Risk of an asthma exacerbation after bariatric surgery in adults

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Background: Research on nonsurgical weight loss interventions has failed to demonstrate consistent efficacy on asthma control, although these interventions resulted in only modest weight reductions.

Objective: We sought to test the hypothesis that bariatric surgery is associated with a rapid and sustained decrease in risk of asthma exacerbation.

Methods: We performed a self-controlled case series study of 2261 obese patients with asthma aged 18 to 54 years who underwent bariatric surgery using the population-based emergency department (ED) and inpatient sample in 3 states (California, Florida, and Nebraska). The primary outcome was an ED visit or hospitalization for asthma exacerbation from 2005 through 2011. We used conditional logistic regression to compare each patient's risk of the outcome event during sequential 12-month periods using presurgery months 13 to 24 as the reference period.

Results: During the reference period, 22.0% (95% CI, 20.3% to 23.7%) of patients had an ED visit or hospitalization for asthma exacerbation. In the subsequent 12-month presurgery period, the risk did not materially change (21.7%; 95% CI, 20.0% to 23.4%), with an odds ratio (OR) of 0.98 (95% CI, 0.85-1.13) compared with the reference period. By contrast, significantly fewer ED visits or hospitalizations for asthma exacerbation occurred within 12 months after bariatric surgery (10.9%; 95% CI, 9.6% to 12.2%), corresponding to an OR of 0.42 (95% CI, 0.35-0.50). Similarly, in the subsequent period of 13 to 24 months after bariatric surgery, the risk remained significantly lower (10.9%; 95% CI, 9.6% to 12.2%), corresponding to an OR of 0.42 (95% CI, 0.35-0.50).

Conclusion: In obese patients the risk of an ED visit or hospitalization for asthma exacerbation decreased by half after bariatric surgery. This reduction suggests the effectiveness of significant weight loss on asthma morbidity. (J Allergy Clin Immunol 2015;■■■:■■■-■■■.)

Key words: *Acute asthma, emergency department, hospitalization, obesity, bariatric surgery, weight reduction, self-controlled case series study*

Asthma and obesity are important public health problems in the United States. The prevalence of asthma remains at historically high levels, affecting 26 million Americans.[1] In parallel the United States is in the midst of an obesity epidemic, with 35% of US adults obese in 2011-2012.[2] Epidemiologic studies have reported associations of obesity with the development of asthma,[3-5] increased risk of exacerbations,[6-8] and higher risk of hospitalization.[9,10] Therefore obesity is considered a potential risk factor for asthma control and health care use.[11]

However, little is known about the effect of weight reduction on asthma morbidities. Previous trials of nonsurgical weight loss interventions have failed to demonstrate consistent efficacy on asthma control, although these interventions resulted in only modest weight reductions.[12] Therefore it is possible that the amount of weight reduction achieved by using these nonsurgical measures was too small to improve asthma control. In contrast, bariatric surgery is the most effective weight loss option for morbidly obese patients among the various approaches.[13] National guidelines recommend that bariatric surgery is indicated in adults with a body mass index (BMI) of 40 kg/m^2 or greater and those with a BMI of 35 to 39.9 kg/m^2 with comorbidities, such as asthma.[14,15]

In this context we designed this study to use bariatric surgery as an instrument for examining the causal effect of a large weight reduction on asthma control. More specifically, we tested the hypothesis that bariatric surgery would be associated with a rapid and sustained decrease in the risk of emergency department (ED) visits or hospitalizations for asthma exacerbation using large population-based databases from 3 diverse states. A better understanding of the role of major weight reductions in asthma morbidity would inform strategies for obese patients with asthma.

METHODS

Study design and setting

This is a self-controlled case series study using data from the Healthcare Cost and Utilization Project (HCUP) State Emergency Department Databases (SEDD) and State Inpatient Databases (SID). This study method relies on intraperson comparisons in a population of subjects with both the exposure and outcome of interest. This method allows each patient to serve as his or her own control subject, and therefore no separate control subjects are needed. Additionally, it has advantages that effects of any time-invariant covariates (eg, patient characteristics) are implicitly controlled, thereby minimizing unmeasured confounding.[16] In this study we compared each patient's risk of

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Abbreviations used
BMI: Body mass index
ED: Emergency department
HCUP: Healthcare Cost and Utilization Project
ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification
OR: Odds ratio
RCT: Randomized controlled trial
SEDD: State Emergency Department Databases
SID: State Inpatient Databases

an ED visit or hospitalization for an asthma exacerbation during a 4-year period (ie, 2-year period before and 2-year period after bariatric surgery).

The data from California, Florida, and Nebraska HCUP SEDD and SID from 2005 to 2011 were used. The HCUP is a family of health care databases developed through a federal-state-industry partnership and sponsored by the Agency for Healthcare Research and Quality. HCUP includes the largest collection of longitudinal hospital care data in the United States with all-payer, encounter-level information. The SEDD includes all treat-and-release and transfer ED visits from short-term, acute-care, nonfederal hospitals in participating states. The SID includes all inpatient discharges from short-term, acute-care, nonfederal, general, and other specialty hospitals, including those admitted from the ED. Taken together, we identified all ED visits regardless of disposition and all hospitalizations regardless of source. Additional details of the HCUP SEDD and SID can be found elsewhere.[17,18] These 3 states were selected for their high data quality and mainly because their databases included unique encrypted patient identifiers that enable follow-up of specific patients across years. The Institutional Review Board of Massachusetts General Hospital waived review of this study.

Study population

Using the databases from 3 states, we identified all obese patients with asthma who underwent bariatric surgery. First, we defined the patients with asthma as adults aged 18 to 54 years with at least 1 ED visit or hospitalization for an asthma exacerbation between January 1, 2005, and December 31, 2011, by using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic code for asthma (493.xx) in the primary diagnosis field. We used this case definition to focus on adults with poorly controlled asthma rather than those with well-controlled asthma (ie, patients with no ED visits or hospitalizations). We excluded patients aged 55 year or older because of potential difficulty distinguishing between asthma and chronic obstructive pulmonary disease.

Then, among these asthmatic patients, we further identified those hospitalized for a bariatric surgery with a concurrent diagnosis of obesity from January 1, 2007, to December 31, 2009, by using the Current Procedural Terminology codes for bariatric surgery (43.89, 44.31, 44.38, 44.39, 44.50, 44.68, 44.69, 44.93, 44.95, 44.99, 45.51, 45.90) with the ICD-9-CM diagnostic code for obesity (278.0-278.2, V77.8, V85.3x, and V85.4).[19] We excluded patients with diagnostic codes for cancer (150.0-159.9).[19] We also excluded out-of-state residents, patients who died at hospitalization for bariatric surgery or died in the hospital during the postsurgery period, and those who had multiple bariatric surgeries during the study period.

Data of patient identifiers were available from January 1, 2005, through December 31, 2011. Therefore to accommodate analyses of the 2-year presurgery and 2-year postsurgery period, we included patients with a bariatric surgery between January 1, 2007, and December 31, 2009.

Measurements

The databases contain information on patients' characteristics, including demographics (age, sex, and race/ethnicity), primary insurance type, estimated household income, ICD-9-CM diagnosis, and procedures. The SEDD database also includes ED disposition. The patients' characteristics were determined at the time of hospitalization for bariatric surgery. Primary insurance types were categorized into Medicaid, Medicare, private sources, and "other." Race/ethnicity was categorized into non-Hispanic white, non-Hispanic black, Hispanic, and "other." Quartile classifications of estimated median household income of residents in the patient's ZIP code were examined. These values were derived from the annual ZIP code demographic data and included in the SEDD and SID databases.

Outcome measures

The primary outcome was a composite of ED visit or hospitalization for asthma exacerbation. Additionally, for the secondary outcome, we separately assessed an ED visit with asthma exacerbation and a hospitalization with asthma exacerbation.

Statistical analysis

All analyses used SAS version 9.3 software (SAS Institute, Cary, NC), and results are presented with 95% CIs, when appropriate. A 2-sided P value of less than .05 was considered statistically significant. For the graphic presentation, we calculated the proportion with an outcome event and the 95% CI for the 2 years before and after surgery in 3-month intervals. Using presurgery days 366 to 730 as the reference period, we fit a conditional logistic regression model to calculate odds ratios (ORs) for presurgery days 1 to 365, postsurgery days 0 to 365, and postsurgery days 365 to 730 because each patient was matched to his or her own reference period. We chose the use of 12-month intervals in the regression model to account for potential seasonal variations in the risk of asthma exacerbation.[8]

We performed a series of sensitivity analyses to assess the consistency of the change in risk of asthma exacerbation. First, we stratified the analysis by age group, sex, race/ethnicity, and season of bariatric surgery.

Second, we modeled the outcomes as count variables. Because there was no evidence of excess zeros or overdispersion for both the number of ED visits and the number of hospitalizations, we fit a Poisson regression model with the generalized estimating equations to account for the correlation over time.

Third, we repeated the analysis using a more restrictive definition of obesity, excluding patients with ICD-9-CM diagnostic codes of V853, 278.00, 278.02, or 278.1 at the time of bariatric surgery.

Fourth, to address the potential effect of loss to follow-up (eg, out-of-hospital deaths and emigration from the 3 states), we conducted a subgroup analysis limited to the patients who had any ED visits or hospitalizations (regardless of reason) during postsurgery days 731 through 1095 (ie, 25-36 months after the surgery). This subgroup analysis ensured that all patients were alive in the state until at least 24 months after bariatric surgery.

Lastly, to address the possibility that any decreased risk of asthma exacerbation was associated with elective abdominal surgery rather than bariatric surgery *per se* we repeated the analysis using 2 different surgical populations. We identified all adults aged 18 to 54 years who were hospitalized not through the ED for a cholecystectomy (ICD-9-CM codes 51.21-51.24 and 51.41-51.59) or hysterectomy (ICD-9-CM codes 68.31-68.79 and 68.9) with the ICD-9-CM diagnostic codes for obesity from January 1, 2007, to December 31, 2009, and who had at least 1 ED visit or hospitalization for asthma exacerbation between January 1, 2005, and December 31, 2011. Then we repeated a self-controlled case series analysis to compare the risk of asthma exacerbation during periods before and after nonbariatric surgery. These 2 surgeries were selected because of their large sample size, similar characteristics (ie, elective abdominal surgery), and absence of plausible relationships with a risk of asthma exacerbation.

RESULTS

All asthmatic patients aged 18 to 54 years who underwent bariatric surgery between January 1, 2007, and December 31, 2009, were identified from the California, Florida, and Nebraska databases (n = 2378). From this population, 105 patients who underwent multiple bariatric surgeries and 12 patients who died in

TABLE I. Baseline characteristics of asthmatic patients who underwent bariatric surgery (n = 2261)

Characteristics	
Age (y), median (IQR)	41 (33-47)
18-34	674 (29.8)
35-44	746 (33.0)
45-54	841 (37.2)
Female sex	1959 (86.6)
Race/ethnicity*	
Non-Hispanic white	1298 (57.4)
Non-Hispanic black	307 (13.6)
Hispanic	413 (18.3)
Other	61 (2.7)
Primary insurance	
Medicare	313 (13.8)
Medicaid	308 (13.6)
Private	1448 (64.0)
Other	192 (8.5)
Quartiles for median household income of patient's ZIP code	
1 (lowest)	624 (27.6)
2	605 (26.8)
3	541 (23.9)
4 (highest)	445 (19.7)
Season of bariatric surgery	
January-March	512 (22.6)
April-June	544 (24.1)
July-September	608 (26.9)
October-December	597 (26.4)
State	
California	1538 (68.0)
Florida	647 (28.6)
Nebraska	76 (3.4)

Data were expressed as numbers (percentages), unless otherwise indicated.
IQR, Interquartile range.
*Analyzed for 2079 (92.0%) patients with race/ethnicity data. Race/ethnicity data were not available in Nebraska.

the hospital during the postsurgery period were excluded, leaving 2261 patients eligible for analysis. Table I shows demographic characteristics. The median age of patients was 41 years, and most patients were women.

Fig 1 describes the risk of an ED visit or hospitalization for asthma exacerbation during the presurgery and postsurgery period by 3-month intervals. In the reference period (ie, 13-24 months before bariatric surgery) 22.0% of patients had at least 1 ED visit or hospitalization caused by an asthma exacerbation (Table II). In the subsequent period of 1 to 12 months before surgery, the risk did not materially change (21.7%), with an OR of 0.98 (95% CI, 0.85-1.13; $P = .80$). By contrast, the risk of an ED visit or hospitalization because of asthma exacerbation decreased significantly after bariatric surgery. Compared with the reference period, significantly fewer ED visits or hospitalizations for asthma exacerbation occurred within 12 months after bariatric surgery (10.9%), corresponding to an OR of 0.42 (95% CI, 0.35-0.50; $P < .001$). Similarly, in the subsequent period of 13 to 24 months after bariatric surgery, the risk remained significantly lower (10.9%), corresponding to an OR of 0.42 (95% CI, 0.35-0.50; $P < .001$).

In the analysis of secondary outcomes, the risk of asthma exacerbation after bariatric surgery decreased for 2 component events individually: ED visits and hospitalizations (Table II). The decrease in the risk after bariatric surgery was especially prominent for the hospitalization outcome. Compared with the reference period, the risk of hospitalization for asthma exacerbation was significantly less within 12 months after bariatric surgery (OR, 0.29; 95% CI, 0.21-0.40; $P < .001$) and in the period of 13 to 24 months after surgery (OR, 0.29; 95% CI, 0.21-0.41; $P < .001$).

Series of sensitivity analyses demonstrated the robustness of our findings. The temporal pattern in the risk of asthma exacerbation persisted with stratification by age, sex, race/ethnicity, and season (see Tables E1-E4 in this article's Online Repository at www.jacionline.org), modeling the outcomes as count variables (see Table E5 in this article's Online Repository at www.jacionline.org) and using the more restrictive definition of obesity (see Table E6 in this article's Online Repository at www.jacionline.org). Additionally, in a subgroup analysis that included only patients known to be alive until at least 2 years after bariatric surgery, this temporal pattern was essentially unchanged (Table III). Furthermore, in separate self-controlled case series analyses using obese adults with asthma who underwent a cholecystectomy (n = 1842) or hysterectomy (n = 1344), the risk of an ED visit or hospitalization for asthma exacerbation did not change after this nonbariatric surgery (see Table E7 in this article's Online Repository at www.jacionline.org).

DISCUSSION

In this population-based study from a 3-state population, we found that risk of an ED visit or hospitalization for asthma exacerbation decreased by half after bariatric surgery and remained significantly lower for at least 2 years. The observed decreases in risk of an asthma exacerbation were large and persisted across several different analytic assumptions. By contrast, we found no significant change in risk of asthma exacerbation after nonbariatric surgery in obese adults with asthma.

Results in context

Our data were consistent with findings from several much smaller cohort studies of obese adults with asthma who underwent bariatric surgery (n < 260). These studies suggested that bariatric surgery is associated with an improvement in pulmonary function (eg, forced vital capacity and FEV1)[20,21] and asthma control score[20,22] and a reduction in asthma medication needs.[22-25] Additionally, a single-center study of 32 morbidly obese patients with asthma reported a decreased risk of hospitalizations for asthma exacerbation after bariatric surgery.[26] Our much larger study with longer follow-up corroborated these findings and extended prior research by demonstrating the robustness of the observed benefit.

The validity of our findings is buttressed by the self-controlled case series design. This study design allows each patient to serve as his as her own control subject, thereby reducing the unmeasured confounding that can occur with traditional case-control or cohort studies.[16] Furthermore, this design is more efficient than other observational study designs because interperson variations are effectively removed from the data. Therefore the estimates of effects can be more precise. Our study meets the assumptions of these self-controlled designs in that we

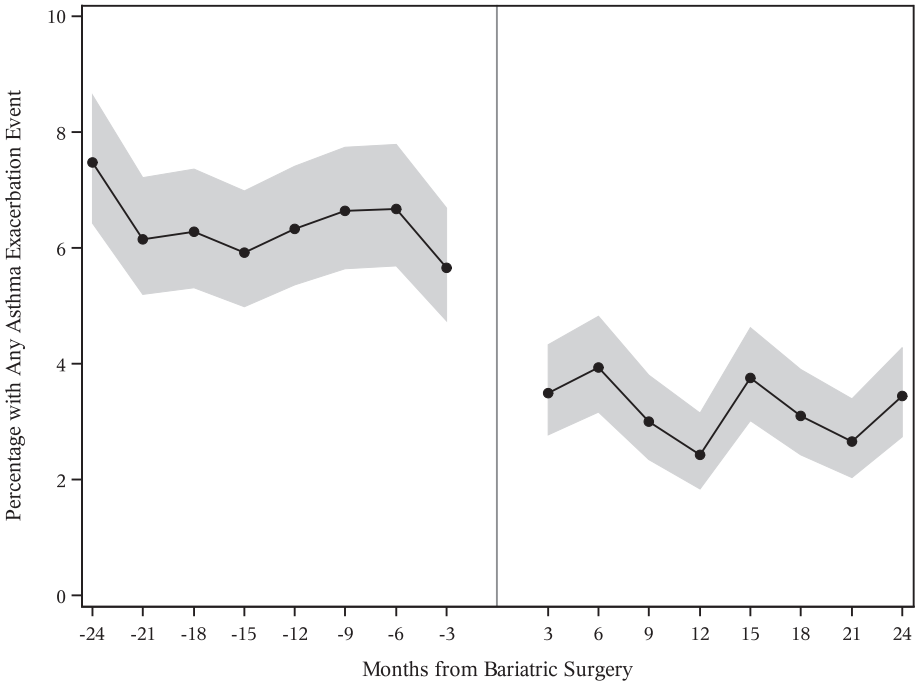

FIG 1. Risk of an asthma exacerbation before and after bariatric surgery in a 3-month interval. Shown is the proportion with a composite primary outcome of an ED visit or hospitalization with asthma exacerbation and the 95% CI for the 2 years before and after surgery in 3-month intervals. The periods were centered around the date of bariatric surgery of each patient. The results of conditional regression analysis are presented in Table E8.

TABLE II. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation, according to 12-month periods

Time interval and outcome	No. of patients (n = 2261)	Risk, % (95%)	OR (95% CI)*	*P* value
13-24 mo before bariatric surgery				
ED visit or hospitalization†	498	22.0 (20.3-23.7)	Reference	—
ED visit‡	382	16.9 (15.4-18.4)	Reference	—
Hospitalization§	165	7.3 (6.2-8.4)	Reference	—
1-12 mo before bariatric surgery				
ED visit or hospitalization†	491	21.7 (20.0-23.4)	0.98 (0.85-1.13)	.80
ED visit‡	373	16.5 (15.0-18.0)	0.97 (0.83-1.14)	.72
Hospitalization§	159	7.0 (6.0-8.1)	0.96 (0.75-1.22)	.71
0-12 mo after bariatric surgery				
ED visit or hospitalization†	247	10.9 (9.6-12.2)	0.42 (0.35-0.50)	<.001
ED visit‡	204	9.0 (7.8-10.2)	0.47 (0.39-0.57)	<.001
Hospitalization§	61	2.7 (2.0-3.4)	0.29 (0.21-0.40)	<.001
13-24 mo after bariatric surgery				
ED visit or hospitalization†	246	10.9 (9.6-12.2)	0.42 (0.35-0.50)	<.001
ED visit‡	202	8.9 (7.8-10.1)	0.47 (0.39-0.56)	<.001
Hospitalization§	62	2.7 (2.1-3.4)	0.29 (0.21-0.41)	<.001

*ORs are for each 12-month period versus the reference period (ie, 13-24 months before bariatric surgery), as calculated with conditional logistic regression.
†Composite of at least 1 ED visit or hospitalization for asthma exacerbation.
‡At least 1 ED visit for asthma exacerbation not resulting in hospitalization.
§At least 1 hospitalization for asthma exacerbation.

modeled a transient and discrete exposure and outcome that was defined by an acute event.[16]

Link between bariatric surgery and reduced risks of asthma exacerbation

An important unanswered question relates to the mechanism by which bariatric surgery reduces asthma morbidity. A potential explanation includes that bariatric surgery–associated weight loss reversed some of the obesity-asthma link. Prior research has linked obesity with increased levels of proinflammatory cytokines and adipokines (eg, leptin),[27] adipokine-induced airway remodeling and reactivity,[28] neutrophilic airway inflammation,[29] higher prevalence of comorbidities (eg, gastroesophageal reflux),[11] reduced corticosteroid responsiveness,[30] and decreased expiratory reserve volume in asthmatic patients.[31] A cohort study

TABLE III. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation among patients with any health care use during 25 to 36 months after bariatric surgery

Time interval and outcome	No. of patients (n = 830)	Risk, % (95% CI)	OR (95% CI)*	*P* value
13-24 mo before bariatric surgery				
ED visit or hospitalization†	209	25.2 (22.3-28.3)	Reference	—
ED visit‡	153	18.4 (15.9-21.2)	Reference	—
Hospitalization§	75	9.0 (7.1-11.2)	Reference	—
1-12 mo before bariatric surgery				
ED visit or hospitalization†	204	24.6 (21.7-27.7)	0.97 (0.77-1.21)	.78
ED visit‡	157	18.9 (16.3-21.7)	1.03 (0.80-1.33)	.80
Hospitalization§	72	8.7 (6.8-10.8)	0.95 (0.65-1.38)	.77
0-12 mo after bariatric surgery				
ED visit or hospitalization†	102	12.3 (10.1-14.7)	0.40 (0.30-0.52)	<.001
ED visit‡	82	9.9 (7.9-12.1)	0.47 (0.35-0.63)	<.001
Hospitalization§	29	3.5 (2.4-5.0)	0.28 (0.17-0.46)	<.001
13-24 mo after bariatric surgery				
ED visit or hospitalization†	110	13.3 (11.0-15.8)	0.44 (0.33-0.57)	<.001
ED visit‡	94	11.3 (9.2-13.7)	0.55 (0.41-0.73)	<.001
Hospitalization§	22	2.7 (1.7-4.0)	0.19 (0.11-0.34)	<.001

*ORs are for each 12-month period versus the reference period (ie, 13-24 months before bariatric surgery), as calculated with conditional logistic regression.
†Composite of at least 1 ED visit or hospitalization for asthma exacerbation. Among all ED visits and hospitalizations (regardless of reason) in this group of patients, asthma was the most frequent reason for the ED visits and hospitalizations (8.5%).
‡At least 1 ED visit for an asthma exacerbation not resulting in hospitalization.
§At least 1 hospitalization for asthma exacerbation.

of obese patients who underwent bariatric surgery reported that the pattern of increased proinflammatory markers in asthmatic patients was reversed with surgery.[28]

The literature also documented that bariatric surgery leads to significant weight loss. For example, in patients undergoing a Roux-en-Y gastric bypass, weight loss occurs rapidly over the first few months and then continues over the next 1 to 1.5 years until weight loss reaches a plateau, a mean weight loss of 35% (excess weight loss of 68%).[32] Although our data did not include the patient's BMI, the expected changes in body weight after bariatric surgery reported in the literature were paralleled by the rapid and sustained decrease in the risk of asthma exacerbation in our study. By contrast, a Cochrane systematic review of 4 randomized controlled trials (RCTs) of nonsurgical interventions demonstrated modest weight loss (1% to 15% weight loss) in the intervention groups and an improvement of asthma symptom scores in one of the 4 trials.[12] Therefore this systematic review concluded that the benefit of nonsurgical weight loss interventions for asthma control remains uncertain. In conjunction with these studies of surgical and nonsurgical interventions, our data suggest that large and sustained weight loss might be required to reverse the obesity-specific mechanisms in asthma morbidity.

High-quality RCTs of bariatric surgery in morbidly obese patients with asthma would be helpful to further establish the causality of the observed "beneficial" association between bariatric surgery and asthma outcomes. However, such trials are logistically and methodologically challenging.[12] Additionally, studies show that patients who consent to participate in the controlled framework of an RCT might be systematically different from the general population,[33,34] which raises questions about generalizability. As an alternative, our population-based data reflect the effectiveness of bariatric surgery in the natural setting of a real population and current clinical practice, therefore enhancing the potential generalizability of the findings. We also note multiple much smaller studies arrived at similar conclusions despite differing designs and populations. Furthermore, there are plausible mechanisms to support these findings. Taken together, our data lend significant support to the concept that bariatric surgery is an effective intervention to improve asthma morbidity among obese adults with asthma.

Limitations

Our study has several potential limitations. First, as with any studies using administrative data, there might be some misclassification of encounters. However, HCUP data are rigorously tested and widely used to estimate diagnoses and visit frequency.[19,35] Furthermore, assuming that the frequency of misclassifications does not vary significantly between the presurgery and postsurgery periods, this nondifferential misclassification would not have biased our inference.

Second, SEDD and SID do not include several helpful clinical covariates, such as patient's BMI, access to ambulatory health care, outpatient management, and asthma education. Therefore one might hypothesize that the observed decreased risk of asthma exacerbation was the result of perisurgical intensified asthma management and education for elective surgery in general rather than bariatric surgery *per se*. However, we think that this is unlikely because the risk of asthma exacerbation did not change after surgery in the analysis of obese adults with asthma who underwent an elective nonbariatric surgery. Furthermore, in patients who underwent bariatric surgery, a substantial (>2-fold) and rapid reduction of risk was observed only after bariatric surgery (see Table E8 in this article's Online Repository at www.jacionline.org). Therefore it is difficult to postulate that perisurgical intensified asthma management fully explains the observed reduction in the risk of asthma exacerbation.

Third, the probability of exposure (ie, bariatric surgery) might not be independent from a previous event (ie, asthma exacerbation). For instance, it is possible that an occurrence of asthma exacerbation would have made a patient less likely to

undergo bariatric surgery. However, this would have upwardly biased the risk in the postsurgery period,[16] thereby biasing our conclusions toward the null.

Fourth, we examined the risk of asthma exacerbation as measured by asthma-related ED visits or hospitalizations, and some patients might have presented with exacerbations to urgent care or other ambulatory care sites. One might hypothesize that patients with asthma exacerbations might have used these non-ED resources more frequently after their bariatric surgery, thereby downwardly biasing our estimates in the postsurgery period. However, we also observed a significant decrease in the risk of hospitalizations not limited to hospitalizations through the ED, which argue against this potential bias.

Fifth, patients might have been progressively lost to follow-up after their bariatric surgery, and this would also have downwardly biased our estimates. Yet we think that this is unlikely because we found consistent results in a subgroup analysis that was limited to patients known to be alive until at least 2 years after bariatric surgery.

Finally, the study population was comprised of obese adults with an ED visit or hospitalization for asthma exacerbation during the study period. Therefore our inferences might not be generalizable to patients with well-controlled asthma. However, our study population (ie, patients with poorly controlled asthma) contributes to a substantial public health burden[1] and therefore is the one for which targeted interventions are most urgently warranted.

Conclusions

Using large population-based databases from 3 diverse US states, we found that bariatric surgery was associated with a significantly decreased risk of ED visits or hospitalizations for asthma exacerbation; this risk reduction was sustained for at least 2 years after surgery. The trials of nonsurgical management for obesity and asthma have only provided a modest weight loss and insufficient evidence about their efficacy.[12] By contrast, in conjunction with the findings of much smaller cohort studies that demonstrated the benefit of weight loss achieved by means of bariatric surgery, our data collectively support the effectiveness of large and sustained weight loss on reduction of asthma morbidities. Because the benefit of bariatric surgery might be offset by the initial high cost and risks of surgical complications, our finding also emphasizes the importance of developing safe, effective, nonsurgical approaches to achieve major weight loss, which would likely benefit millions of obese patients with asthma. Such research should proceed concurrently with vigorous public health campaigns to prevent obesity in the first place.

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Clinical implications: In obese patients the risk of asthma exacerbation decreased by half after bariatric surgery, suggesting the effectiveness of large and sustained weight loss on the reduction of asthma morbidities.

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TABLE E1. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation stratified by age group

Time interval and age group	No. of patients*	Risk, % (95% CI)	OR (95% CI)†	*P* value
13-24 mo before bariatric surgery				
18-34 y	143	21.2 (18.1-24.3)	Reference	—
35-44 y	178	23.9 (20.8-26.9)	Reference	—
45-54 y	177	21.1 (18.3-23.8)	Reference	—
1-12 mo before bariatric surgery				
18-34 y	146	21.7 (18.5-24.8)	1.03 (0.79-1.33)	.84
35-44 y	165	22.1 (19.1-25.1)	0.91 (0.71-1.15)	.43
45-54 y	180	21.4 (18.6-24.2)	1.02 (0.81-1.29)	.86
0-12 mo after bariatric surgery				
18-34 y	88	13.1 (10.5-15.6)	0.55 (0.41-0.74)	<.001
35-44 y	76	10.2 (8.0-12.4)	0.35 (0.26-0.47)	<.001
45-54 y	83	9.9 (7.9-11.9)	0.39 (0.29-0.52)	<.001
13-24 mo after bariatric surgery				
18-34 y	68	10.1 (7.8-12.4)	0.40 (0.29-0.56)	<.001
35-44 y	85	11.4 (9.1-13.7)	0.40 (0.30-0.53)	<.001
45-54 y	93	11.1 (8.9-13.2)	0.45 (0.34-0.59)	<.001

*Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.

†ORs are for each 12-month period versus the reference period (ie, 13-24 months before bariatric surgery), as calculated with conditional logistic regression.

TABLE E2. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation stratified by sex

Time interval and sex	No. of patients*	Risk, % (95% CI)	OR (95% CI)†	*P* value
13-24 mo before bariatric surgery				
Female	440	22.5 (20.7-24.4)	Reference	—
Male	57	19.8 (15.2-24.4)	Reference	—
1-12 mo before bariatric surgery				
Female	442	22.6 (20.7-24.4)	1.01 (0.87-1.17)	.94
Male	47	16.3 (12.0-20.6)	0.80 (0.53-1.21)	.30
0-12 mo after bariatric surgery				
Female	223	11.4 (10.0-12.8)	0.43 (0.36-0.51)	<.001
Male	22	7.6 (4.6-10.7)	0.35 (0.21-0.59)	<.001
13-24 mo after bariatric surgery				
Female	222	11.3 (9.9-12.7)	0.42 (0.35-0.51)	<.001
Male	23	8.0 (4.8-11.1)	0.37 (0.22-0.61)	<.001

*Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.

†ORs are for each 12-month period versus the reference period (ie, 13-24 months before bariatric surgery), as calculated with conditional regression.

TABLE E3. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation stratified by race/ethnicity

Time interval and race/ethnicity	No. of patients*	Risk, % (95% CI)	OR (95% CI)†	*P* value
13-24 mo before bariatric surgery				
Non-Hispanic white	276	21.3 (19.0-23.5)	Reference	—
Non-Hispanic black	82	26.7 (21.7-31.7)	Reference	—
Hispanic	97	23.5 (19.4-27.6)	Reference	—
1-12 mo before bariatric surgery				
Non-Hispanic white	273	21.0 (18.8-23.3)	0.99 (0.82-1.19)	.89
Non-Hispanic black	80	26.1 (21.1-31.0)	0.97 (0.68-1.38)	.86
Hispanic	89	21.6 (17.6-25.5)	0.90 (0.65-1.24)	.51
0-12 mo after bariatric surgery				
Non-Hispanic white	147	11.3 (9.5-13.0)	0.46 (0.37-0.57)	<.001
Non-Hispanic black	34	11.1 (7.5-14.6)	0.32 (0.21-0.51)	<.001
Hispanic	44	10.7 (7.7-13.6)	0.39 (0.26-0.57)	<.001
13-24 mo after bariatric surgery				
Non-Hispanic white	146	11.3 (9.5-13.0)	0.45 (0.36-0.57)	<.001
Non-Hispanic black	31	10.1 (6.7-13.5)	0.29 (0.18-0.46)	<.001
Hispanic	46	11.1 (8.1-14.2)	0.41 (0.28-0.60)	<.001

*Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.

†ORs are for each 12-month period versus the reference period (ie, 13-24 months before bariatric surgery), as calculated with conditional logistic regression.

TABLE E4. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation stratified by season

Time interval and season	No. of patients*	Risk, % (95% CI)	OR (95% CI)†	*P* value
13-24 mo before bariatric surgery				
January-March	101	19.7 (16.3-23.2)	Reference	—
April-June	134	24.6 (21.0-28.3)	Reference	—
July-September	142	23.4 (20.0-26.7)	Reference	—
October-December	121	20.3 (17.0-23.5)	Reference	—
1-12 mo before bariatric surgery				
January-March	119	23.2 (19.6-26.9)	1.25 (0.92-1.70)	.16
April-June	116	21.3 (17.9-24.8)	0.83 (0.62-1.10)	.19
July-September	138	22.7 (19.4-26.0)	0.97 (0.74-1.26)	.79
October-December	118	19.8 (16.6-23.0)	0.97 (0.73-1.28)	.83
0-12 mo after bariatric surgery				
January-March	52	10.2 (7.5-12.8)	0.41 (0.28-0.61)	<.001
April-June	60	11.0 (8.4-13.7)	0.36 (0.26-0.51)	<.001
July-September	74	12.2 (9.6-14.8)	0.45 (0.33-0.61)	<.001
October-December	61	10.2 (7.8-12.7)	0.46 (0.33-0.63)	<.001
13-24 mo after bariatric surgery				
January-March	51	10.0 (7.4-12.6)	0.40 (0.27-0.59)	<.001
April-June	62	11.4 (8.7-14.1)	0.38 (0.27-0.53)	<.001
July-September	56	9.2 (6.9-11.5)	0.32 (0.23-0.45)	<.001
October-December	77	12.9 (10.2-15.6)	0.59 (0.43-0.80)	<.001

*Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.

†ORs are for each 12-month period versus the reference period (ie, 13-24 months before bariatric surgery), as calculated with conditional logistic regression.

TABLE E5. Rate ratios of ED visits or hospitalizations for asthma exacerbation in obese patients

Time interval and outcome	Rate ratio (95% CI)*	*P* value
13-24 mo before bariatric surgery		
ED visit or hospitalization†	Reference	—
ED visit‡	Reference	—
Hospitalization§	Reference	—
1-12 mo before bariatric surgery		
ED visit or hospitalization†	0.99 (0.88-1.12)	.90
ED visit‡	1.00 (0.87-1.15)	1.00
Hospitalization§	0.98 (0.80-1.19)	.82
0-12 mo after bariatric surgery		
ED visit or hospitalization†	0.50 (0.43-0.58)	<.001
ED visit‡	0.54 (0.45-0.65)	<.001
Hospitalization§	0.40 (0.30-0.53)	<.001
13-24 mo after bariatric surgery		
ED visit or hospitalization†	0.47 (0.41-0.55)	<.001
ED visit‡	0.53 (0.44-0.63)	<.001
Hospitalization§	0.36 (0.27-0.47)	<.001

*Rate ratios are for each 12-month period versus the reference period (ie, 13-24 months before the bariatric surgery), as calculated with the Poisson regression model with generalized estimating equations.
†Number of ED visits and hospitalizations for asthma exacerbation.
‡Number of ED visits for asthma exacerbation not resulting in hospitalization.
§Number of hospitalizations for asthma exacerbation.

TABLE E6. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation using more restrictive criteria

Time interval	No. of patients* (n = 2257)	Risk,† % (95% CI)	OR (95% CI)‡	*P* value
13-24 mo before bariatric surgery	498	22.1 (20.4-23.8)	Reference	—
1-12 mo before bariatric surgery	493	21.8 (20.1-23.5)	0.99 (0.86-1.14)	.86
0-12 mo after bariatric surgery	247	10.9 (9.7-12.2)	0.42 (0.35-0.50)	<.001
13-24 mo after bariatric surgery	244	10.8 (9.5-12.1)	0.41 (0.35-0.49)	<.001

*Analysis excluding the patients who underwent bariatric surgery with ICD-9-CM diagnostic codes V853, 278.00, 278.02, and 278.1.
†Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.
‡ORs are for each 12-month period versus the reference period (ie, 13-24 months before surgery), as calculated with conditional regression.

TABLE E7. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation among obese patients who underwent a nonbariatric surgery

Time interval and surgery	No. of patients	Risk, % (95% CI)*	OR (95% CI)†	*P* value
Cholecystectomy (n = 1842)				
13-24 mo before surgery	356	19.3 (17.5-21.1)	Reference	—
1-12 mo before surgery	381	20.7 (18.8-22.5)	1.09 (0.93-1.29)	.29
0-12 mo after surgery	376	20.4 (18.6-22.3)	1.07 (0.91-1.27)	.40
13-24 mo after surgery	363	19.7 (17.9-21.5)	1.03 (0.87-1.21)	.77
Hysterectomy (n = 1344)				
13-24 mo before surgery	249	18.5 (16.5-20.7)	Reference	—
1-12 mo before surgery	245	18.2 (16.2-20.4)	0.98 (0.80-1.20)	.84
0-12 mo after surgery	237	17.6 (15.6-19.8)	0.94 (0.77-1.15)	.54
13-24 mo after surgery	232	17.3 (15.3-19.4)	0.91 (0.75-1.12)	.38

*Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.
†ORs are for each 12-month period versus the reference period (ie, 13-24 months before surgery), as calculated with conditional logistic regression.

TABLE E8. Number and risk of patients with an ED visit or hospitalization for asthma exacerbation according to 3-month periods

Time interval	No. of patients (n = 2261)	Risk,* % (95% CI)	OR (95% CI)†	*P* value
22-24 mo before bariatric surgery	169	7.5 (6.4-8.6)	Reference	—
19-21 mo before bariatric surgery	139	6.2 (4.2-7.2)	0.80 (0.63-1.02)	.07
16-18 mo before bariatric surgery	142	6.3 (5.3-7.4)	0.82 (0.65-1.04)	.10
13-15 mo before bariatric surgery	134	5.9 (5.0-7.0)	0.77 (0.60-0.98)	.03
10-12 mo before bariatric surgery	143	6.3 (5.4-7.4)	0.83 (0.65-1.05)	.12
7-9 mo before bariatric surgery	150	6.6 (5.6-7.7)	0.87 (0.69-1.10)	.26
4-6 mo before bariatric surgery	151	6.7 (5.7-7.8)	0.88 (0.70-1.11)	.28
1-3 mo before bariatric surgery	128	5.7 (4.7-7.0)	0.73 (0.57-0.93)	.01
0-3 mo after bariatric surgery	79	3.5 (2.8-4.3)	0.43 (0.32-0.56)	<.001
4-6 mo after bariatric surgery	89	3.9 (3.2-4.8)	0.49 (0.37-0.64)	<.001
7-9 mo after bariatric surgery	68	3.0 (2.3-3.8)	0.36 (0.27-0.48)	<.001
10-12 mo after bariatric surgery	55	2.4 (1.8-3.2)	0.29 (0.21-0.39)	<.001
13-15 mo after bariatric surgery	85	3.8 (3.0-4.6)	0.46 (0.35-0.61)	<.001
16-18 mo after bariatric surgery	70	3.1 (2.4-3.9)	0.37 (0.28-0.50)	<.001
19-21 mo after bariatric surgery	60	2.7 (2.0-3.4)	0.31 (0.23-0.43)	<.001
22-24 mo after bariatric surgery	78	3.5 (2.7-4.3)	0.42 (0.32-0.56)	<.001

*Outcome is the composite of at least 1 ED visit or hospitalization for asthma exacerbation.

†ORs are for each 3-month period versus the reference period (ie, 22-24 months before the index bariatric surgery), as calculated with conditional regression.