, Y. Kaneko, K. Iino, M. Ishida, T. Kosaka, Y. Motohashi, H. Ito, Impact of obesity on plasma B-type natriuretic peptide levels in Japanese community-based subjects, *Heart Vessels*. 27 (2012) 287–294. <https://doi.org/10.1007/s00380-011-0143-3>.
- [6] C. Kistorp, J. Faber, S. Galatius, F. Gustafsson, J. Frystyk, A. Flyvbjerg, P. Hildebrandt, Plasma adiponectin, body mass index, and mortality in patients with chronic heart failure, *Circulation*. 112 (2005) 1756–1762. <https://doi.org/10.1161/CIRCULATIONAHA.104.530972>.
- [7] M. Saitoh, Y. Takahashi, D. Okamura, M. Akiho, H. Suzuki, N. Noguchi, Y. Yamaguchi, K. Hori, Y. Adachi, T. Takahashi, Prognostic impact of hospital-acquired disability in elderly patients with heart failure, *ESC Heart Fail*. 8 (2021) 1767–1774. <https://doi.org/10.1002/ehf2.13356>.
- [8] K.E. Covinsky, E. Pierluissi, C.B. Johnston, Hospitalization-associated disability: “She was probably able to ambulate, but I’m not sure”, *JAMA*. 306 (2011) 1782–1793. <https://doi.org/10.1001/jama.2011.1556>.



- [9] H.K. Vincent, K.R. Vincent, K.M. Lamb, Obesity and mobility disability in the older adult, *Obes. Rev.* 11 (2010) 568–579. <https://doi.org/10.1111/j.1467-789X.2009.00703.x>.
- [10] H. Wakabayashi, K. Maeda, S. Nishioka, H. Shamoto, R. Momosaki, Impact of body mass index on activities of daily living in inpatients with acute heart failure, *J. Nutr. Health Aging.* 23 (2019) 151–156. <https://doi.org/10.1007/s12603-018-1111-8>.
- [11] S. Yasuda, K. Nakao, K. Nishimura, Y. Miyamoto, Y. Sumita, T. Shishido, T. Anzai, H. Tsutsui, H. Ito, I. Komuro, Y. Saito, H. Ogawa; on the behalf of JROAD Investigators, The current status of cardiovascular medicine in Japan – Analysis of a large number of health records from a nationwide claim-based database, JROAD-DPC, *Circ. J.* 80 (2016) 2327–2335. <https://doi.org/10.1253/circj.CJ-16-0196>.
- [12] S. Yasuda, Y. Miyamoto, H. Ogawa, Current status of cardiovascular medicine in the aging society of Japan, *Circulation.* 138 (2018) 965–967. <https://doi.org/10.1161/CIRCULATIONAHA.118.035858>.
- [13] M. Nakai, Y. Iwanaga, Y. Sumita, K. Kanaoka, R. Kawakami, M. Ishii, K. Uchida, N. Nagano, T. Nakayama, K. Nishimura, K. Tsuchihashi, K. Kimura, Y. Saito, K. Tsujita, H. Ogawa, Y. Miyamoto, S. Yasuda; on the behalf of the JROAD Investigators, Validation of acute myocardial infarction and heart failure diagnoses in hospitalized patients with the nationwide claim-based JROAD-DPC database. *Circ Rep.* 3, 131–136 (2021), *Circ. Rep.* 3 (2021) 131–

136. <https://doi.org/10.1253/circrep.CR-21-0004>.

[14] M. Konishi, Y. Matsuzawa, T. Ebina, M. Kosuge, M. Gohbara, K. Nishimura, M. Nakai, Y. Miyamoto, Y. Saito, H. Tsutsui, I. Komuro, H. Ogawa, K. Tamura, K. Kimura, Impact of population density on mortality in patients hospitalized for heart failure – JROAD-DPC Registry Analysis, *J. Cardiol.* 75 (2020) 447–453. <https://doi.org/10.1016/j.jjcc.2019.09.008>.

[15] *Regional Office for the Western P, The Asia-Pacific Perspective: Redefining Obesity and Its Treatment.*

[16] F.I. Mahoney, D.W. Barthel, Functional evaluation: The Barthel index, *Md State Med. J.* 14 (1965) 61–65.

[17] Y. Takara, M. Saitoh, T. Morisawa, T. Takahashi, N. Yoshida, M. Sakiyama, R. Nakamura, I. Tei, T. Fujiwara, Clinical characteristics of older heart failure patients with hospital-acquired disability: A preliminary, single-center, observational study, *Cardiol. Res.* 12 (2021) 293–301. <https://doi.org/10.14740/cr1306>.

[18] Statistics of Japan, The Portal Site of Official Statistics of Japan. <https://www.e-stat.go.jp/en/>.

[19] W. Zheng, D.F. McLerran, B. Rolland, X. Zhang, M. Inoue, K. Matsuo, J. He, P.C. Gupta, K. Ramadas, S. Tsugane, F. Irie, A. Tamakoshi, Y.T. Gao, R. Wang, X.O. Shu, I. Tsuji, S. Kuriyama, H. Tanaka, H. Satoh, C.J. Chen, J.M. Yuan, K.Y. Yoo, H. Ahsan, W.H. Pan, D. Gu, M.S. Pednekar, C. Sauvaget, S. Sasazuki, T. Sairenchi, G. Yang, Y.B. Xiang, M. Nagai, T.

Suzuki, Y. Nishino, S.L. You, W.P. Koh, S.K. Park, Y. Chen, C.Y. Shen, M. Thornquist, Z. Feng, D. Kang, P. Boffetta, J.D. Potter, Association between body-mass index and risk of death in more than 1 million Asians, *N. Engl. J. Med.* 364 (2011) 719–729. <https://doi.org/10.1056/NEJMoa1010679>.

[20] T.M. Powell-Wiley, J. Ngwa, S. Kebede, D. Lu, P.J. Schulte, D.L. Bhatt, C. Yancy, G.C. Fonarow, M.A. Albert, Impact of body mass index on heart failure by race/ethnicity from the get with the guidelines–heart failure (GWTG–HF) registry, *JACC Heart Fail.* 6 (2018) 233–242. <https://doi.org/10.1016/j.jchf.2017.11.011>.

[21] M. Kato, Y. Mori, D. Watanabe, h. Onoda, K. Fujiyama, M. Toda, K. Kito, Relationship between average daily rehabilitation time and decline in instrumental activity of daily living among older patients with heart failure: A preliminary analysis of a multicenter cohort study, SURUGA-CARE, *PLOS ONE.* 16 (2021) e0254128. <https://doi.org/10.1371/journal.pone.0254128>.

[22] K. Takabayashi, S. Kitaguchi, K. Iwatsu, Y. Morikami, T. Ichinohe, T. Yamamoto, K. Takenaka, H. Takenaka, H. Muranaka, R. Fujita, O. Nakajima, R. Yokoyama, Y. Terasaki, H. Nishio, M. Masai, H. Koito, M. Okuda, H. Uwatoko, Y. Kawakami, S. Matsumoto, T. Kitamura, R. Nohara, A decline in activities of daily living due to acute heart failure is an independent risk factor of hospitalization for heart failure and mortality, *J. Cardiol.* 73 (2019)

522–529. <https://doi.org/10.1016/j.jjcc.2018.12.014>.

[23] Jackson AS, Janssen I, Sui X, Church TS, Blair SN, Longitudinal changes in body composition associated with healthy ageing: men, aged 20–96 years, *Br J Nutr.* 107 (2012) 1085–1091. <https://doi.org/10.1017/S0007114511003886>

[24] A. Lena, M.S. Anker, J. Springer, Muscle wasting and sarcopenia in heart failure-the current state of science, *Int. J. Mol. Sci.* 21 (2020) 6549. <https://doi.org/10.3390/ijms21186549>.

[25] M. Urbich, G. Globe, K. Pantiri, M. Heisen, C. Bennison, H.S. Wirtz, G.L. Di Tanna, A systematic review of medical costs associated with heart failure in the USA (2014–2020), *Pharmacoeconomics.* 38 (2020) 1219–1236. <https://doi.org/10.1007/s40273-020-00952-0>.

[26] P.A. Heidenreich, N.M. Albert, L.A. Allen, D.A. Bluemke, J. Butler, G.C. Fonarow, J.S. Ikonomidis, O. Khavjou, M.A. Konstam, T.M. Maddox, G. Nichol, M. Pham, I.L. Piña, J.g. Trogon, American Heart Association Advocacy Coordinating Committee, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Cardiovascular Radiology and Intervention, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Stroke Council, Forecasting the impact of heart failure in the United States: A policy statement from the American Heart Association, *Circ. Heart Fail.* 6 (2013) 606–619. <https://doi.org/10.1161/HHF.0b013e318291329a>.

[27] Kono Y, Izawa H, Aoyagi Y, Ishikawa A, Sugiura T, Mori E, Yanohara R, Ishiguro T,

Yamada R, Okumura S, Fujiwara W, Hayashi M, Saitoh E, Predictive impact of early mobilization on rehospitalization for elderly Japanese heart failure patients, *Heart Vessels*. 35 (2020) 531–536.

<https://doi.org/10.1007/s00380-019-01517-8>

[28] Fleming LM, Zhao X, DeVore AD, Heidenreich PA, Yancy CW, Fonarow GC, Hernandez AF, Kociol RD. Early ambulation among hospitalized heart failure patients is associated with reduced length of stay and 30-day readmissions, *Circ Heart Fail*. 11 (2018) e004634.

<https://doi.org/10.1161/CIRCHEARTFAILURE.117.004634>

[29] Katano S, Hashimoto A, Ohori K, Watanabe A, Honma R, Yanase R, Ishigo T, Fujito T, Ohnishi H, Tsuchihashi K, Ishiai S, Miura T, Nutritional status and energy intake as predictors of functional status after cardiac rehabilitation in elderly inpatients with heart failure - A retrospective cohort study, *Circ J*. 82 (2018) 1584–1591.

<https://doi.org/10.1253/circj.CJ-17-1202>

[30] K. Kamiya, T. Yamamoto, M. Tsuchihashi-Makaya, T. Ikegame, T. Takahashi, Y. Sato, N. Kotooka, Y. Saito, H. Tsutsui, H. Miyata, M. Isobe. Nationwide Survey of Multidisciplinary Care and Cardiac Rehabilitation for Patients With Heart Failure in Japan—An Analysis of the AMED-CHF Study. *Circ J*. 83 (2019) 1546–1552. <https://doi.org/10.1253/circj.CJ-19-0241>

[31] Kanaoka K, Okayama S, Nakai M, Sumita Y, Nishimura K, Kawakami R, Okura H,

1 Miyamoto Y, Yasuda S, Tsutsui H, Komuro I, Ogawa H, Saito Y. Hospitalization costs for  
2 patients with acute congestive heart failure in Japan, *Circ. J.* 83 (2019) 1025–1031.  
3 <https://doi.org/10.1253/circj.CJ-18-1212>

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## **Figure legends**

### **Figure 1. Study flowchart**

A flowchart of patient enrollment in this study shows the exclusion criteria and the number of patients excluded at each stage of data collection. JROAD-DPC, Japanese Registry of All Cardiac and Vascular Diseases-Diagnosis Procedure Combination; ADL, activities of daily living; BMI, body mass index; NYHA, New York Heart Association

### **Figure 2. Multilevel mixed-effect logistic regression analysis for hospital-associated disability**

A multiple logistic regression analysis, using institution as a random intercept, was performed to examine the association between the incidence of HAD and each variable. The results are shown as odds ratios (OR) with 95% confidence intervals. Overweight and obesity I and II BMI categories showed an OR of less than 1. All other variables showed an OR of greater than 1.

### **Figure 3. Association between body mass index (BMI) and the risk of hospital-associated disability (HAD) and hospitalization costs among the three age subgroups**

Restricted cubic spline models were adjusted for age, sex, Charlson comorbidity index, NYHA class, the number of hospital bed, implementation of cardiac rehabilitation, and BI on admission. Spline curves were stratified into three age subgroups ( $20 \leq \text{age} < 65$ ,  $65 \leq \text{age} < 75$ , and  $\geq 75$  years). (A) shows the association between BMI and the risk of HAD, the dotted vertical line is

22.0 kg/m<sup>2</sup> and denotes the referent BMI; (B) shows the association between BMI and hospitalization costs.

CI: confidence interval

#### **Figure S1. The prevalence of hospital-associated disability stratified by BMI category**

This image shows the prevalence of hospital-associated disability (HAD) for each body mass index (BMI) category. The underweight category had the highest incidence of HAD, which decreased for each subsequent BMI category, with the obese II category having the lowest HAD incidence.

#### **Figure S2. The association between BMI and the risk of HAD**

Restricted cubic spline models were used to assess the relationship between BMI and risk of developing HAD. The blue line represents the univariate analysis between BMI and the risk of HAD. The red line represents multivariable analysis adjusted for age, sex, Charlson comorbidity index, NYHA class, number of hospital beds, implementation of cardiac rehabilitation, and BI on admission.



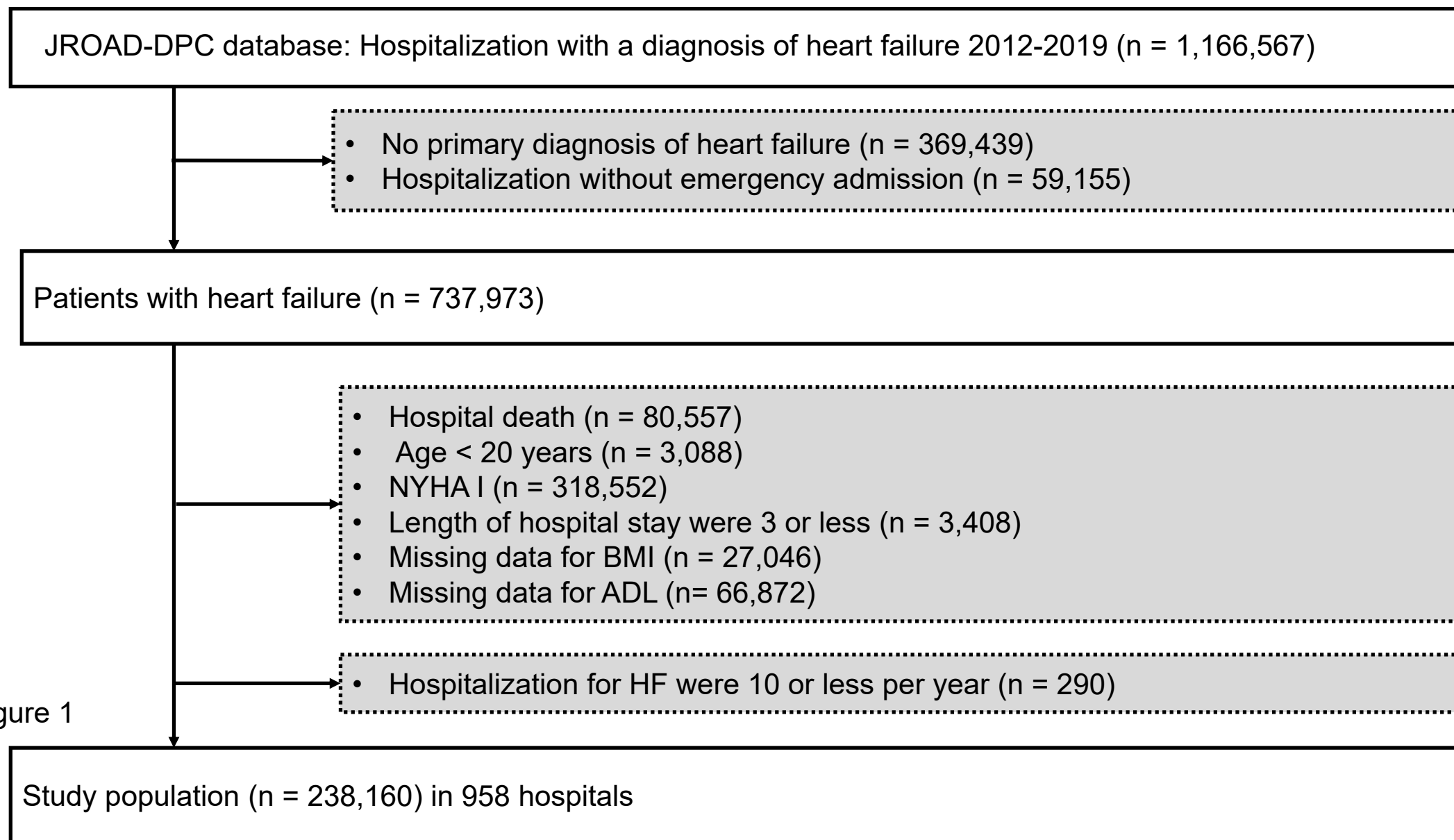


Figure 1

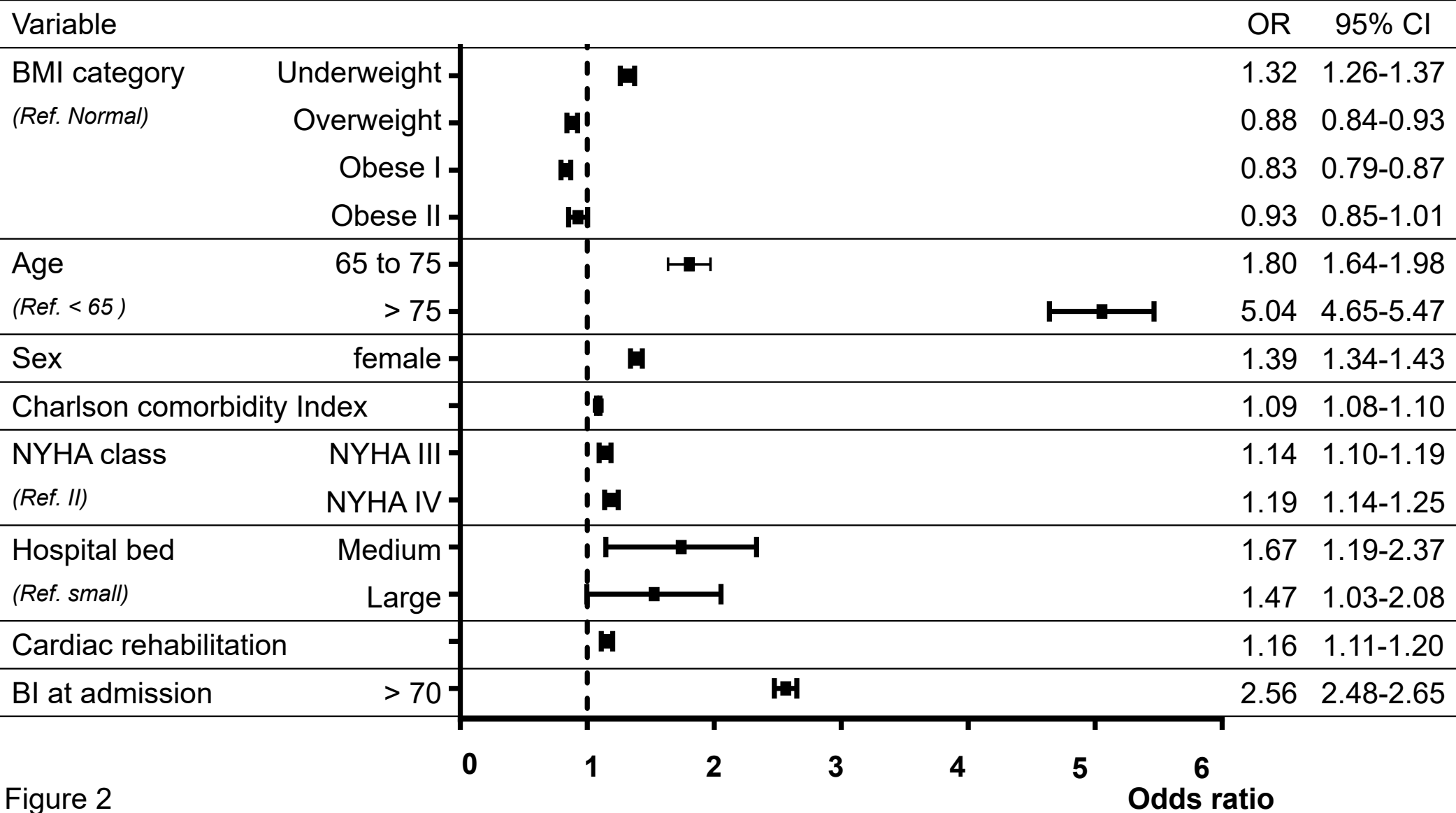


Figure 2

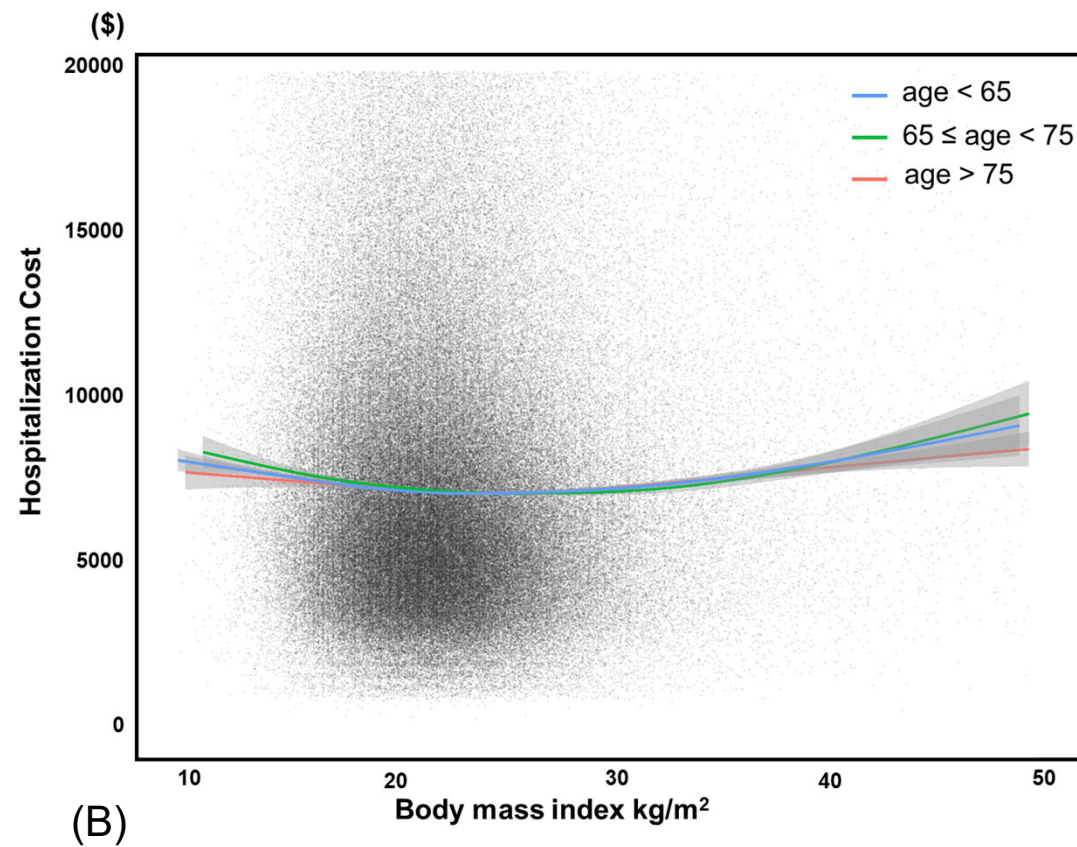
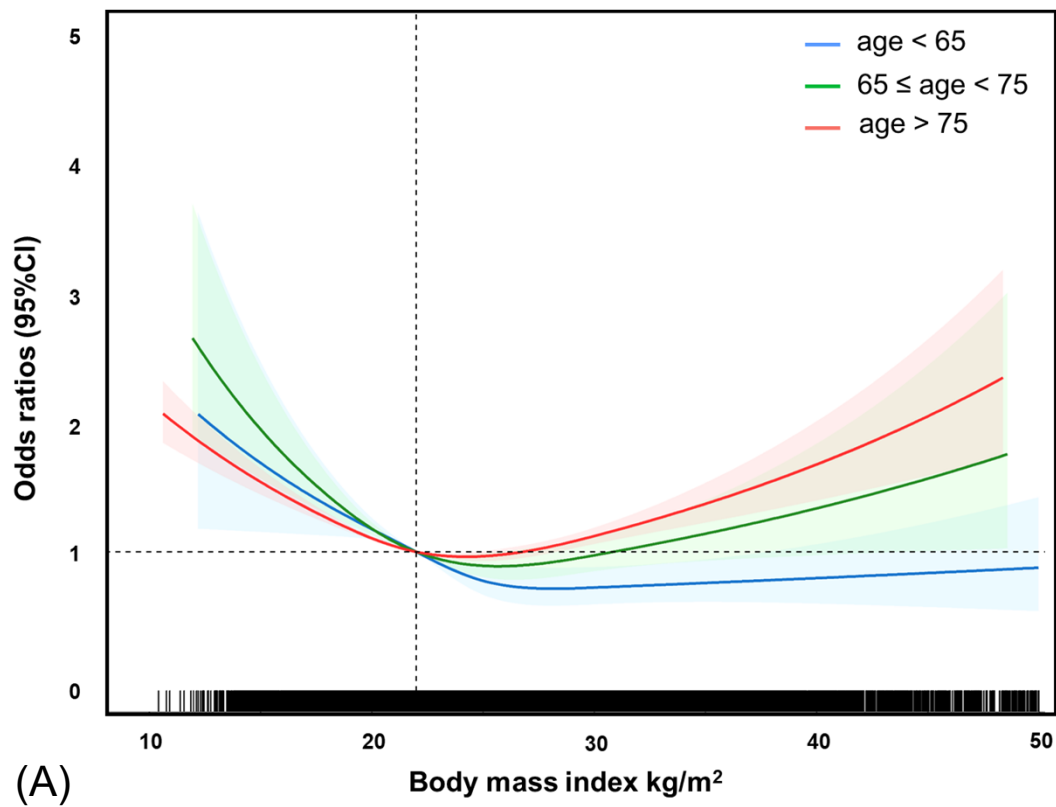


Figure 3

**Table 1.** Patient characteristics according to the WHO Asian BMI classification

	Underweight	Normal	Overweight	Obese I	Obese II
Sample size, n	37,344	100,650	39,737	46,116	14,313
Age, median(IQR)	84.0 (78.0–89.0)	82.0 (75.0–88.0)	80.0 (71.0–86.0)	77.0 (67.0–84.0)	68.0 (54.0–79.0)
Women, %	62.1	46.6	38.6	39.7	43.6
BMI, median (IQR)	17.2 (16.1–17.9)	20.9 (19.8–22.0)	23.9 (23.5–24.4)	26.7 (25.8–28.0)	32.5 (31.0–35.2)
Charlson score, median (IQR)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)
NYHA class, II/ III/ IV, %	25.6/ 38.6/ 35.8	27.2/ 38.9/ 33.9	28.4/ 39.4/ 32.2	27.9/ 39.6/ 32.5	26.7/ 38.8/ 34.4
<b>Comorbidity, %</b>					
Diabetes	16.7	25.3	31.8	38.3	48.5
Chronic respiratory disease	10.2	8.0	7.6	7.2	8.1
Hypertension	50.9	55.6	58.5	60.8	64.2
Atrial fibrillation	30.6	32.2	34.1	34.0	31.1
Stroke	2.1	1.9	1.8	1.7	1.2

Dyslipidemia	14.7	20.0	23.8	26.7	29.2
Hyperuricemia	7.1	8.9	9.6	10.7	12.4
Chronic kidney disease	11.6	14.0	13.7	13.6	12.9
Hemodialysis	3.3	4.0	3.8	3.4	3.4
<b>Hospital Beds, %</b>					
Large (> 400)	37.6	37.3	36.9	36.7	37.0
Medium (200–399)	61.3	61.4	61.6	61.7	61.5
Small (< 199)	1.1	1.3	1.4	1.6	1.5
<b>Medications, %</b>					
β-blocker	55.2	59.6	61.9	64.2	67.8
ACE-I	25.8	26.0	25.7	25.3	26.6
ARB	24.2	30.9	35.5	39.7	46.0
Statin	18.6	26.6	31.7	35.7	38.7
<b>Treatment, %</b>					

Respirator	17.6	19.7	19.9	21.0	23.7
IABP	0.4	0.6	0.7	0.7	0.7
PCI	2.3	3.8	5.0	4.8	4.2
Open surgery	0.4	0.5	0.6	0.5	0.4
ICD/CRT	0.2	0.4	0.5	0.4	0.4
Cardiac Rehabilitation	39.8	40.0	38.9	38.4	38.9
<b>Discharge dislocations, %</b>					
Home	73.8	82.5	86.9	89.2	91.7
Transfer	11.9	7.3	5.0	3.5	2.0
Nursing facility	14.0	10.0	7.9	7.1	6.2
Hospital stay, days, median (IQR)	19.0 (13.0–30.0)	17.0 (12.0–27.0)	17.0 (12.0–25.0)	17.0 (12.0–25.0)	18.0 (12.0–26.0)
Hospital cost, \$, median (IQR)	6,883	6,600	6,497	6,536	6,876
	(4,780–10,273)	(4,591–9,974)	(4,500–9,837)	(4,541–9,834)	(4,800–10,322)
Hospital cost, Yen, median (IQR)	825,988	792,000	779,590	784,400	825,121

	(573,622–	(550,936–	(539,884–	(544,919–	(576,141–
	1,232,803)	1,196,949)	1,180,325)	1,180,091)	1,238,579)
BI on admission, point, median (IQR)	45.0 (0.0–90.0)	55.0 (10.0–100.0)	65.0 (15.0–100.0)	70.0 (20.0–100.0)	75.0 (25.0–100.0)
BI on discharge, point, median (IQR)	80.0 (40.0–100.0)	100.0 (60.0–100.0)	100.0(75.0–100.0)	100.0(85.0–100.0)	100.0(90.0–100.0)
Hospital associated disability, %	9.9	7.8	6.7	5.9	5.1

WHO, World Health Organization; BMI, body mass index; NYHA, New York Heart Association; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; VAD, ventricular assist device; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve implantation; ICD, implantable cardioverter defibrillator; CRT, cardiac resynchronization therapy; BI, Barthel index; IQR, interquartile range

## Hospital-Associated Disability

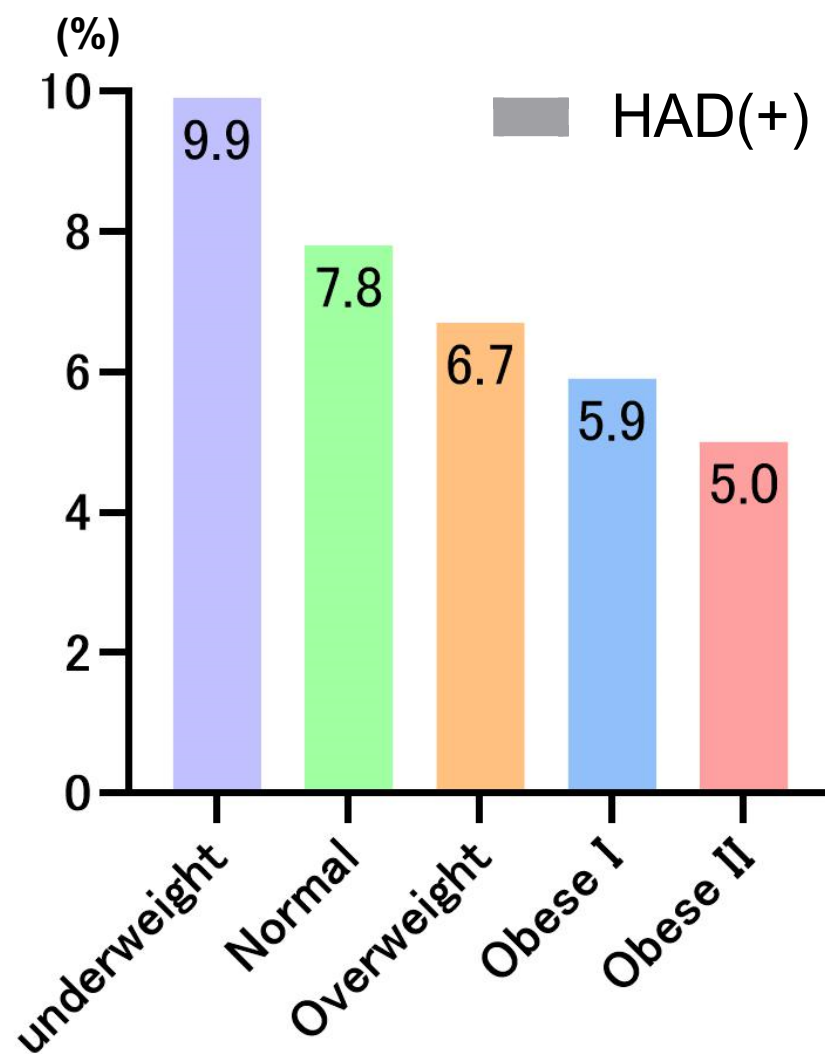


Figure S1



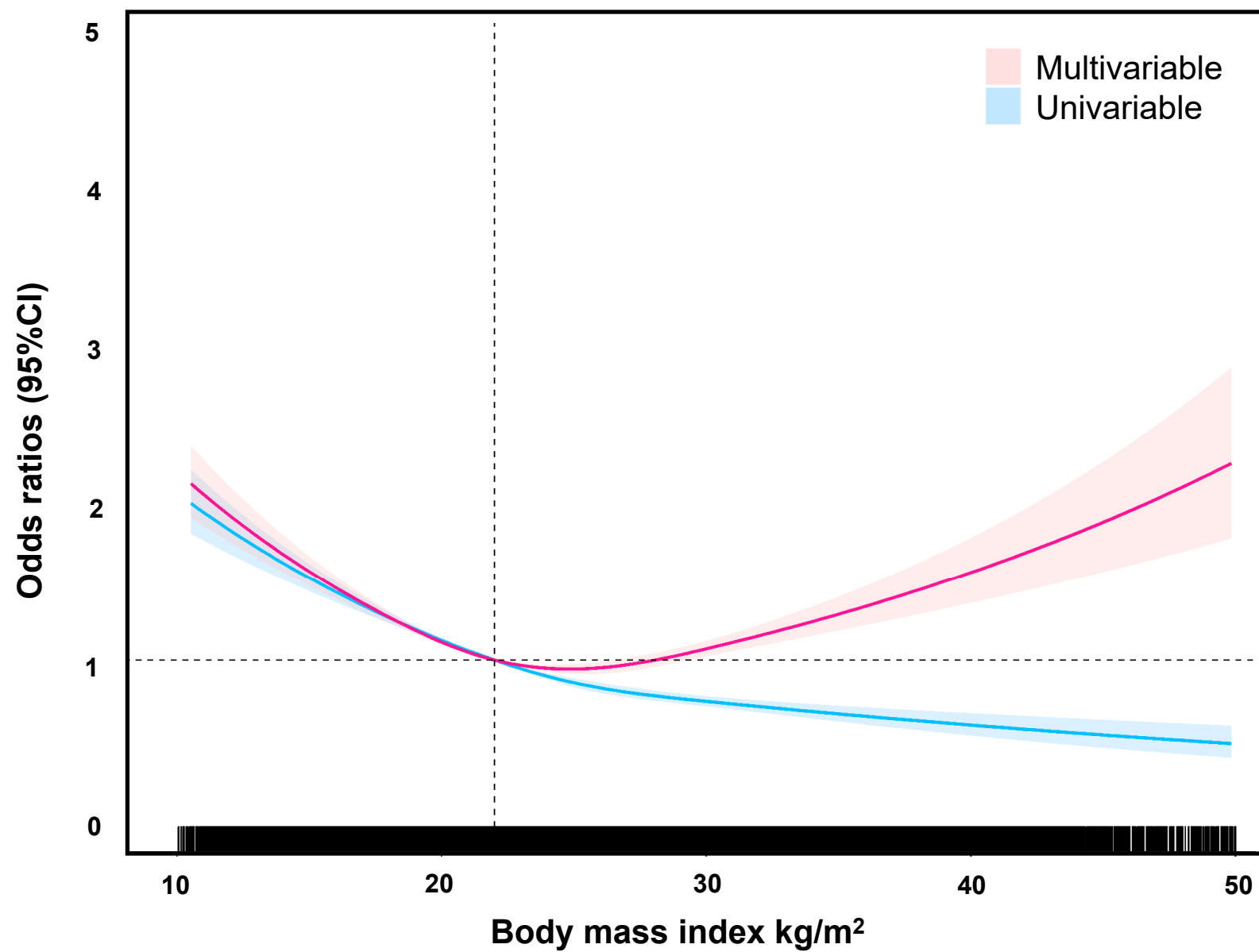


Figure S2

Patient's characteristics based on WHO Asian-BMI classification stratified by HAD													
			Underweight		Normal range		Overweight		Obese I		Obese II		
			HAD(+)	HAD(-)	HAD(+)	HAD(-)	HAD(+)	HAD(-)	HAD(+)	HAD(-)	HAD(+)	HAD(-)	
Hospital cost, \$,	cost,	\$,	3,694	33,650	7,859	92,791	2,673	37,064	2,737	43,379	727	13,586	
			7,464	6,816	7,325	6,547	7,403	6,441	7,030	6,514	7,816	6,845	
			median (IQR)	(5,083–	(4,750–	(4,912–	(4,565–	(4,965–	(4,466–	(4,811–	(4,528–	(5,195–	(4,780–
Hospital cost, Yen,	cost,	Yen,	895,752	817,998	878,946	785,647	888,358	772,936	843,548	781,698	937,934	821,451	
			median (IQR)	(609,961–	(569,951–	(589,533–	(547,830–	(595,814–	(535,951–	(577,367–	(543,307–	(623,393–	(573,643–
			1,407,116)	1,217,128)	1,364,976)	1,184,025)	1,404,920)	1,165,572)	1,363,152)	1,167,326)	1,485,090)	1,226,138)	
Hospital stay, days,	stay,	days,	22.0										
			median (IQR)	(14.0–	19.00	21.0	17.0	21.0	17.0	20.0	17.0	22.0	17.0
			36.0)	(13.0–29.0)	(13.0–35.0)	(12.0–26.0)	(14.0–35.0)	(11.0–25.0)	(13.0–34.0)	(11.0–25.0)	(14.0–36.0)	(12.0–25.0)	

WHO, World Health Organization; BMI, body mass index; HAD, hospital associated disability; IQR, interquartile range