

Association Between Obesity and Acute Severity Among Patients Hospitalized for Asthma Exacerbation



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What is already known about this topic? The literature has linked obesity to incident asthma and chronic morbidity (eg, suboptimal asthma control, frequent exacerbations, and increased use of oral corticosteroids).

What does this article add to our knowledge? We found that obese adults hospitalized for asthma exacerbation were more likely to have higher acute severity (ie, overall mechanical ventilation use, noninvasive positive pressure ventilation use, and longer hospital length-of-stay) in comparison with nonobese adults.

How does this study impact current management guidelines? Our findings illustrate that obesity is associated with acute severity of asthma exacerbation and underscore the importance of continued public health campaigns against obesity, which might curb asthma-related healthcare utilization.

BACKGROUND: Although studies have demonstrated relations between obesity and incident asthma, little is known about the association of obesity with acute severity in adults hospitalized for asthma exacerbation.

OBJECTIVES: To investigate the association of obesity with acute severity of asthma exacerbation.

METHODS: This is a retrospective cohort study using population-based data of 8 geographically diverse US states from 2010 through 2013. We included adults (age 18-54 years) hospitalized for asthma exacerbation. The outcome measures were markers of acute severity—use of mechanical ventilation (defined by noninvasive positive pressure

ventilation and/or invasive mechanical ventilation) and hospital length of stay. To determine the association of obesity with each outcome, we fit multivariable models adjusting for patient-level confounders (eg, age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, and comorbidities) and potential patient clustering within hospitals.

RESULTS: Among the 72,086 patients hospitalized for asthma exacerbation, 24% were obese. Obesity was associated with a significantly higher risk of any mechanical ventilation use (8.3% vs 5.0%; adjusted odds ratio [OR], 1.77; 95% CI, 1.63-1.92; $P < .001$) driven by the higher risk of noninvasive positive pressure ventilation use (7.2% vs 3.4%; adjusted OR, 2.14; 95% CI, 1.96-2.35; $P < .001$). Likewise, obese patients were more likely to have a hospital length of stay of 3 or more days compared with nonobese patients (59.4% vs 46.5%; adjusted OR, 1.37; 95% CI, 1.32-1.43; $P < .001$). These findings were consistent with stratifications by age, sex, and race/ethnicity.

CONCLUSIONS: In this population-based study of adults hospitalized for asthma exacerbation, obesity was associated with higher acute severity. © 2018 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;6:1936-41)

Key words: Asthma; Adults; Obesity; Acute severity; Hospitalization

INTRODUCTION

Asthma and obesity are major health problems, with a significant impact on the US health care system. The prevalence of asthma remains high, affecting 8% (18 million) of American adults.¹ In addition, the burden of asthma-related health care utilization is substantial—approximately 385,000 annual

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Conflicts of interest: C. A. Camargo has provided asthma-related consulting services to AstraZeneca, GlaxoSmithKline, Novartis, and Teva. K. Hasegawa has received grants for asthma-related research from Novartis and Teva. The rest of the authors declare that they have no relevant conflicts of interest.

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Abbreviations used

HCUP- Healthcare Cost and Utilization Project
ICD-9-CM- International Classification of Diseases, Ninth
Revision, Clinical Modification
IPW- Inverse probability weighting
NIPPV- Noninvasive positive pressure ventilation
OR- Odds ratio

hospitalizations with \$2.3 billion direct cost each year.² In parallel, the United States has also experienced an obesity epidemic.³ It is anticipated that there will be a 33% increase in obesity prevalence over the next 2 decades.⁴

The literature has linked obesity to incident asthma⁵ and chronic morbidity (eg, suboptimal asthma control, frequent exacerbations,⁶ and increased use of oral corticosteroids^{7,8}). In contrast, only a few studies have examined the relations between obesity and acute asthma severity in adults.⁹⁻¹² Studies of emergency department patients with asthma exacerbation have reported that, in obese adults, the risk of hospitalization—a marker for acute severity—is no different^{12,13} or higher^{9,10} than in nonobese patients. However, the inferences may have been limited by the small sample sizes, confounding, and potential issues of generalizability. Despite the clinical and public importance of asthma exacerbation, the relation of obesity with in-hospital acute severity in adults remains largely unclear.

In this context, we used large, population-based, all-payer databases from 8 US states to investigate the association of obesity with the markers for acute severity and in-hospital mortality in adults hospitalized for asthma exacerbation. Specifically, we hypothesized *a priori* that obese adults hospitalized for asthma exacerbation have higher acute severity (defined by the use of mechanical ventilations and hospital length of stay [LOS]) when compared with nonobese patients.

METHODS

Study design and setting

We performed a retrospective cohort study using the Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases from 8 racially/ethnically and geographically diverse US states (Arkansas, California, Florida, Iowa, Nebraska, New York, Utah, and Washington) from January 2010 through December 2013. The HCUP is the largest administrative longitudinal health care database containing all-payer encounter-level information in the United States. It is managed by the Agency for Healthcare Research and Quality and developed through a federal-state-industry partnership. The HCUP State Inpatient Databases include all inpatient discharge records, regardless of source or disposition, from all acute care, nonfederal, general, and other specialty hospitals within the states. Additional information of HCUP State Inpatient Databases can be found elsewhere.¹⁴ The 8 states were selected considering their geographic distribution and high data quality. The study period was chosen on the basis of availability of databases. This study was approved by the institutional review board of Massachusetts General Hospital.

Study population

We included all adult patients (age 18-54 years) who had an unplanned hospitalization with a principal diagnosis of asthma, defined by the *International Classification of Diseases, Ninth Revision*,

Clinical Modification (ICD-9-CM) diagnosis code of 493.xx.⁹ We included only the first hospitalization for asthma exacerbation for each patient during the study period. We excluded patients who were underweight (defined as *ICD-9-CM* codes 783.2, 783.21, 783.22, and v85.0)¹⁵ because these patients may represent a unique phenotype compared with normal or overweight counterparts.^{16,17} In addition, we excluded patients who were 55 years or older, due to the difficulty of distinguishing asthma from chronic obstructive pulmonary disease,⁹ and those who left hospital against medical advice.

Measurements

The databases include patient characteristics such as demographic characteristics (age, sex, race/ethnicity), primary insurance type, quartiles for estimated median household income, patient residence, *ICD-9-CM* diagnoses, patient comorbidities, procedures, hospital course, and disposition. Quartile classifications of estimated median household income of residents were based on the patient's ZIP code. Patient comorbidities were measured by the Elixhauser comorbidity measures,^{11,18} a method of identifying comorbidities on the basis of *ICD-9-CM* diagnoses. The residential status was defined according to the National Center for Health Statistics.

Primary exposure

The primary exposure was obesity, as defined by *ICD-9-CM* diagnosis codes of 278.00, 278.01, v85.31-v85.39, and v85.41-85.45.¹⁹⁻²¹ These *ICD-9-CM* codes have a high specificity and positive predictive value to identify obesity (both >90%).²²

Outcome measures

The primary outcome measures were markers of acute severity—the use of mechanical ventilation (defined by noninvasive positive pressure ventilation [NIPPV] and/or invasive mechanical ventilation) and hospital LOS. The secondary outcome measure was in-hospital mortality during the hospitalization for asthma exacerbation. The use of NIPPV was identified by *ICD-9-CM* procedure code 93.90; the use of invasive mechanical ventilation was identified by the codes 96.04 and 96.70 to 96.72.²³

Statistical analysis

We compared the patient characteristics between the obesity and nonobesity groups by using chi-square and Wilcoxon signed rank test as appropriate. To examine the association between obesity and each outcome, we fit unadjusted and adjusted logistic regression models for each of the binomial responses with the use of generalized estimating equations accounting for potential clustering of patients within hospitals. In the primary analysis, we modeled hospital LOS as a binomial response based on the median LOS (ie, ≤ 2 days vs ≥ 3 days). The cutoff value of 3 days was decided on the basis of previous literature of patients hospitalized for asthma exacerbation where the overall mean hospital LOS was 2.7 days.²⁴ In addition, the overall median LOS was 3 days in our data. In the adjusted models, we adjusted for age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities (29 Elixhauser comorbidity measures¹⁸ and arrhythmia¹¹), hospital state, and calendar year. A set of potential confounders was chosen *a priori* on the basis of clinical plausibility and *a priori* knowledge.

To examine the robustness of inferences, we performed a series of sensitivity analyses. First, we repeated the analysis with stratification by age (<40 and ≥ 40 years), sex, and race/ethnicity (non-Hispanic white, non-Hispanic black, and Hispanic). Next, to examine the association between obesity and hospital LOS as a count variable, we

fit unadjusted and adjusted negative binomial regression models with the use of generalized estimating equations. This model has advantages of no need to define an arbitrary cutoff point of LOS and accounts for overdispersion of data. Finally, to estimate the average causal effect of obesity on each outcome, we used stabilized inverse probability weighting (stabilized IPW).²⁵ Weighting the inverse probability to have an exposure (obesity) creates a synthetic sample where the exposure becomes independent from measured baseline covariates. Consequently, in the synthetic sample, obese and non-obese individuals become exchangeable. While conventional IPW may have a greater variability of the estimated effects in subjects with a very low or high probability score, stabilized IPW enables us to directly estimate both the main effect and variance from conventional regression models.²⁵ All analyses were performed by STATA 14.0 (STATA Corp, College Station, Texas). All *P* values were 2-tailed and considered statistically significant with *P* values of less than .05.

RESULTS

We identified 72,086 patients hospitalized for asthma exacerbation in the 8 US states from January 2010 through December 2013. Overall, the median age was 43 years (interquartile range, 33–49 years), 70.2% were women, and 44.7% were non-Hispanic white. Among these, 17,479 patients (24.3%) were obese (Table I). The patient characteristics differed by obesity status. For example, obese patients were more likely to be women, Medicare beneficiaries, and living in lower household income areas compared with nonobese patients (all *P* < .001). In addition, obese patients were more likely to have several comorbidities, such as congestive heart failure, depression, and diabetes (all *P* < .001), compared with nonobese patients.

Figure 1 illustrates the unadjusted and adjusted associations between obesity and each outcome. Obesity was associated with a significantly higher risk of overall mechanical ventilation use (8.3% vs 5.0%; unadjusted odds ratio [OR], 1.89; 95% CI, 1.76–2.03; *P* < .001). This association remained significant after adjusting for patient-level potential confounders (age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities, hospital state, and calendar year) and potential clustering of patients within hospitals. When dividing overall mechanical ventilation use into NIPPV and invasive mechanical ventilation, obesity was associated with a significantly higher risk of NIPPV use in both unadjusted (7.2% vs 3.4%; unadjusted OR, 2.53; 95% CI, 2.32–2.75; *P* < .001) and adjusted (adjusted OR, 2.14; 95% CI, 1.96–2.35; *P* < .001) models. There was no statistically significant association with risk of invasive mechanical ventilation use in the adjusted model (*P* = .12). As for hospital LOS, obese patients were more likely to have a hospital LOS of 3 or more days compared with nonobese patients (59.4% vs 46.5%; adjusted OR, 1.37; 95% CI, 1.32–1.43; *P* < .001). The number of asthma deaths was low (*n* = 116), which limited statistical power, but there was no significant difference in in-hospital mortality between obesity and nonobesity groups (0.15% vs 0.16%, respectively; *P* = .97).

In the sensitivity analyses, these results persisted with stratification by age, sex, and race/ethnicity (see Table E1 in this article's Online Repository at www.jaci-inpractice.org) except for a lower risk of invasive mechanical ventilation use among obese men. Although there were some statistically significant

TABLE I. Characteristics of patients hospitalized for asthma exacerbation, according to obesity status

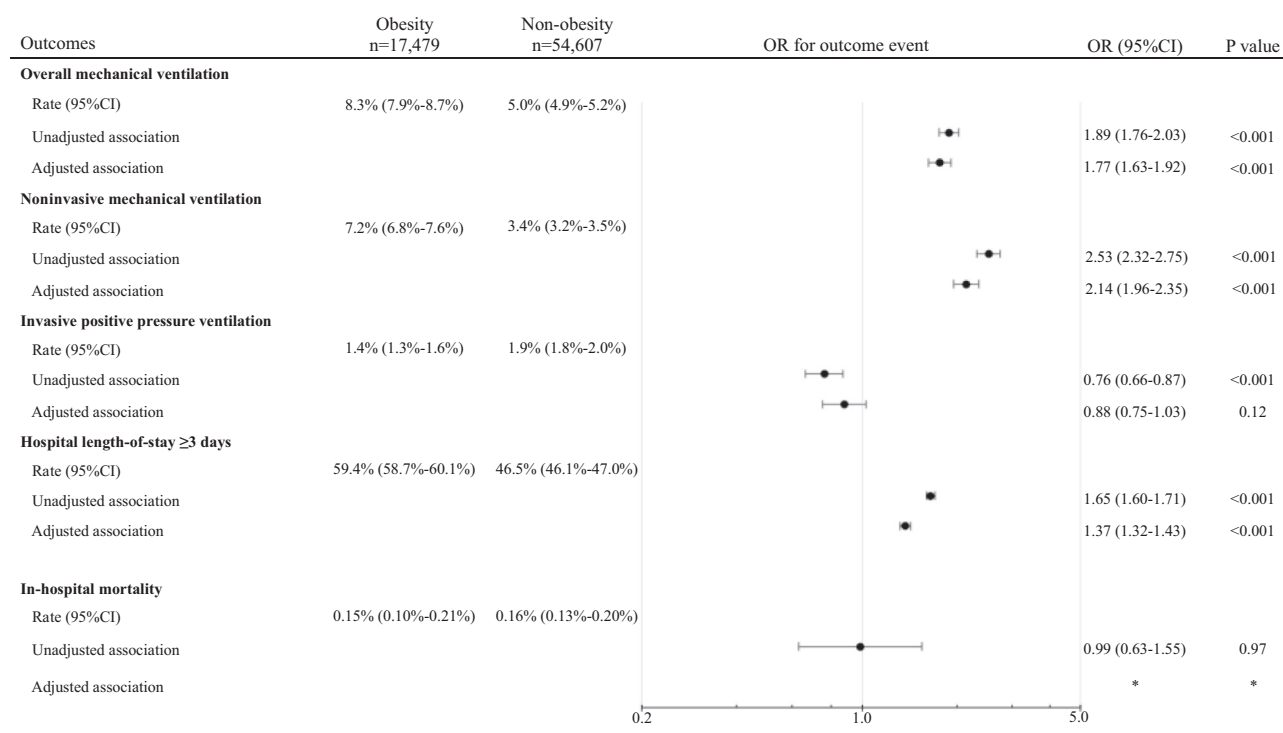
Characteristic	Obesity (n = 17,479 [24.3%])	Nonobesity (n = 54,607 [75.7%])	<i>P</i> value
Age (year), median (IQR)	45 (37–50)	43 (32–49)	<.001
Female sex	13,798 (79.0)	36,586 (67.3)	<.001
Race/ethnicity			<.001
Non-Hispanic white	7,667 (45.3)	23,199 (44.5)	
Non-Hispanic black	5,154 (30.4)	14,154 (27.2)	
Hispanic	3,225 (19.1)	10,855 (20.8)	
Others	887 (5.2)	3,877 (7.4)	
Primary health insurance			<.001
Medicare	3,030 (17.4)	6,000 (11.0)	
Medicaid	6,387 (36.6)	18,271 (33.5)	
Private	5,069 (29.0)	17,399 (31.9)	
No insurance	2,033 (11.6)	9,214 (16.9)	
No charge	333 (1.9)	1,208 (2.2)	
Others	613 (3.5)	2,489 (4.6)	
Median household income quartile			<.001
1 (lowest)	6,921 (41.4)	19,408 (37.8)	
2	4,161 (24.9)	12,691 (24.7)	
3	3,497 (20.9)	11,363 (22.1)	
4 (highest)	2,125 (12.7)	7,940 (15.5)	
Patient residence			.90
Metropolitan	16,148 (92.7)	50,369 (92.7)	
Nonmetropolitan	1,270 (7.3)	3,978 (7.3)	
Selected comorbidities*			
Congestive heart failure	1,767 (10.1)	1,766 (3.2)	<.001
Depression	3,097 (17.7)	6,941 (12.7)	<.001
Diabetes	5,915 (33.8)	6,734 (12.3)	<.001
Drug abuse	1,064 (6.1)	4,835 (8.9)	<.001
Hypertension	9,292 (53.2)	15,421 (28.2)	<.001
Renal failure	644 (3.7)	1,017 (1.9)	<.001
Hospital state			<.001
Arkansas	471 (2.7)	1,739 (3.2)	
California	3,287 (18.8)	8,753 (16.0)	
Florida	6,516 (37.3)	16,544 (30.3)	
Iowa	382 (2.2)	1,147 (2.1)	
Nebraska	199 (1.1)	836 (1.5)	
New York	5,286 (30.2)	21,296 (39.0)	
Utah	171 (1.0)	930 (1.7)	
Washington	1,167 (6.87)	3,362 (6.2)	
Hospitalization year			.054
2010	19,828 (36.3)	6,301 (36.1)	
2011	15,282 (28.0)	4,865 (27.8)	
2012	10,511 (19.3)	3,286 (18.8)	
2013	8,986 (16.5)	3,027 (17.3)	

IQR, Interquartile range.

Data are shown as n (%) unless otherwise specified.

*Selected from 29 Elixhauser comorbidity measures and arrhythmia.

interactions of obesity with age and sex in the setting of large sample size (see Table E2 in this article's Online Repository at www.jaci-inpractice.org), there was no substantial heterogeneity (or clinically meaningful interactions) in the observations across the age, sex, and race/ethnicity strata. Likewise, the associations



Abbreviations: CI, confidence interval; OR, odds ratio

* Adjusted model was not constructed because of the relatively small number of in-hospital mortality (n=116)

FIGURE 1. Unadjusted and adjusted associations of obesity with acute severity markers of asthma exacerbation and in-hospital mortality. In patients hospitalized for asthma exacerbation, obese patients were more likely to have markers of higher acute severity, including any mechanical ventilation use, noninvasive mechanical ventilation use, and hospital LOS of 3 or more days, when compared with nonobesity. These associations remained significant after adjusting for the potential confounders and potential clustering within the hospitals. The number of asthma deaths was low (n = 116), which limited statistical power, but there was no significant association between obesity and in-hospital mortality. * Adjusted model was not constructed because of the relatively small number of in-hospital mortality (n = 116).

were also consistent across the median household income and patient residence strata (see Table E3 in this article's Online Repository at www.jaci-inpractice.org). In addition, consistent with the primary analysis, the analysis modeling hospital LOS as a count variable (see Table E4 in this article's Online Repository at www.jaci-inpractice.org) also showed that obese patients had a significantly longer hospital LOS, corresponding to a 24% increase (95% CI, 22%-27% increase) in the unadjusted model and 13% increase (95% CI, 11%-16% increase) in the adjusted model. Last, in the analysis using the stabilized IPW method, the results were consistent with the primary analysis, suggesting the causal association of obesity with acute severity of asthma exacerbation (see Table E5 in this article's Online Repository at www.jaci-inpractice.org).

DISCUSSION

By analyzing population-based data from 72,086 patients hospitalized for asthma exacerbation in 8 US states, we found that obese patients had significantly higher acute severity, including overall mechanical ventilation use and longer hospital LOS, when compared with nonobese patients. In contrast, there was no significant difference in in-hospital mortality between obese and non-obese patients although the number of asthma deaths was very low, which limited statistical power. These associations were consistent across the several sensitivity analyses with different statistical

assumptions, including stabilized IPW. To our knowledge, this is the first study that has investigated the relations of obesity with acute severity in adults hospitalized for asthma exacerbation.

Consistent with our inferences, within the limited literature, studies in the emergency department setting have reported the association of obesity and higher acute severity.^{9,10} For example, a US-based multicenter chart-review study of 1227 emergency department adult patients with asthma exacerbation reported that obesity was associated with a higher risk of hospitalization compared with nonobesity.⁹ Similarly, another single-center study of 426 adults with asthma exacerbation in Uruguay reported significant obesity-hospitalization risk associations.¹⁰ Likewise, an analysis of administrative data of US children (aged 2-18 years) hospitalized for asthma exacerbation demonstrated that obesity is associated with a higher risk of mechanical ventilation use and longer hospital LOS.²⁶ In addition, the literature of all-cause hospitalizations has documented that obese individuals have longer hospital LOS through an increased prevalence of comorbidities, complications, and longer recovery.^{27,28} Our study corroborates these previous studies, and extends them by demonstrating, in a large population-based data set, the robust association between obesity and acute severity in patients hospitalized for asthma exacerbation.

The underlying mechanism(s) of the observed obesity-acute severity relation warrants investigation. The literature has linked

obesity to increased systemic inflammation by adipocyte-derived proinflammatory mediators (eg, leptin),²⁹⁻³¹ increased airway obstruction and inflammation,³²⁻³⁴ decreased corticosteroid responsiveness,³⁵⁻³⁹ altered gut microbiome modulating host immune response,⁴⁰ obesity-associated restrictive ventilatory patterns and reduced expiratory reserve volume,⁴¹ and higher prevalence of comorbidities (eg, gastroesophageal reflux). Previous studies of bariatric surgery—the most effective weight reduction measure—and asthma have shown that bariatric surgery improves airway hyperresponsiveness in obese patients with asthma,⁴² and that bariatric surgery reverses the obesity-related increased proinflammatory mediator profiles,²⁹ both supporting the obesity-asthma morbidity causal link. Each of these mechanisms may affect this particular population to develop altered pulmonary pathophysiology and higher acute severity, resulting in higher use of mechanical ventilation and longer LOS.^{43,44} Interestingly, our study showed no significant association between obesity and the risk of invasive mechanical ventilation use even with sufficient statistical power (1303 outcome events). This observation might be explained, at least in part, by the possibility that clinicians were more reluctant to attempt tracheal intubations on obese patients because obesity is a known risk factor for difficult intubation and extubation.⁴⁵⁻⁴⁸

We found no significant associations between obesity and in-hospital mortality despite the observed obesity-acute severity association. A study of adults (aged >40 years) hospitalized with several conditions (eg, asthma, cardiovascular diseases, and cancer) reported that a higher body mass index was associated with an increased risk of in-hospital mortality,⁴⁹ whereas a meta-analysis of 17 studies has shown that obesity is associated with favorable survival outcomes in other respiratory conditions, such as chronic obstructive pulmonary disease.⁵⁰ This apparent discrepancy in the literature might be partially attributable to the differences in study population, study designs, settings, or any combination of these factors. Alternatively, a limited statistical power from the low rate of in-hospital mortality among obese and nonobese patients in the present study (0.15% vs 0.16%) may be an explanation for not detecting a statistically significant difference in this outcome measure. The potential protective effect of obesity on asthma merits further research.

Potential limitations

The study has several potential limitations. First, the lack of information on body mass index may have underestimated the prevalence of obesity. The sensitivity of *ICD-9-CM* codes for identifying obesity is shown to be poor,^{51,52} while the specificity and positive predictive value for identifying obesity are both 90% or more.²² It is possible that those classified as obese had a very high body mass index, and that our inferences of obese patients having a higher acute severity may not be generalizable to patients with mild-to-moderate obesity. Second, as with any observational studies, the observed associations may be confounded by unmeasured factors, such as smoking status, chronic severity of asthma, and institutional variability in resource use. In addition, the observed associations between obesity and acute severity markers of asthma exacerbation remained significant after accounting for patient clustering at the hospital level. Furthermore, the significant associations persisted in the stabilized IPW, supporting causality in the association of interest. Third, the studied data were not a random sample of the entire population in the United States. However, the data were

racially/ethnically and geographically diverse. In addition, the 8 states together represent approximately 30% of the US population,⁵³ thereby supporting the generalizability of our inferences. Finally, because our study sample consisted of patients hospitalized for asthma exacerbation, our inferences may not be generalizable to patients with less severe asthma exacerbations. However, our findings remain highly relevant to the population of approximately 400,000 US adults hospitalized for asthma each year, involving high morbidity and health care utilization.²

CONCLUSIONS

By analyzing population-based data from 72,086 patients hospitalized for asthma exacerbation, we found that obese patients were more likely to have a higher acute severity—that is, overall mechanical ventilation use and a longer hospital LOS—in comparison with nonobese patients. These associations persisted after adjusting for potential confounders and across the sensitivity analyses with different statistical assumptions. Our findings should facilitate further research into the mechanisms underlying the observed obesity-acute severity link to develop therapeutic interventions in this high-risk population. Last, our observations also underscore the importance of continued public health campaigns against obesity, which might curb asthma-related health care utilization.

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TABLE E1. Unadjusted and adjusted associations of obesity with acute severity markers of asthma exacerbation and in-hospital mortality

Outcomes and strata	Obesity (95% CI)	Nonobesity (95% CI)	Unadjusted OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
Overall (n = 72,086)						
Mechanical ventilation	8.3% (7.9%-8.7%)	5.0% (4.9%-5.2%)	1.89 (1.76-2.03)	<.001	1.77 (1.63-1.92)	<.001
Noninvasive	7.2% (6.8%-7.6%)	3.4% (3.2%-3.5%)	2.53 (2.32-2.75)	<.001	2.14 (1.96-2.35)	<.001
Invasive	1.4% (1.3%-1.6%)	1.9% (1.8%-2.0%)	0.76 (0.66-0.87)	<.001	0.88 (0.75-1.03)	.12
Hospital LOS ≥ 3 d	59.4% (58.7%-60.1%)	46.5% (46.1%-47.0%)	1.65 (1.60-1.71)	<.001	1.37 (1.32-1.43)	<.001
In-hospital mortality	0.15% (0.10%-0.21%)	0.16% (0.13%-0.20%)	0.99 (0.63-1.55)	.97	†	†
Age <40 y (n = 27,855)						
Mechanical ventilation	7.3% (6.6%-8.0%)	5.1% (4.8%-5.4%)	1.60 (1.41-1.80)	<.001	1.61 (1.40-1.85)	<.001
Noninvasive	6.0% (5.4%-6.7%)	3.0% (2.8%-3.2%)	2.28 (1.98-2.63)	<.001	2.05 (1.74-2.41)	<.001
Invasive	1.5% (1.2%-1.8%)	2.3% (2.1%-2.5%)	0.66 (0.52-0.84)	.001	0.82 (0.63-1.07)	.14
Hospital LOS ≥ 3 d	50.1% (48.8%-51.4%)	38.9% (38.2%-39.5%)	1.55 (1.46-1.64)	<.001	1.30 (1.22-1.39)	<.001
In-hospital mortality	0.07% (0.001%-0.01%)	0.13% (0.08%-0.18%)	0.55 (0.19-1.62)	.28	†	†
Age ≥ 40 y (n = 44,231)						
Mechanical ventilation	8.8% (8.3%-9.3%)	4.9% (4.7%-5.2%)	2.03 (1.86-2.22)	<.001	1.85 (1.67-2.04)	<.001
Noninvasive	7.7% (7.2%-8.2%)	3.6% (3.4%-3.8%)	2.56 (2.32-2.83)	<.001	2.19 (1.96-2.44)	<.001
Invasive	1.4% (1.2%-1.6%)	1.6% (1.5%-1.8%)	0.85 (0.71-1.02)	.09	0.89 (0.72-1.09)	.25
Hospital LOS ≥ 3 d	63.9% (63.0%-64.8%)	51.8% (51.2%-52.3%)	1.64 (1.57-1.71)	<.001	1.40 (1.34-1.47)	<.001
In-hospital mortality	0.19% (0.11%-0.27%)	0.18% (0.14%-0.23%)	1.09 (0.67-1.77)	.74	†	†
Male (n = 21,421)†						
Mechanical ventilation	11.3% (10.2%-12.3%)	6.5% (6.1%-6.8%)	2.00 (1.76-2.26)	<.001	1.71 (1.48-1.97)	<.001
Noninvasive	10.2% (9.3%-11.2%)	4.2% (3.9%-4.5%)	2.93 (2.54-3.37)	<.001	2.25 (1.92-2.63)	<.001
Invasive	1.3% (1.0%-1.7%)	2.6% (2.4%-2.8%)	0.50 (0.36-0.68)	<.001	0.53 (0.37-0.76)	<.001
Hospital LOS ≥ 3 d	55.6% (54.0%-57.2%)	42.0% (41.3%-42.8%)	1.67 (1.55-1.79)	<.001	1.36 (1.25-1.47)	<.001
In-hospital mortality	0.25% (0.17%-0.32%)	0.25% (0.09%-0.41%)	1.01 (0.49-2.08)	.98	†	†
Female (n = 50,384)†						
Mechanical ventilation	7.5% (7.1%-8.0%)	4.3% (4.1%-4.5%)	1.96 (1.80-2.14)	<.001	1.79 (1.63-1.97)	<.001
Noninvasive	6.4% (6.0%-6.8%)	3.0% (2.8%-3.1%)	2.49 (2.25-2.76)	<.001	2.09 (1.87-2.33)	<.001
Invasive	1.5% (1.3%-1.7%)	1.6% (1.5%-1.7%)	0.93 (0.79-1.09)	.367	1.04 (0.86-1.25)	.71
Hospital LOS ≥ 3 d	60.4% (59.6%-61.3%)	48.9% (48.4%-49.4%)	1.59 (1.52-1.65)	<.001	1.37 (1.31-1.44)	<.001
In-hospital mortality	0.12% (0.09%-0.16%)	0.13% (0.07%-0.19%)	1.10 (0.63-1.93)	.74	†	†
Non-Hispanic white (n = 30,866)§						
Mechanical ventilation	6.8% (6.3%-7.4%)	4.3% (4.1%-4.6%)	1.63 (1.46-1.82)	<.001	1.54 (1.36-1.75)	<.001
Noninvasive	5.7% (5.2%-6.2%)	2.7% (2.5%-2.9%)	2.20 (1.93-2.50)	<.001	1.92 (1.66-2.22)	<.001
Invasive	1.4% (1.2%-1.7%)	1.9% (1.7%-2.0%)	0.75 (0.60-0.93)	.01	0.81 (0.63-1.04)	.10
Hospital LOS ≥ 3 d	62.1% (61.0%-63.1%)	50.0% (49.4%-50.7%)	1.64 (1.56-1.73)	<.001	1.40 (1.32-1.49)	<.001
In-hospital mortality	0.11% (0.06%-0.20%)	0.13% (0.09%-0.22%)	0.88 (0.42-1.86)	.74	†	†
Non-Hispanic black (n = 19,308)§						
Mechanical ventilation	10.3% (9.5%-11.2%)	5.9% (5.5%-6.2%)	2.03 (1.79-2.29)	<.001	1.81 (1.57-2.08)	<.001
Noninvasive	9.2% (8.4%-10.0%)	4.1% (3.8%-4.5%)	2.66 (2.31-3.06)	<.001	2.22 (1.89-2.60)	<.001
Invasive	1.5% (1.2%-1.8%)	2.0% (1.8%-2.3%)	0.73 (0.56-0.95)	.02	0.78 (0.58-1.05)	.11
Hospital LOS ≥ 3 d	57.4% (56.1%-58.8%)	43.8% (43.0%-44.6%)	1.68 (1.58-1.79)	<.001	1.31 (1.22-1.41)	<.001
In-hospital mortality	0.17% (0.09%-0.33%)	0.19% (0.13%-0.28%)	0.91 (0.42-1.94)	.80	†	†
Hispanic (n = 14,080)§						
Mechanical ventilation	8.4% (7.5%-9.4%)	4.2% (3.9%-4.6%)	2.27 (1.94-2.27)	<.001	2.02 (1.68-2.43)	<.001
Noninvasive	7.5% (6.6%-8.4%)	3.0% (2.7%-3.4%)	2.88 (2.39-3.46)	<.001	2.42 (1.97-2.97)	<.001
Invasive	1.2% (0.9%-1.7%)	1.5% (1.3%-1.8%)	0.85 (0.60-1.19)	.34	0.82 (0.55-1.22)	.32
Hospital LOS ≥ 3 d	59.1% (57.4%-60.8%)	45.3% (44.4%-46.3%)	1.75 (1.61-1.89)	<.001	1.45 (1.33-1.59)	<.001
In-hospital mortality	0.15% (0.06%-0.37%)	0.17% (0.11%-0.26%)	0.94 (0.35-2.57)	.91	†	†

Unadjusted and adjusted logistic regression models to account for patient clustering within hospitals.

*Adjusted for age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities, hospital state, and calendar year.

†Adjusted models were not constructed because of the relatively small number of in-hospital mortality (n = 116).

‡Two hundred eighty-one patients were excluded because sex variable was missing.

§The other races (Asian, Pacific Islander, and Native American) were excluded in this analysis because of the few number.

TABLE E2. Interactions of obesity with age, sex, and race/ethnicity

Interaction term and outcomes	<i>P</i> value for interactions
Obesity × Age	
Mechanical ventilation	.03
Noninvasive	.15
Invasive	.85
Hospital LOS ≥3 d	.03
In-hospital mortality	.06
Obesity × Sex	
Mechanical ventilation	.71
Noninvasive	.32
Invasive	.001
Hospital LOS ≥3 d	.80
In-hospital mortality	.61
Obesity × Race/ethnicity	
Mechanical ventilation	.12
Noninvasive	.31
Invasive	.72
Hospital LOS ≥3 d	.63
In-hospital mortality	.92

Adjusted for age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities, hospital state, and calendar year as well as each of the interaction terms.

TABLE E3. Unadjusted and adjusted associations of obesity with acute severity markers of asthma exacerbation and in-hospital mortality, according to the estimated median household income and patient residence

Outcomes and strata	Obesity (95% CI)	Nonobesity (95% CI)	Unadjusted OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
Median household income quartile 1 (lowest) (n = 26,329) [†]						
Mechanical ventilation	8.6% (7.9%-9.2%)	5.2% (4.9%-5.6%)	1.88 (1.67-2.10)	<.001	1.74 (1.53-1.99)	<.001
Noninvasive	7.4% (6.8%-8.1%)	3.6% (3.4%-3.9%)	2.48 (2.17-2.84)	<.001	2.17 (1.87-2.52)	<.001
Invasive	1.5% (1.3%-1.8%)	1.9% (1.7%-2.1%)	0.80 (0.64-1.00)	.05	0.84 (0.65-1.09)	.19
Hospital LOS ≥3 d	59.4% (58.3%-60.6%)	45.8% (45.1%-46.5%)	1.68 (1.59-1.77)	<.001	1.40 (1.32-1.49)	<.001
In-hospital mortality	0.18% (0.11%-0.32%)	0.20% (0.15%-0.28%)	0.93 (0.48-1.81)	.83	‡	‡
Median household income quartile 2 (n = 16,852) [†]						
Mechanical ventilation	7.2% (6.4%-8.0%)	4.5% (4.2%-4.9%)	1.65 (1.43-1.92)	<.001	1.61 (1.36-1.91)	<.001
Noninvasive	6.1% (5.4%-6.9%)	3.0% (2.7%-3.3%)	2.19 (1.85-2.59)	<.001	1.91 (1.57-2.31)	<.001
Invasive	1.2% (0.9%-1.6%)	1.9% (1.6%-2.1%)	0.65 (0.48-0.88)	.01	0.76 (0.52-1.09)	.14
Hospital LOS ≥3 d	59.2% (57.7%-60.7%)	47.2% (46.4%-48.1%)	1.63 (1.51-1.75)	<.001	1.33 (1.23-1.44)	<.001
In-hospital mortality	0.19% (0.09%-0.38%)	0.14% (0.09%-0.23%)	1.47 (0.63-3.41)	.37	‡	‡
Median household income quartile 3 (n = 14,860) [†]						
Mechanical ventilation	7.7% (6.8%-8.6%)	4.8% (4.4%-5.2%)	1.75 (1.50-2.04)	<.001	1.62 (1.36-1.93)	<.001
Noninvasive	6.4% (5.6%-7.2%)	3.3% (3.0%-3.6%)	2.20 (1.84-2.62)	<.001	1.89 (1.55-2.29)	<.001
Invasive	1.5% (1.2%-2.0%)	1.8% (1.6%-2.1%)	0.85 (0.63-1.16)	.31	0.91 (0.64-1.29)	.58
Hospital LOS ≥3 d	59.7% (58.1%-61.3%)	47.7% (46.8%-48.6%)	1.64 (1.52-1.77)	<.001	1.39 (1.28-1.52)	<.001
In-hospital mortality	0.08% (0.03%-0.26%)	0.14% (0.09%-0.23%)	0.58 (0.17-1.597)	.39	‡	‡
Median household income quartile 4 (highest) (n = 10,065) [†]						
Mechanical ventilation	8.4% (7.3%-9.6%)	4.5% (4.1%-5.0%)	2.04 (1.69-2.46)	<.001	2.03 (1.64-2.51)	<.001
Noninvasive	7.3% (6.3%-8.5%)	2.7% (2.4%-3.1%)	3.01 (2.41-3.75)	<.001	2.73 (2.14-3.48)	<.001
Invasive	1.5% (1.0%-2.1%)	2.1% (1.8%-2.4%)	0.71 (0.48-1.05)	.083	0.76 (0.49-1.18)	.23
Hospital LOS ≥3 d	62.2% (60.1%-64.2%)	49.4% (48.3%-50.5%)	1.72 (1.56-1.90)	<.001	1.43 (1.29-1.59)	<.001
In-hospital mortality	0.09% (0.02%-0.37%)	0.11% (0.06%-0.22%)	0.80 (0.18-3.65)	.78	‡	‡
Metropolitan residents (n = 66,516)						
Mechanical ventilation	8.4% (8.0%-8.9%)	5.1% (4.9%-5.3%)	1.89 (1.76-2.03)	<.001	1.74 (1.60-1.89)	<.001
Noninvasive	7.3% (6.9%-7.7%)	3.5% (3.3%-3.6%)	2.52 (2.32-2.75)	<.001	2.12 (1.93-2.33)	<.001
Invasive	1.4% (1.3%-1.6%)	1.9% (1.8%-2.1%)	0.75 (0.65-0.87)	<.001	0.85 (0.72-1.00)	.048
Hospital LOS ≥3 d	59.6% (58.8%-60.3%)	46.4% (46.0%-46.9%)	1.67 (1.62-1.74)	<.001	1.39 (1.33-1.47)	<.001
In-hospital mortality	0.16% (0.11%-0.24%)	0.17% (0.14%-0.21%)	1.01 (0.65-1.58)	.06	‡	‡
Nonmetropolitan residents (n = 5,570)						
Mechanical ventilation	6.6% (5.4%-8.1%)	3.5% (2.9%-4.0%)	1.80 (1.34-2.40)	<.001	1.94 (1.38-2.74)	<.001
Noninvasive	5.0% (4.0%-6.3%)	2.0% (1.6%-2.4%)	2.37 (1.66-3.38)	<.001	2.36 (1.55-3.58)	<.001
Invasive	1.6% (1.1%-2.4%)	1.7% (1.3%-2.1%)	0.91 (0.54-1.53)	.73	1.16 (0.63-2.12)	.63
Hospital LOS ≥3 d	58.4% (55.8%-61.0%)	46.3% (44.8%-47.8%)	1.58 (1.39-1.80)	<.001	1.26 (1.08-1.46)	.003
In-hospital mortality	0	0.11% (0.05%-0.29%)	—	—	‡	‡

Unadjusted and adjusted logistic regression models to account for patient clustering within hospitals.

*Adjusted for age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities, hospital state, and calendar year.

†Three thousand nine hundred eighty patients were excluded because the patient residence variable was missing.

‡Adjusted models were not constructed because of the relatively small number of in-hospital mortality (n = 116).

TABLE E4. Unadjusted and adjusted associations of obesity with hospital LOS among patients hospitalized with asthma exacerbation

Strata	Obesity hospital LOS (d), median (IQR)	Nonobesity hospital LOS (d), median (IQR)	Unadjusted % increase in hospital LOS compared with nonobesity (95% CI)*	P value	Adjusted % increase in hospital LOS compared with nonobesity (95% CI)*	P value
Overall	3 (2-5)	2 (1-4)	24% (22%-27%)	<.001	13% (11%-16%)	<.001
Age category						
<40 y	3 (2-4)	2 (1-3)	20% (16%-25%)	<.001	11% (7%-15%)	<.001
≥40 y	3 (2-5)	2 (2-4)	23% (20%-26%)	<.001	14% (11%-17%)	<.001
Sex						
Male	3 (2-4)	2 (1-3)	26% (21%-31%)	<.001	14% (8%-19%)	<.001
Female	3 (2-5)	2 (2-4)	22% (20%-25%)	<.001	13% (10%-16%)	<.001

IQR, Interquartile range.

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

*Adjusted for age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities, hospital state, and calendar year.

TABLE E5. Associations of obesity with acute severity markers of asthma exacerbation and in-hospital death using stabilized IPW method

Outcomes	OR (95% CI)	P value
Mechanical ventilation	1.70 (1.54-1.87)	<.001
Noninvasive	2.08 (1.85-2.32)	<.001
Invasive	0.85 (0.72-1.00)	.055
Hospital LOS ≥3 d	1.36 (1.30-1.43)	<.001
In-hospital mortality	0.95 (0.57-1.59)	.86

IPW was calculated by using age, sex, race/ethnicity, primary insurance, quartiles for household income, residential status, patient comorbidities, hospital state, and calendar year.

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