Association of Obesity With Severity of Heart Failure Exacerbation: A Population-Based Study

Atsushi Hirayama, MD, MPH; Tadahiro Goto, MD, MPH; Yuichi J. Shimada, MD, MPH; Mohammad Kamal Faridi, MPH; Carlos A. Camargo Jr MD, DrPH; Kohei Hasegawa, MD, MPH

***Background*—**Obesity and heart failure (HF) are important public health problems in the United States. Although studies have reported the association between obesity and higher chronic morbidity of HF, little is known about the relations of obesity with severity of HF exacerbation and in-hospital mortality; therefore, we aimed to investigate the associations of obesity with severity of HF exacerbation and in-hospital mortality.

***Methods and Results*—**This retrospective cohort study of adults hospitalized for HF exacerbation used population-based data sets (the State Inpatient Databases) of 7 US states from 2012 to 2013. The outcomes were acute severity measures—use of positive pressure ventilation and hospital length of stay—and in-hospital mortality. We determined the associations between obesity and these outcomes, including adjustment for sociodemographic factors and comorbidities. We identified 219 465 patients hospitalized for HF exacerbation. Of those, 37 539 (17.1%) were obese. Obese patients had a significantly higher risk of positive pressure ventilation use compared with nonobese patients (13.6% versus 8.8%), with a corresponding adjusted odds ratio of 1.61 (95% confidence interval, 1.55–1.68; $P<0.001$). Likewise, obese patients were more likely to have hospital length of stay of ≥4 days compared with nonobese patients (62.5% versus 56.7%), with an adjusted odds ratio of 1.40 (95% confidence interval, 1.37–1.44; $P<0.001$). In contrast, obese patients had significantly lower in-hospital mortality compared with nonobese patients (1.7% versus 3.3%), with an adjusted odds ratio of 0.87 (95% confidence interval, 0.80–0.95; $P=0.002$).

***Conclusions*—**Based on large population-based data sets of patients with HF exacerbation, obesity was associated with higher acute severity measures but lower in-hospital mortality. **(*J Am Heart Assoc*. 2018;7:e008243. DOI: 10.1161/JAHA.117.008243.)**

Key Words: acute severity • epidemiology • heart failure • obesity

Heart failure (HF) affects approximately 2% (6.5 million) of Americans and is responsible for 1 million hospitalizations each year.[1] In parallel, the United States is in the midst of obesity epidemic with 35% (105 million) of adults obese.[2] Furthermore, the societal burdens of HF and obesity are rising, with estimates of >8 million Americans having HF[1] and 125 million being obese by 2030.[3]

Emerging evidence indicates a link between obesity and chronic morbidity with HF. Obese patients with HF have a greater risk of chronic comorbidities of HF (eg, arrhythmia, coronary heart disease)[4] and increased frequency of HF exacerbation.[5] In contrast to associations seen in the general population, obesity is associated to a certain degree with lower long-term mortality compared with healthy weight among patients with HF.[6,7] Despite the public health and clinical importance of HF exacerbation, little is known about the relationship of obesity with severity of HF exacerbation and in-hospital mortality.

To address this knowledge gap, we used population-based data to investigate the association of obesity with acute severity measures and in-hospital mortality among patients hospitalized for HF exacerbation. We considered use of

From the Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA (A.H., T.G., M.K.F., C.A.C., K.H.); Division of Cardiology, Department of Medicine, Columbia University Medical Center, New York, NY (Y.J.S.); Harvard T.H. Chan School of Public Health, Boston, MA (C.A.C.); Harvard Medical School, Boston, MA (C.A.C., K.H.).

Accompanying Tables S1 through S3 are available at http://jaha.ahajournals.org/content/7/6/e008243/DC1/embed/inline-supplementary-material-1.pdf

Correspondence to: Atsushi Hirayama, MD, MPH, Department of Emergency Medicine, Massachusetts General Hospital, 125 Nashua Street, Suite 920, Boston, MA. E-mail: ath877@mail.harvard.edu

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Clinical Perspective

What Is New?

- In the analysis of population-based data sets with 219 465 patients hospitalized for heart failure exacerbation, obesity was associated with acute severity of heart failure (ie, higher use of positive pressure ventilation and longer hospital length of stay) but lower in-hospital mortality compared with nonobesity.

What Are the Clinical Implications?

- Our study suggested that obesity is an important clinical factor in both long-term and acute care of heart failure.
- Our observations should encourage further research into the mechanisms linking obesity to severity of heart failure exacerbation and mortality.

positive pressure ventilation (PPV) and hospital length of stay (LOS) as the measures of severity of hospitalization, based on previous literature.[8–12]

Methods

Study Design and Setting

We conducted a retrospective cohort study using large, population-based, multi-payer data from the Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases (SID) of 7 geographically dispersed US states (Arkansas, Florida, Iowa, Nebraska, New York, Utah, and Washington) between 2012 and 2013. The HCUP is a family of healthcare databases developed through a federal, state, and industry partnership and sponsored by the US Agency for Healthcare Research and Quality. The data, analytic methods, and study materials have been made available to other researchers for purposes of reproducing the results or replicating the procedure. HCUP's Nationwide and State-Specific Databases are available for purchase from the online HCUP distributor.[13] HCUP is the largest collection of longitudinal hospital care data in the United States, with all-payer, encounter-level information. The SID captures all hospitalizations, regardless of source, from short-term, acute care, nonfederal, general, and other specialty hospitals. Additional details of the HCUP SID can be found elsewhere.[13] These 7 states were selected for their geographic distribution and high data quality and because their data included unique encrypted patient identifiers that enable longitudinal follow-up of specific individuals across years. The institutional review board of Massachusetts General Hospital approved this study, and the requirement for informed consent was waived.

Study Population

We identified all hospitalized adult patients (aged ≥18 years) with a principal discharge diagnosis of HF exacerbation, as defined by the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis codes of 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.0.[14,15] These *ICD-9-CM* codes have high specificity and positive predictive value to identify HF (both ≥90%).[16] We included only the first nonelective hospitalization for HF exacerbation for each patient during the study period. We excluded patients who left the hospital against medical advice and those who were underweight (defined by *ICD-9-CM* diagnosis codes of 783.2, 783.21, 783.22, and v85.0).[17]

Measurements

The SID contains information on the patient characteristics, including demographics (age, sex, and race/ethnicity), primary insurance type (payer), estimated household income, patient residence, *ICD-9-CM* diagnosis and procedure codes, patient comorbidities, hospital LOS, in-hospital death, and disposition. Quartile classifications of estimated median household income of residents in the patient's ZIP code were examined. Patient residence status was defined according to the National Center for Health Statistics.[18]

Primary Exposure

The primary exposure was obesity (body mass index ≥30) at the index hospitalization for HF exacerbation, as defined by the *ICD-9-CM* diagnosis codes of 278.00, 278.01, V85.3x, and V85.4x in any diagnosis field.[9] These *ICD-9-CM* codes have high specificity and positive predictive value to identify obesity (both >90%).[16]

Outcome Measures

The primary outcomes were acute severity measures—namely, use of PPV (including both noninvasive and invasive PPV) during hospitalization and hospital LOS—and in-hospital mortality. The use of noninvasive PPV was identified by *ICD-9-CM* procedure code 93.90, and the use of invasive PPV was identified by codes 96.04 and 96.70 to 96.72.[9,19]

Statistical Analyses

First, we compared the patient characteristics between the obesity and nonobesity groups using the Wilcoxon rank sum test or the χ^2 test, as appropriate. Second, to examine the associations of obesity with the acute severity measures and

Table 1. Characteristics of Patients Hospitalized for HF Exacerbation by Obesity Status

Characteristics	Obesity n=37 539 (17.1%)	Nonobesity n=181 926 (82.9%)	*P* Value
Age, y, median (IQR)	67 (57–76)	79 (68–87)	<0.001
Women	19 308 (51.4)	89 634 (49.3)	<0.001
Race/ethnicity			<0.001
Non-Hispanic white	23 223 (63.3)	121 685 (70.0)	
Non-Hispanic black	8148 (22.2)	24 846 (14.3)	
Hispanic	3641 (9.9)	17 052 (9.8)	
Asian or Pacific Islander	248 (0.7)	2737 (1.6)	
Native American	132 (0.4)	487 (0.3)	
Others	1318 (3.6)	7070 (4.1)	
Primary health insurance			<0.001
Medicare	24 678 (65.7)	146 520 (80.5)	
Medicaid	4460 (11.9)	11 580 (6.4)	
Private	5.702 (15.2)	15 936 (8.8)	
No insurance	1625 (4.3)	4143 (2.3)	
No charge	318 (0.9)	704 (0.4)	
Others	756 (2.0)	3037 (1.7)	
Quartiles for median household income			<0.001
1 (lowest)	12 679 (34.7)	51 426 (29.0)	
2	9752 (26.7)	46 574 (26.3)	
3	8428 (23.1)	43 175 (24.4)	
4 (highest)	5654 (15.5)	36 092 (20.4)	
Patient residence			<0.001
Metropolitan	25 825 (84.0)	155 837 (85.8)	
Nonmetropolitan	4913 (16.0)	32 558 (17.3)	
Selected comorbidities*			
Cardiac arrhythmia	19 200 (51.2)	107 444 (59.1)	<0.001
Chronic pulmonary disease	21 250 (56.6)	82 870 (45.6)	<0.001
Diabetes mellitus	23 769 (63.3)	70 307 (38.9)	<0.001
Depression	4897 (13.1)	17 609 (9.7)	<0.001
Hypertension	32 018 (85.3)	143 090 (78.7)	<0.001
Peripheral vascular disease	3879 (10.3)	21 247 (11.7)	<0.001
Renal failure	15 444 (41.1)	73 202 (40.2)	<0.001
Valvular disease	8363 (22.3)	58 410 (32.1)	<0.001
Hospital state			<0.001
Arkansas	1816 (4.8)	10 076 (5.5)	
Florida	18 061 (48.1)	72 047 (39.6)	
Iowa	1520 (4.1)	8124 (4.5)	
Nebraska	340 (0.9)	4965 (2.7)	
New York	11 700 (31.2)	65 596 (36.1)	
Utah	316 (0.8)	4428 (2.4)	
Washington	3786 (10.1)	16 690 (9.2)	

Continued

Table 1. Continued

Data are shown as n (%) unless otherwise specified. HF indicates heart failure; IQR, interquartile range.
*Selected from Elixhauser comorbidity measures.

in-hospital mortality, we constructed unadjusted and adjusted logistic regression models with generalized estimating equations accounting for clustering of patients within hospitals. In the multivariable models, we adjusted for age, sex, race/ethnicity, primary insurance, quartiles for median household income, residential status, 27 comorbidities (Elixhauser comorbidity measures[20] except for congestive HF and obesity) and arrhythmia, and hospital state. In this primary analysis, the hospital LOS was modeled as a binomial response ($\leq$3 versus $\geq$4 days) based on the median LOS in the study population.

To examine the robustness of our inference, we performed a series of sensitivity analyses. First, to examine the association between obesity and hospital LOS as a count variable, we constructed negative binomial regression models with generalized estimating equations. Second, we repeated the analyses with stratification by age (19–39, 40–64, and $\geq$65 years), sex (men, women), and diabetes mellitus status (defined by using Elixhauser comorbidity measures). In addition, we repeated the analyses with stratification by obstructive sleep apnea status because obstructive sleep apnea is associated with obesity.[21] Last, we used stabilized inverse probability weighting (IPW) to estimate the causal relation of obesity with the outcomes in this observational study. Weighting participants by the inverse probability of having an exposure (obesity) creates a synthetic sample in which the exposure is independent from the measured baseline covariates—that is, in the synthetic sample, obese and nonobese individuals are exchangeable.[22] Although conventional IPW enables us to obtain estimates of average effects of the exposure on outcomes, participants with very low or high probability increase the variability of the estimated effects. Instead, stabilized IPW addresses this issue and directly estimates both the main effect and its variance from conventional regression models. All analyses used STATA 14.0 (StataCorp). All *P* values were 2-tailed, with $P<0.05$ considered statistically significant.

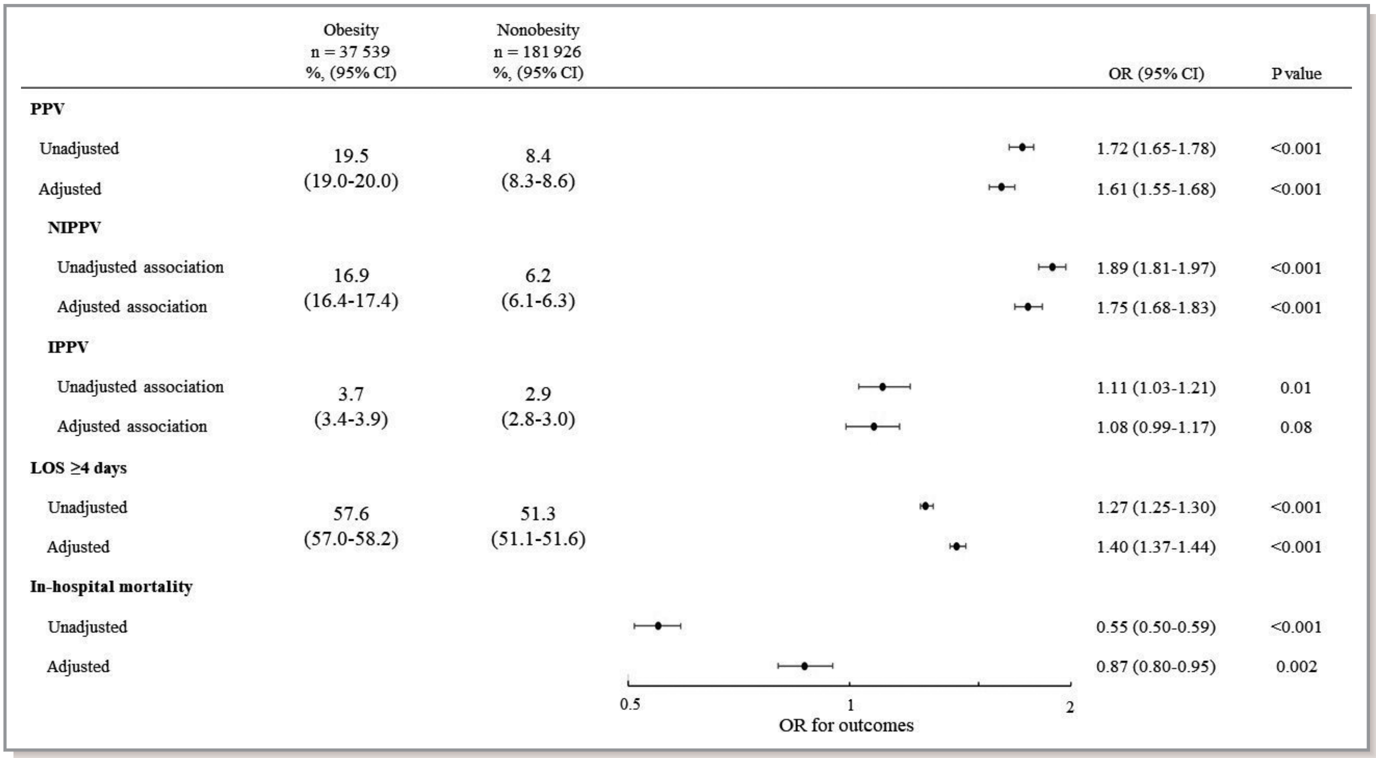

Figure. Unadjusted and adjusted associations of obesity with acute severity measures and in-hospital mortality in patients hospitalized for heart failure exacerbation. Obesity was associated with a higher risk of positive pressure ventilation (PPV) use and longer hospital length of stay (LOS) compared with nonobesity. In contrast, obesity was associated with lower in-hospital mortality compared with nonobesity. CI indicates confidence interval; IPPV, invasive positive pressure ventilation; NIPPV, noninvasive positive pressure ventilation; OR, odds ratio.

Results

Patient Characteristics

We identified 223 380 patients with nonelective hospitalization for HF exacerbation in the 7 states between January 2012 and December 2013. Of these, we excluded 2755 patients who left the hospital against medical advice and 1160 who were diagnosed as underweight. A total of 219 465 patients were eligible for the analysis. The median age was 77 years (interquartile range: 66–86 years), 49.6% were female, and 17.1% were obese. Patient characteristics differed between the obese and nonobese groups (Table 1). For example, obese patients were younger and were more likely to be non-Hispanic black and to have chronic pulmonary disease, diabetes mellitus, depression, and hypertension compared with nonobese patients (all $P<0.001$).

Association of Obesity With Acute Severity Measures and In-Hospital Mortality

Figure summarizes the unadjusted and adjusted associations of obesity with each outcome. Obese patients had a higher risk of PPV use compared with nonobese patients (13.6% versus 8.8%) in both unadjusted (odds ratio [OR]: 1.72) and adjusted (adjusted OR: 1.61) models. Likewise, obese patients had a significantly higher risk of noninvasive PPV use (adjusted OR: 1.75) and nonsignificantly higher risk of invasive PPV use (adjusted OR: 1.08). Similarly, obese patients were more likely to have hospital LOS ≥4 days (62.5% versus 56.7%), with a corresponding adjusted OR of 1.40. In the analysis modeling hospital LOS as a count variable, obese patients also had significantly longer hospital LOS, corresponding to an 11% increase in the adjusted model (95% confidence interval, 10–13% increase; $P<0.001$; Table S1). In the sensitivity analyses stratified by age (Table 2), sex (Table 3), obstructive sleep apnea status (Table 4), and diabetes mellitus status (Table S2) and in the analysis with stabilized IPW (Table S3), all of these associations were consistent.

In contrast, obesity was associated with significantly lower in-hospital mortality compared with nonobesity (1.7% versus 3.3%; unadjusted OR: 0.55). The magnitude of the association attenuated after adjusting for patient sociodemographic factors and comorbidities (adjusted OR: 0.87). Likewise, in the sensitivity analyses stratified by age (Table 2), sex (Table 3), obstructive sleep apnea status (Table 4), and

Table 2. Unadjusted and Adjusted Associations of Obesity With Acute Severity Measures and In-Hospital Mortality of HF Exacerbation by Age Category

Outcomes and Age Groups	Obesity, % (95% CI)	Nonobesity, % (95% CI)	Unadjusted OR (95% CI)	*P* Value	Adjusted OR* (95% CI)	*P* Value
Aged 18–39 y (n=3784)						
PPV use	12.3 (10.7–14.1)	6.5 (5.6–7.6)	2.21 (1.74–2.80)	<0.001	3.24 (2.42–4.35)	<0.001
NIPPV	10.2 (8.0–11.8)	3.4 (2.7–4.2)	3.29 (2.46–4.41)	<0.001	4.05 (2.86–5.71)	<0.001
IPPV	2.6 (1.8–3.5)	3.4 (2.7–4.2)	0.90 (0.60–1.35)	0.60	1.83 (1.10–3.03)	0.02
Hospital LOS ≥4 d	51.7 (49.1–54.3)	51.9 (49.8–53.9)	1.03 (0.91–1.18)	0.614	1.17 (0.99–1.36)	0.051
In-hospital mortality	1.0 (0.6–1.6)	1.5 (1.0–1.9)	0.73 (0.39–1.37)	0.32	...†	...†
Aged 40–64 y (n=46 696)						
PPV use	13.7 (13.2–14.3)	9.1 (8.7–9.4)	1.73 (1.62–1.85)	<0.001	1.72 (1.60–1.84)	<0.001
NIPPV	11.7 (11.5–12.2)	6.3 (6.0–6.6)	2.16 (2.00–2.33)	<0.001	1.97 (1.82–2.13)	<0.001
IPPV	2.6 (2.3–2.9)	3.2 (3.0–3.4)	0.81 (0.71–0.92)	0.001	0.98 (0.85–1.12)	0.73
Hospital LOS ≥4 d	59.8 (59.0–60.6)	52.8 (52.3–53.4)	1.34 (1.29–1.39)	<0.001	1.41 (1.34–1.47)	<0.001
In-hospital mortality	1.1 (1.0–1.3)	1.5 (1.4–1.7)	0.79 (0.66–0.97)	0.01	0.97 (0.80–1.18)	0.77
Aged ≥65 y (n=168 985)						
PPV use	13.6 (13.1–14.1)	8.8 (8.7–9.0)	1.72 (1.64–1.80)	<0.001	1.59 (1.51–1.67)	<0.001
NIPPV	11.8 (11.4–12.3)	7.2 (7.1–7.3)	1.85 (1.75–1.94)	<0.001	1.65 (1.56–1.73)	<0.001
IPPV	2.3 (2.1–2.5)	1.9 (1.8–2.0)	1.20 (1.09–1.33)	<0.001	1.24 (1.12–1.38)	<0.001
Hospital LOS ≥4 d	64.9 (64.3–65.6)	57.6 (57.3–57.9)	1.37 (1.33–1.42)	<0.001	1.35 (1.30–1.39)	<0.001
In-hospital mortality	2.1 (2.0–2.3)	3.7 (3.6–3.8)	0.60 (0.55–0.66)	<0.001	0.69 (0.63–0.77)	<0.001

CI indicates confidence interval; HF, heart failure; IPPV, invasive positive pressure ventilation; LOS, length of stay; NIPPV, noninvasive positive pressure ventilation; OR, odds ratio; PPV, positive pressure ventilation.
*Logistic regression model with generalized estimating equations to account for patient clustering within hospitals, adjusting for sex, race/ethnicity, primary insurance, quartiles for household income, residential status, 28 comorbidity measures, and hospital state.
†Not computed because of the small number of outcome events (n=48).

diabetes mellitus status and in the analysis with stabilized IPW (Table S3), obese patients tended to have lower in-hospital mortality.

Discussion

In this population-based study of 219 465 patients hospitalized for HF exacerbation, we found that obesity was associated with a higher risk of PPV use and longer hospital LOS and that these significant associations persisted after adjustment for potential confounders. In contrast, obesity was associated with lower in-hospital mortality. These findings were consistent across different statistical assumptions, including the stabilized IPW method. To the best of our knowledge, this study is the first that has comprehensively investigated the relation of obesity with acute severity in patients with HF exacerbation. The findings have both clinical and research importance.

Although prior epidemiologic studies have reported associations between obesity and higher chronic HF severity (eg, incident coronary heart disease, frequent HF exacerbation),[15] surprisingly little is known about the impact of obesity on the severity of HF exacerbation. The underlying mechanisms of our new findings—the observed link between obesity and acute HF exacerbation—are likely multifactorial. Although obesity-related comorbidities (eg, the higher prevalence of chronic pulmonary diseases in obese patients) played a role, the associations remained significant after adjustment for these comorbidities. Alternatively, obesity-related physiological and biological changes—for example, left ventricular hypertrophy and diastolic dysfunction,[23] activation of the renin–angiotensin–aldosterone axis,[24] increased sympathetic tone,[25] hyperleptinemia,[26] and systemic inflammation[27]—may have contributed to the severity of HF exacerbation. In addition, obesity and acute severity (higher PPV use and longer hospital LOS) was observed in other population (ie, patients hospitalized for chronic obstructive pulmonary disease).[9] Our study builds on prior epidemiologic and mechanistic studies of the obesity–HF link and extends them by demonstrating the association of obesity with acute severity measures in this large population-based sample of HF exacerbation.

Table 3. Unadjusted and Adjusted Associations of Obesity With Acute Severity Measures and In-Hospital Mortality of HF Exacerbation by Sex

Outcomes and Sex Groups	Obesity, % (95% CI)	Nonobesity, % (95% CI)	Unadjusted OR (95% CI)	*P* Value	Adjusted OR* (95% CI)	*P* Value
Men (n=110 523)						
PPV use	13.4 (12.9–13.9)	8.5 (8.3–8.7)	1.78 (1.68–1.87)	<0.001	1.72 (1.63–1.83)	<0.001
NIPPV	11.6 (11.1–12.0)	6.4 (6.3–6.6)	2.04 (1.92–2.16)	<0.001	1.93 (1.81–2.05)	<0.001
IPPV	2.5 (2.2–2.7)	2.4 (2.3–2.5)	1.03 (0.93–1.15)	0.55	1.06 (0.95–1.20)	0.29
Hospital LOS ≥4 d	59.9 (59.2–60.7)	55.4 (55.1–55.7)	1.21 (1.17–1.25)	<0.001	1.36 (1.31–1.42)	<0.001
In-hospital mortality	1.7 (1.5–1.9)	3.3 (3.2–3.4)	0.53 (0.47–0.60)	<0.001	0.88 (0.77–0.99)	0.04
Women (n=108 942)						
PPV use	13.7 (13.2–14.2)	9.2 (9.0–9.4)	1.64 (1.56–1.72)	<0.001	1.51 (1.43–1.60)	<0.001
NIPPV	11.9 (11.4–12.3)	7.6 (7.4–7.7)	1.73 (1.63–1.83)	<0.001	1.61 (1.52–1.71)	<0.001
IPPV	2.4 (2.2–2.6)	2.0 (1.9–2.1)	1.22 (1.09–1.36)	0.001	1.06 (0.94–1.20)	0.32
Hospital LOS ≥4 d	64.8 (64.1–65.5)	58.0 (57.7–58.4)	1.34 (1.30–1.38)	<0.001	1.45 (1.39–1.50)	<0.001
In-hospital mortality	1.7 (1.5–1.9)	3.2 (3.1–3.3)	0.56 (0.50–0.63)	<0.001	0.86 (0.75–0.97)	0.02

CI indicates confidence interval; HF, heart failure; IPPV, invasive positive pressure ventilation; LOS, length of stay; NIPPV, noninvasive positive pressure ventilation; OR, odds ratio; PPV, positive pressure ventilation.

*Logistic regression model with generalized estimating equations to account for patient clustering within hospitals, adjusting for age, race/ethnicity, primary insurance, quartiles for household income, residential status, 28 comorbidity measures, and hospital state.

The paradoxical relation of obesity with in-hospital mortality is novel but consistent with prior studies showing that obese patients with HF have favorable long-term survival outcomes compared with nonobese patients with HF. A cohort study of 6142 patients, for example, reported that obese patients with HF had significantly lower 30-day and 1-year mortality rates.[28] In addition, within the limited literature, few studies also investigated the relation of obesity with in-hospital mortality. In the analysis of 108 927 hospitalizations for HF exacerbation in the United States, higher body mass index was associated with lower in-hospital mortality.[29] The reasons for the association between obesity

Table 4. Unadjusted and Adjusted Associations of Obesity With Acute Severity Measures and In-Hospital Mortality of HF Exacerbation by OSA Status

Outcomes and OSA Groups	Obesity, % (95% CI)	Nonobesity, % (95% CI)	Unadjusted OR (95% CI)	*P* Value	Adjusted OR* (95% CI)	*P* Value
OSA (n=20 732)						
PPV use	19.5 (18.4–20.7)	13.0 (11.9–14.1)	1.48 (1.38–1.60)	<0.001	1.39 (1.28–1.52)	<0.001
NIPPV	16.6 (15.9–17.3)	11.3 (10.7–12.0)	1.49 (1.37–1.61)	<0.001	1.36 (1.25–1.49)	<0.001
IPPV	3.1 (2.8–3.4)	2.0 (1.8–2.3)	1.50 (1.25–1.81)	<0.001	1.58 (1.27–1.96)	<0.001
Hospital LOS ≥4 d	61.9 (61.0–62.8)	54.1 (53.0–55.1)	1.33 (1.26–1.41)	<0.001	1.45 (1.36–1.56)	<0.001
In-hospital mortality	2.0 (1.7–2.3)	2.7 (2.4–3.1)	0.71 (0.59–0.85)	<0.001	1.00 (0.80–1.25)	0.99
Non-OSA (n=198 733)						
PPV use	10.4 (9.9–11.2)	8.6 (8.3–9.0)	1.18 (1.12–1.24)	<0.001	1.19 (1.12–1.26)	<0.001
NIPPV	7.1 (6.7–7.4)	6.0 (5.9–6.1)	1.22 (1.15–1.30)	<0.001	1.22 (1.15–1.31)	<0.001
IPPV	3.4 (3.2–3.6)	3.2 (3.1–3.3)	1.10 (1.00–1.21)	0.04	1.10 (0.99–1.22)	0.07
Hospital LOS ≥4 d	62.6 (62.0–63.2)	57.0 (56.7–57.3)	1.22 (1.19–1.25)	<0.001	1.35 (1.30–1.39)	<0.001
In-hospital mortality	1.7 (1.6–1.9)	3.6 (3.4–3.6)	0.55 (0.50–0.60)	<0.001	0.86 (0.77–0.95)	0.002

CI indicates confidence interval; HR, heart failure; IPPV, invasive positive pressure ventilation; LOS, length of stay; NIPPV, noninvasive positive pressure ventilation; OSA, obstructive sleep apnea; OR, odds ratio; PPV, positive pressure ventilation.

*Logistic regression model with generalized estimating equations to account for patient clustering within hospitals, adjusting for age, race/ethnicity, primary insurance, quartiles for household income, residential status, 28 comorbidity measures, and hospital state.

and lower in-hospital mortality remain to be elucidated. The observed attenuation of the association after adjustment indicates that the covariates in the model (eg, younger age in obese patients) partially explain the association. Another possible explanation is that obese patients were more likely to have PPV therapy, and it mediated the association between obesity and in-hospital mortality. The use of PPV has been shown to improve clinical outcomes in patients with severe respiratory function impairment.[30] In addition, the observed association may be attributable to biological factors, such as lower production of circulating natriuretic peptides and greater clearance, that potentially lead to obese patients becoming symptomatic earlier.[31] Greater metabolic reserve from acute HF–induced catabolic state[32] may also explain the protective role of obesity. Moreover, unless they have sarcopenic obesity, obese patients have typically increased lean mass associated with excess body fat, and lean mass is associated with greater cardiorespiratory fitness in HF,[33–35] which may also explain the protective role of obesity. Furthermore, it is possible that obese patients were hospitalized with relatively lower severity compared with nonobese patients, thereby inflating their denominator. Any combination of these factors may have contributed, at least in part, to the observed association between obesity and lower in-hospital mortality in this population.

Potential Limitations

Our study has several potential limitations. First, although the HCUP data are thought to be accurate and are widely used to capture diagnoses and hospitalizations,[15,36] misclassifications are possible. However, the *ICD-9-CM* codes that are used to identify obesity and HF have been validated[14,15] and are known to have high specificity and positive predictive value (both >90%).[16] Furthermore, the prevalence of obesity in our cohort (17%) was comparable to the prevalence of obesity in previous HF cohorts (15–28%).[28,37–39] In addition, assuming misclassification occurred equally regardless of the outcomes, the results would have biased our estimates toward the null. Second, our data did not include the category of obesity or detailed left ventricular function. Because previous studies have indicated that the effect of obesity on clinical outcome differs between morbidly obese and less severely obese participants,[40] caution should be used in generalizing the current results. Third, as with any observational study, the causal inference of obesity with acute severity measures and in-hospital mortality might be confounded by unmeasured factors (eg, etiology of HF, left ventricular function, chronic severity, and institutional variation in resource use); however, the observed associations between obesity and outcomes remained significant after accounting for patient clustering within hospitals. Fourth, the studied data are limited by not being a random sample of the entire nation; however, the data are racially/ethnically and geographically diverse. The 7 states together represent approximately 20% of the US population, thereby supporting the generalizability of our inferences. Finally, the study population comprised only patients hospitalized for HF exacerbation. Consequently, our inferences might not be generalizable to patients with less severe HF exacerbation that does not require hospitalization. Nevertheless, our data remain highly relevant for the 1 million patients hospitalized for HF in the United States each year,[41] a population with high morbidity and healthcare utilization.

Conclusions

By using population-based data sets with 219 465 patients hospitalized for HF exacerbation across 7 US states, we found that obese patients had higher acute severity measures, such as more use of PPV and longer hospital LOS, while also having lower in-hospital mortality. These associations persisted across different statistical assumptions. Our observations should encourage further research into the mechanisms linking obesity to severity of HF exacerbation and mortality. Furthermore, given the obesity and HF epidemic in the United States, our findings underscore the importance of continued efforts to develop effective treatment strategies for obese patients with HF exacerbation.

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Disclosures

None.

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Supplemental Material

Table S1. Unadjusted and adjusted associations of obesity with hospital length-of-stay among patients hospitalized with heart failure exacerbation.

	Obesity Hospital LOS, median (IQR), day	**Non-obesity** Hospital LOS, median (IQR), day	**Unadjusted % change in hospital LOS*** (95%CI)	**P value**	**Adjusted % change in hospital LOS*** (95%CI)	**P value**
Overall	4 (3-7)	4 (2-6)	9% (7% to 10%)	<0.001	11% (10% to 13%)	<0.001
Age group						
18-39 years	4 (2-6)	4 (2-6)	-9% (-17% to -5%)	<0.001	4% (-4% to 13%)	0.31
40-64 years	4 (3-7)	4 (2-6)	5% (3% to 7%)	<0.001	11% (9% to 14%)	<0.001
≥65 years	5 (3-7)	4 (3-6)	13% (11% to 14%)	<0.001	12% (10% to 14%)	<0.001
Sex						
Male	4 (3-7)	4 (2-6)	6% (4% to 8%)	<0.001	10% (8% to 12%)	<0.001
Female	5 (3-7)	4 (3-6)	12% (10% to 14%)	<0.001	12% (10% to 14%)	<0.001

Abbreviations: CI, confidence interval; LOS, length-of-stay

* Unadjusted and adjusted negative binomial regression models using generalized estimating equations to account for patient clustering within hospitals.

Table S2. Unadjusted and adjusted associations of obesity with acute severity measures and in-hospital mortality of heart failure exacerbation, according to diabetes mellitus status.

Outcomes and DM groups	Obesity (95%CI)	Non-obesity (95%CI)	Unadjusted OR (95%CI)	P value	Adjusted OR* (95%CI)	P value
DM (n=94,076)						
Positive pressure ventilation use	14.5% (13.7%-15.2%)	9.3% (9.0%-9.7%)	1.69 (1.57-1.81)	<0.001	1.59 (1.46-1.74)	<0.001
NIPPV	12.4% (11.7%-13.1%)	7.7% (7.3%-8.0%)	1.85 (1.73-1.97)	<0.001	1.70 (1.55-1.87)	<0.001
IPPV	2.7% (2.4%-3.0%)	2.4% (2.2%-2.6%)	1.15 (0.84-1.27)	0.76	1.13 (0.95-1.35)	0.17
Hospital LOS ≥4 days	63.9% (62.9%-64.9%)	56.9% (56.2%-57.5%)	1.30 (1.21-1.39)	<0.001	1.38 (1.30-1.47)	<0.001
In-hospital mortality	1.6% (1.2%-2.0%)	3.0% (2.7%-3.3%)	0.61 (0.51-0.72)	<0.001	0.83 (0.69-1.01)	0.06
Non-DM (n=125,389)						
Positive pressure ventilation use	12.4% (11.6-13.2%)	8.4% (8.1%-8.8%)	1.59 (1.46-1.73)	<0.001	1.56 (1.46-1.74)	<0.001
NIPPV	10.5% (9.5%-11.5%)	6.7% (6.3%-8.1%)	1.80 (1.66-1.97)	<0.001	1.76 (1.57-1.98)	<0.001
IPPV	2.2% (1.9%-2.7%)	2.1% (2.0%-2.3%)	1.03 (0.88-1.23)	0.76	0.92 (0.73-1.16)	0.48
Hospital LOS ≥4 days	59.5% (58.2%-60.9%)	53.2% (52.7%-53.7%)	1.30 (1.21-1.38)	<0.001	1.52 (1.41-1.63)	<0.001
In-hospital mortality	1.7% (1.3%-2.1%)	4.0% (3.9%-4.1%)	0.48 (0.39-0.57)	<0.001	0.73 (0.58-0.92)	0.01

Abbreviations: OR, odds ratio; CI, confidence interval; DM, diabetes mellitus; NIPPV, non-invasive positive pressure ventilation; IPPV, invasive positive pressure ventilation; LOS, length-of-stay.

* Logistic regression model with generalized estimating equations to account for patient clustering within hospitals, adjusting for age, race/ethnicity, primary insurance, quartiles for household income, residential status, 28 comorbidity measures, and hospital state.

Table S3. Associations of obesity with acute severity measures of heart failure exacerbation and in-hospital mortality using stabilized inverse probability weighting method.

Outcomes	**Odds Ratio** (95%CI)	**P value**
Positive pressure ventilation use	1.59 (1.50-1.69)	<0.001
NIPPV	1.73 (1.62-1.86)	<0.001
IPPV	1.10 (0.98-1.23)	0.11
Hospital LOS ≥4 days	1.39 (1.33-1.45)	<0.001
In-hospital mortality	0.85 (0.74-0.97)	0.02

Abbreviations: OR, odds ratio; CI, confidence interval; NIPPV, non-invasive positive pressure ventilation; IPPV, invasive positive pressure ventilation; LOS, length-of-stay.