The Obesity Paradox in Patients with Severe Soft Tissue Infections

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Abstract

Background: The "obesity paradox" has been demonstrated in chronic diseases but not in acute surgery. We sought to determine whether obesity is associated with improved outcomes in patients with severe soft tissue infections (SSTIs).

Methods: The 2006-2010 Nationwide Inpatient Sample was used to identify adult patients with SSTIs. Patients were categorized into non-obese and obese (non-morbid [BMI 30-39.9] and morbid [BMI≥40]). Logistic regression provided risk-adjusted association between obesity categories and in-hospital mortality.

Results: There were 2,868 records with SSTI weighted to represent 14,080 patients. Obese patients were less likely to die in hospital than non-obese patients (odds ratio [OR]=0.42, 95% confidence interval [CI] 0.25-0.70; p=0.001). Subanalysis revealed a similar trend, with lower odds of mortality in non-morbid obesity (OR=0.46, CI 0.23-0.91; p=0.025) and morbid obesity (OR=0.39, CI 0.19-0.80; p=0.011) groups.

Conclusion: Obesity is independently associated with reduced in-hospital mortality in patients with SSTI regardless of the obesity classification. This suggests that the obesity paradox exists in this acute surgical population.

Introduction

Obesity is a growing public health issue that affects 35% of adults in the United States.[1] It is known to be associated with a large range of diseases, including diabetes, dyslipidemia, hypertension, coronary artery disease, stroke, depression, sleep apnea, and a number of malignancies.[2-5] It is also considered a risk factor for poor outcomes following surgical procedures.[6] However, there is a growing body of evidence to support an "obesity paradox", which is a phenomenon that suggests a protective mortality effect of high body mass index (BMI) for some chronic diseases.[2,6,7]

The obesity paradox has been described in a number of acute[8,9] and chronic[10-12] disease populations, as well as following some interventional procedures[2,6,13-16]. However, there is little data to determine if this pattern is seen in surgical patients with severe skin and soft tissue infections (SSTI), including necrotizing soft tissue infections (NSTIs). The latter are rapidly spreading infections within the soft tissue compartment (dermis, subcutaneous tissue, superficial fascia, muscle or deep fascia) that are associated with necrotizing changes.[17,18] Their management typically requires extensive surgical debridement as well resuscitation and intravenous antibiotics.[18,19] As nutritional support plays an important role in patient recovery from SSTIs[18,19], it has been suggested that individuals with higher BMIs have increased nutritional reserves conferring upon them a nutritional advantage that could improve hospital recovery.[20] We conducted a small pilot study (n=148) in a single academic center to examine outcomes in NSTI by nutrition feeding system and observed a trend towards reduced mortality in obese patients regardless of feeding technique. Although this study included a large number of patients with this relatively rare condition, the patients were all treated in one hospital and the results were not necessarily representative of the general population.

In order to examine the association between baseline BMI and hospital mortality in patients with SSTI, we examined hospital records from a nationally representative inpatient administrative database. We hypothesized that obesity will be associated with reduced mortality among these patients particularly in those with SSTI.

Methods

Data source

We used the 2006-2010 National Inpatient Sample (NIS), which is the largest publicly accessible all-payer inpatient database in the United States. This nationally representative dataset includes all discharges from a 20% stratified sample of hospitals from across the United States. It is administered as part of the Healthcare Cost and Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (AHRQ).

Inclusion criteria

Patients with SSTI were defined as those with a primary diagnosis *International Classification of Diseases, Ninth Edition, Clinical Classification* (ICD-9-CM) code pertaining to "gas gangrene" (040.0), "Fournier's disease" (608.83) or "necrotizing fasciitis" (728.86), and a ICD-9-CM procedure code corresponding to excisional or nonexcisional "debridement of wound, infection, or burn" (86.22 and 86.28 respectively). Patients aged <18 years old and those with any burn ICD-9-CM diagnosis code (940.0-949.5) were excluded. The remaining patients therefore had a soft tissue infection that was severe enough to require surgical debridement.[17-19,21]

Variables and outcome measures

Patients were categorized into non-obese or obese by using the AHRQ co-morbidity identifier for obesity. For bivariate and multivariable logistic regression analyses of mortality, obese patients were further stratified into obesity class 1 and 2 (BMI 30-30.9) and morbid obesity (BMI≥40); the latter identified by ICD-9-CM diagnosis code 278.01.

Extracted variables included age (categorized as 18-44, 45-64, 65-84, and ≥84 years), sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian/Pacific Islander, Native American, other and missing), estimated mean household income quartile based on ZIP code ($1-$38,999; $39,000 - $47,999; $48,000 - $62,999; $63,000 or more), primary payer (private, Medicare, Medicaid, self-pay and other), Charlson Comorbidity Index (CCI; 0, 1-2, 3 and ≥4), tube feeding (ICD-9-CM procedure codes 46.32, 46.39 and 96.6), total parenteral nutrition (ICD-9-CM procedure code 99.15), total hospital length-of-stay (coded as 0-3, 4-7 and >7 days), hospital size (NIS-defined large, medium and small bed size), rurality (defined by Core Based Statistical Area codes corresponding to non-metropolitan statistical areas), hospital region (Northeast, Midwest, South, West), hospital teaching status, and hospital affiliation to a multi-hospital system.

The primary outcome measure was in-hospital mortality, which was compared between obese vs. non-obese groups.

Statistical analysis

Categorical variables were compared using Pearson Chi-squared tests. Multivariable logistic regression was used to determine the independent association of obesity with mortality. Models were adjusted for all variables that were $p<0.5$ in bivariate analysis, which included patient- and hospital-level factors: age, race, gender, insurance, CCI, length-of-stay, hospital teaching status and hospital region.

NIS-provided population design weights were used to account for patient clustering within hospitals and to attain nationally weighted effects. Data analyses and management were performed using Stata 13 (College Station, TX, USA) and the threshold for statistical significance was set at $p<0.05$ (two-tailed). The study protocol was approved by the Partners HealthCare Institutional Review Board.

Results

Demographics, clinical and hospital characteristics

There were 2,868 records with SSTI weighted to represent 14,080 patients nationally, of which 75.7% were non-obese and 24.3% were obese. The mean age was 53.5 for non-obese (95% Confidence Interval [CI]: 52.8-54.3) for non-obese and 50.2 (95% CI: 49.2-51.2) for obese patients. Obese patients were more likely to be female, White, privately insured with less comorbidities associated (all p<0.001). Non-obese and obese groups were comparable in terms of income quartile, nutritional support (tube feeding and TPN), length-of-stay, and hospital characteristics (Table 1).

Outcomes

The overall mortality of our sample was 5.4%. In unadjusted bivariate analyses, obesity was associated with lower in-hospital mortality for SSTI patients (p=0.004) (Table 2). After adjusting for all measured confounders, obese patients were less likely to die in hospital than their non-obese counterparts: obesity any-class (odds ratio [OR] 0.42, 95% confidence interval [CI] 0.25-0.70; p=0.001), obesity class 1 and 2 (OR 0.46, CI 0.23-0.91; p=0.025) and morbid obesity (OR 0.39, CI 0.19-0.80; p=0.011).

Discussion

The obesity paradox was first described by in patients undergoing haemodialysis[22] and has since been documented in those with peripheral arterial disease[10], heart failure[23], type 2 diabetes[2,12], coronary artery disease[7], and gastrointestinal malignancies[14]. The mechanism of this association remains unknown and possible explanations include an uncharacterized malnutrition-inflammation syndrome[24], increased muscle strength[25], and improved cardiorespiratory reserves in obese patients. However, the obesity paradox remains controversial and a number of possible explanations have been suggested. These include protein energy wasting in hemodialysis patients and cachexia as a poor prognostic sign in various chronic diseases[23]. The comparative analyses of the present study reveal that the obesity paradox holds in the context of SSTI, as obesity is inversely associated with in-hospital mortality regardless of the obesity substratification.

There have been other explanations of the obesity paradox including attributing it to selection or lag-time biases.[26] The selection bias argument states that most patients with a chronic disease (e.g. heart failure) develop comorbidities (e.g. alcoholic liver disease, coronary artery disease) first but that this step is omitted in obese patients, as obesity itself is a cause of heart failure. Obese heart failure patients are then the “healthiest” and would be expected to have better outcomes. The lag-time bias argument suggests that obese patients may be diagnosed more promptly (e.g. obesity aggravates breathless observed in heart failure) and so at earlier stage in their disease trajectory.[27] These biases may partially account for the obesity paradox observed in peripheral arterial disease, coronary artery disease, heart failure, and type 2 diabetes. However, SSTI is an acute presentation and the obesity paradox in this population is not as readily explained by selection or lag-time biases. It is not immediately apparent that obesity itself should predispose to SSTI or result in earlier diagnosis. Nevertheless, it is feasible that deep wound infections requiring debridement are more common in obese patients.[28,29] Non-obese patients might have other predisposing factors (e.g. poorly controlled diabetes, disseminated malignancy) that were not evident in the obese patients but associated with in-hospital mortality.

An alternative possibility specific to SSTI is that debridement of infected wounds could be a less invasive procedure in obese patients. For example, a non-obese patient undergoing extensive wound debridement may be left with open cavities and/or plastic surgical intervention to facilitate soft tissue coverage. An obese patient could undergo a much more extensive soft tissue debridement without compromising deep structures. Further work should aim to understand the cause(s) of the obesity paradox as this could lead to interventions (e.g. nutritional supplementation) to improve outcomes in the affected patient population.

The limitations of this study arise from our use of an administrative dataset. Although the CCI was included in our multivariable models, this cannot completely control for all co-morbidities. In particular, the use of ICD-9-CM codes within the NIS is insufficiently granular to identify subtle differences in co-morbidity profiles between patients. For example, type 2 diabetes might be well controlled or poorly controlled, which may have implications both for development of SSTI and in-hospital mortality. We identified obese patients from a tag within the NIS. Since the documentation of obesity is dependent on whether the providers decided it was important enough to report it as a diagnosis during the admission, the extent to which this is obesity is captured is unknown. It is therefore possible that some obese patients were included within our non-obese group. However, this would be expected to underestimate any difference between the two groups rather than result in a strong negative association between obesity and in-hospital mortality. Other factors must be considered with the use of administrative data, such as the lack of physiologic data and the potential for misclassification, miscoding, and absent reporting of pertinent events not detectable without individual chart review.

In summary, the obesity paradox remains controversial but has been described across a range of chronic disease populations. To the best of our knowledge, this study represents the first time that the obesity paradox has been described in an acute surgical population. This finding cannot readily be explained by the lag-time bias suggested for the obesity paradox in chronic disease. The persistence of such a strongly apparent protective effect outside the chronic disease setting lends weight to proponents of the obesity paradox as a genuine clinical entity.

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Table 1. Demographic, clinical case-mix, and hospital-level (weighted percentages) of patients with SSTI undergoing surgical debridement by type of nutritional support

Weighted N, (%)	**Non-Obese** 10658 (75.7)	**Obese** 3423 (24.3)	***p***
Patient Characteristics			
Age (%)			**<0.001**
18 – 44	(25.2)	(30.4)	
45 – 64	(53.7)	(57.5)	
65 – 84	(19.1)	(12.0)	
85+	(2.0)	(0.1)	
Gender (%)			**<0.001**
Male	(67.1)	(48.3)	
Female	(32.9)	(51.7)	
Race/Ethnicity (%)			**<0.001**
White	(47.2)	(57.4)	
Black	(14.7)	(12.9)	
Hispanic	(11.7)	(6.2)	
Asian/Pa	(1.5)	(1.1)	
Native A	(0.9)	(0.8)	
Other	(2.7)	(1.7)	
Missing	(21.4)	(19.8)	
Payer (%)			**<0.001**
Private, including HMO	(28.7)	(40.2)	
Medicare	(30.4)	(25.0)	
Medicaid	(17.9)	(18.3)	
Self-pay	(13.1)	(11.6)	
Other	(9.9)	(4.9)	
Income Quartile (%)			0.583
1st	(36.9)	(34.6)	
2nd	(27.2)	(28.7)	
3rd	(20.7)	(22.4)	
4th	(15.2)	(14.3)	
Charlson Comorbidity Index score (%)			**<0.001**
0	(32.4)	(16.5)	
1	(30.3)	(39.6)	
2	(17.4)	(20.6)	
3	(9.0)	(11.3)	
>4	(11.0)	(11.9)	
Tube feeding (%)	(2.4)	(2.4)	0.978
Total parenteral nutrition (%)	(2.5)	(3.0)	0.521
Length of stay (%)			0.169
0-3 days	(7.0)	(4.9)	
3-7 days	(18.0)	(17.4)	
>7 days	(75.1)	(77.6)	
Hospital characteristics			
Bed size (%)*			0.578
Small	(10.7)	(11.4)	
Medium	(23.2)	(25.1)	
Large	(66.0)	(63.5)	
Rural location (%)	(9.4)	(9.7)	0.814
Region (%)			0.209
Northeast	(14.1)	(12.9)	
Midwest	(21.7)	(25.5)	
South	(39.9)	(41.0)	
West	(24.3)	(20.7)	
Teaching status (%)	(57.6)	(52.9)	0.071
Member multihospital system(%)	(63.6)	(65.4)	0.541

Table 2. Mortality of severe skin and soft tissue infection cases by obesity classification.

	Non-Obese (BMI<30)	Obese (BMI 30-39.9)	Morbid-Obese (BMI≥40)	***p***
Weighted N, (%)	10658 (75.7)	1541 (10.9)	1882 (13.4)	
Mortality (%)	(6.2)	(3.2)	(2.6)	**0.004**

	Non-Obese (BMI<30)	Obese (BMI 30-39.9)	Morbid-Obese (BMI≥40)	***p***
Weighted N, (%)	10658 (75.7)	1541 (10.9)	1882 (13.4)	
Mortality (%)	(6.2)	(3.2)	(2.6)	**0.004**

Obesity classification	Non-Obese (BMI<30)	Obesity any class (BMI≥30)		***p***
Weighted N, (%)	10658 (75.7)	3418 (24.7)		
Mortality (%)	(6.2)	(0.3)		**<0.001**
	Non-Obese (BMI<30)	**Obesity class 1 & 2 (BMI 30-39.9)**	**Morbid-Obese (BMI≥40)**	***p***
Weighted N, (%)	10658 (75.7)	1541 (10.9)	1882 (13.4)	
Mortality (%)	(6.2)	(3.2)	(2.6)	**0.004**

Figure 1. Forest plot of risk-adjusted mortality among severe skin and soft tissue infection cases by obesity classification.

Footnote: Non-obesity (BMI<30 kg/m^2); Obesity, any type (BMI≥30 kg/m^2); Non-morbid Obesity (BMI 30-39.9 kg/m^2); Morbid-obesity (BMI≥40 kg/m^2). Models were adjusted for age, gender, race, insurance, Charlson Comorbidity Index, length-of-stay and hospital characteristics.