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ORIGINAL SCIENTIFIC REPORT

The Obesity Paradox in the Trauma Patient: Normal May not Be Better

J. E. Dvorak[1] · E. L. W. Lester[1] · P. J. Maluso[1] · L. Tatebe[1] · V. Schlanser[1] · M. Kaminsky[1] · T. Messer[1] · A. J. Dennis[1] · F. Starr[1] · F. Bokhari[1]

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Abstract

Objective The obesity paradox is the association of increased survival for overweight and obese patients compared to normal and underweight patients, despite an increased risk of morbidity. The obesity paradox has been demonstrated in many disease states but has yet to be studied in trauma. The objective of this study is to elucidate the presence of the obesity paradox in trauma patients by evaluating the association between BMI and outcomes.

Methods Using the 2014–2015 National Trauma Database (NTDB), adults were categorized by WHO BMI category. Logistic regression was used to assess the odds of mortality associated with each category, adjusting for statistically significant covariables. Length of stay (LOS), ICU LOS and ventilator days were also analyzed, adjusting for statistically significant covariables.

Results A total of 415,807 patients were identified. Underweight patients had increased odds of mortality (OR 1.378, $p < 0.001$ 95% CI 1.252–1.514), while being overweight had a protective effect (OR 0.916, $p = 0.002$ 95% CI 0.867–0.968). Class I obesity was not associated with increased mortality compared to normal weight (OR 1.013, $p = 0.707$ 95% CI 0.946–1.085). Class II and Class III obesity were associated with increased mortality risk (Class II OR 1.178, $p = 0.001$ 95% CI 1.069–1.299; Class III OR 1.515, $p < 0.001$ 95% CI 1.368–1.677). Hospital and ICU LOS increased with each successive increase in BMI category above normal weight. Obesity was associated with increased ventilator days; Class I obese patients had a 22% increase in ventilator days (IRR 1.217 95% CI 1.171–1.263), and Class III obese patients had a 54% increase (IRR 1.536 95% CI 1.450–1.627).

Conclusion The obesity paradox exists in trauma patients. Further investigation is needed to elucidate what specific phenotypic aspects confer this benefit and how these can enhance patient care.

Level of evidence Level III, prognostic study

This work has not been presented at a meeting or conference.

✉ J. E. Dvorak
justin.dvorak@cookcountyhhs.org

E. L. W. Lester
Erica.lester@cookcountyhhs.org

P. J. Maluso
Patrick.maluso@cookcountyhhs.org

L. Tatebe
leah.tatebe@cookcountyhhs.org

V. Schlanser
victoria.schlanser@cookcountyhhs.org

M. Kaminsky
mkaminsky2@cookcountyhhs.org

T. Messer
t.messer@cookcountyhhs.org

Introduction

Approximately 40% of American adults and 13% of adults worldwide are now classified as obese, representing a significant burden of disease [1, 2]. Obesity is associated with increased risk of multiple disorders, including diabetes mellitus, hepatic and renal dysfunction, certain cancers, sleep disorders and infertility [3]. Despite this, increasing body mass index (BMI) appears to have a protective effect on mortality in certain disease states, a phenomenon termed the "Obesity Paradox." Several studies have shown either a *U*-shaped or *J*-shaped relationship between BMI and mortality in which overweight and Class I obese patients have increased survival compared to normal weight and underweight patients, with mortality trending upwards in Class II and III obesity. This "paradox" has been seen in patients with Type II diabetes, coronary artery disease, numerous malignancies and in the critically ill [4–12].

While the obesity paradox has been established in numerous clinical areas, the effect of BMI class on trauma mortality remains unclear. Several studies have demonstrated no association between obesity and mortality [13–18], while others have found increased mortality in obese trauma patients [19–25]. A lack of uniform BMI categorization among previous studies renders meta-analysis difficult. Additionally, many studies are single institution, limiting the sample size and generalizability of the results.

The objective of the present study is to elucidate the presence of the obesity paradox in trauma patients by evaluating the association between BMI and in-hospital mortality, length of stay, intensive care unit (ICU) days and ventilator days using a robust national database.

Methods

Using the National Trauma Database (NTDB) between 2014 and 2015, patients age 18 or older were categorized according to the World Health Organization (WHO) BMI categories ("Appendix" section). Outliers of weight and height (weight <30 kg or >600 kg, height <80 cm or >250 cm), as well as patients with incomplete data were removed from the study. Basic descriptive statistics were performed. For the primary analysis, logistic regression was conducted to assess the adjusted mortality odds associated with each WHO category, adjusting for statistically significant covariables and their power transformations and interaction terms to optimize the model as determined by the Box–Tidwell model method. Given its clinical relevance, mechanism of injury was included in the model, though the variable representing blunt injury was not statistically significant. The final model was adjusted for age (transformed), sex, injury severity score (ISS), blunt mechanism, penetrating mechanism, pulse, systolic blood pressure (SBP) and Glasgow Coma Scale (GCS) on arrival, as well as diagnosis of diabetes, COPD, cirrhosis or CHF, and smoking status. Pearson goodness-of-fit test was performed, and area under the receiver operator curve (AUROC) was calculated. The model was then tested using NTDB data from 2013, with AUROC calculated for comparison.

Subgroup analysis of the primary outcome was performed for patients with ISS ≤9 and those with ISS >9, adjusting for the same covariables.

For the secondary analysis, the following categorical variables were assessed in patients that survived to discharge: length of stay (LOS), ICU length of stay (ICU LOS) and ventilator days. By comparing model fits, it was determined that the negative binomial approach was the most appropriate for the LOS analysis, and zero-inflated negative binomial regression for ICU LOS and ventilator days. ISS was the logit component of the zero-inflated model when assessing ICU length of stay, and ICU length of stay was the logit component in the ventilator days model. Each model was adjusted for statistically significant covariables, including age, sex, ISS, pulse, SBP and GCS on arrival, diagnosis of hypertension, diabetes, COPD, cirrhosis or CHF, smoking and ethanol use status. The robust standard error approach was used to determine standard errors. Analyses were conducted using Stata version 13 (Version 13, College Station, Texas).

Results

A total of 415,807 trauma patients with complete data were identified during the study timeframe. Mean (Standard Deviation) age was 53.25 (21.04) years, and 60.86% of patients were male. Mean ISS was 9.59 (8.05), mean SBP and pulse on arrival were 139.76 (26.96) and 88.42 (19.39), respectively, and mean GCS on presentation was 14.20 (2.48). Within the sample of patients analyzed, there were 10,713 mortalities (2.58%). A total of 119,823 (28.82%)

A. J. Dennis
adennis@cookcountyhhs.org

F. Starr
fstarr@cookcountyhhs.org

F. Bokhari
fbokhari@cookcountyhhs.org

[1] Department of Trauma and Burns, John H. Stroger, Jr. Hospital of Cook County, 1950 W. Polk St, Department of Trauma, 8th Floor, Chicago, IL 60613, USA

Table 1 Patient characteristics

Characteristic	Number	Percentage (%)
Total patients	415,807	–
BMI <18.5	18,733	4.51
BMI 18.5–24.9	143,740	34.57
BMI 25.0–29.9	135,067	32.48
BMI 30.0–34.9	67,929	16.34
BMI 35.5–39.9	27,599	6.64
BMI >40.0	22,739	5.47
Age [mean (SD)]	53.25 (21.04)	–
Male sex	253,060	60.86
ISS [mean (SD)]	9.59 (8.05)	–
ED SBP mean (SD)	139.76 (26.96)	–
ED pulse mean (SD)	88.42 (19.39)	–
ED GCS mean (SD)	14.20 (2.48)	–
ICU admissions	119,823	28.82
Ventilated patients	46,377	11.15
Total mortalities	10,713	2.58

patients were admitted to ICU, with 46,377 (11.15%) patients requiring ventilation. A total of 18,733 (4.51%) patients were in the underweight category, 143,740 (34.57%) patients were in the normal weight category, 135,067 (32.48%) patients were in the overweight category, 67,929 (16.34%) patients were in the Class I obese category, 27,599 (6.64%) patients were in the Class II obese category, and 22,739 (5.47%) patients were in the Class III obese category (Table 1).

In the primary analysis of in-hospital mortality, after adjusting for statistically significant covariables and using normal BMI as the reference category, a *U*-shaped relationship between BMI category and adjusted odds of mortality was seen (Fig. 1). Underweight patients had elevated odds of mortality (OR 1.378, $p < 0.001$ 95% CI 1.252–1.514), while being overweight appeared to have a protective effect (OR 0.916, $p = 0.002$ 95% CI 0.867–0.968). There was no statistically significant difference in odds of mortality between the normal weight and Class I obesity groups (OR 1.013, $p = 0.707$ 95% CI 0.946–1.085). Class II and Class III obesity were both associated with increased odds of mortality (Class II OR 1.178, $p = 0.001$ 95% CI 1.069–1.299; Class III OR 1.515, $p < 0.001$ 95% CI 1.368–1.677) (Table 2). The pseudo-R2 was 0.349, and the AUROC was 0.921. When the model was tested using 2013 data, results were consistent and the AUROC was 0.928.

In subgroup analysis of mortality, the *U*-shape curve relationship with BMI category remained in both groups (Figs. 2, 3), with adjusted odds of mortality of 0.892 ($p = 0.052$ 95% CI 0.867–0.968) for overweight patients in ISS $\leq$9 subgroup (Table 3), and 0.935 ($p = 0.035$ 95% CI (0.879–0.995) (Table 4) in the ISS >9 subgroup.

Both hospital and ICU LOS increased with each successive increase in BMI category above normal weight. Obesity was associated with an increase in ventilator days, with Class I obese patients having a 22% increase in ventilator days (IRR 1.217 95% CI 1.171–1.263), Class II obese patients experiencing a 30% increase in ventilator days (IRR 1.295 95% CI 1.228–1.366) and Class III obese patients experiencing a 54% increase in ventilator days (IRR 1.536 95% CI 1.450–1.627). Overweight patients did

Fig. 1 Relationship between BMI category and adjusted mortality

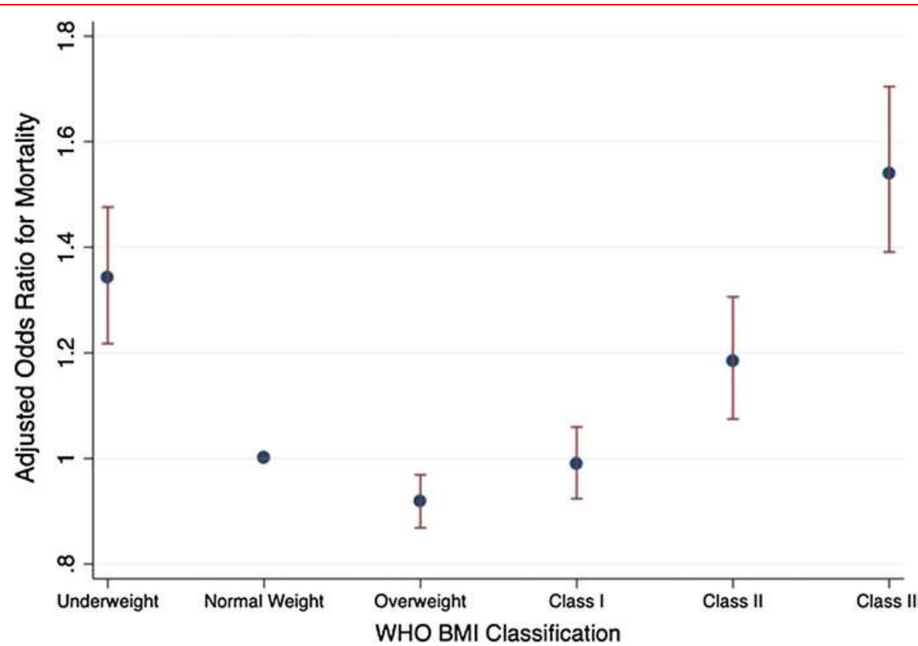

Table 2 Primary outcome by BMI stratum compared to normal BMI

BMI	Mortality (OR 95% CI)	*p*
BMI <18.5	1.378 (1.252–1.514)	<0.001
BMI 18.5–24.9	1.000	–
BMI 25.0–29.9	0.916 (0.867–0.968)	0.002
BMI 30.0–34.9	1.013 (0.946–1.085)	0.707
BMI 35.5–39.9	1.178 (1.069–1.299)	0.001
BMI >40.0	1.515 (1.368–1.677)	<0.001

not have a statistically significant increase in ventilator days compared to normal weight, whereas underweight patients did (Table 5).

Postestimation comparisons of actual and predicted probabilities demonstrated appropriate model specifications for each secondary analysis model, and when tested using 2013 data, results were consistent.

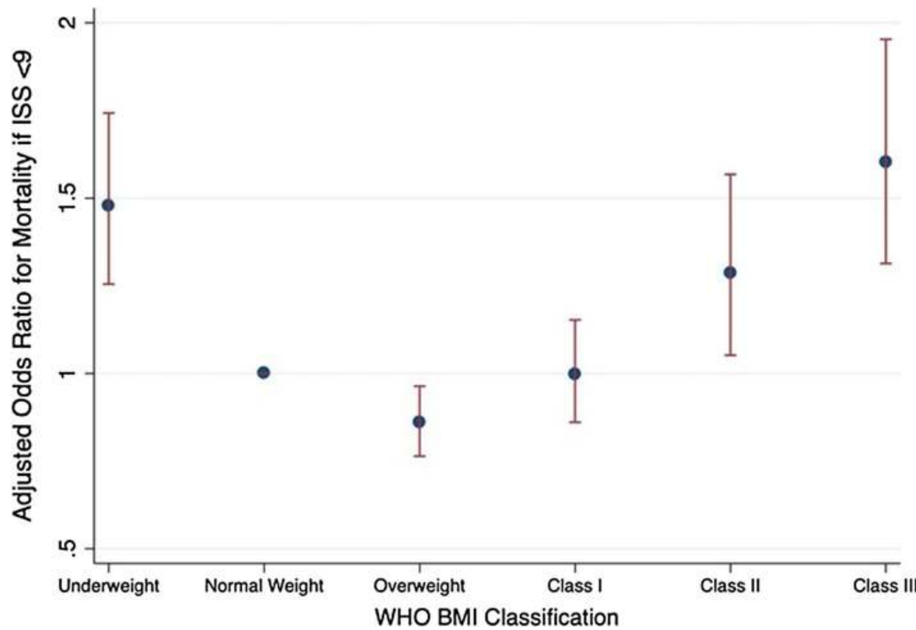

Fig. 2 Relationship between BMI category and adjusted mortality for ISS ≤9

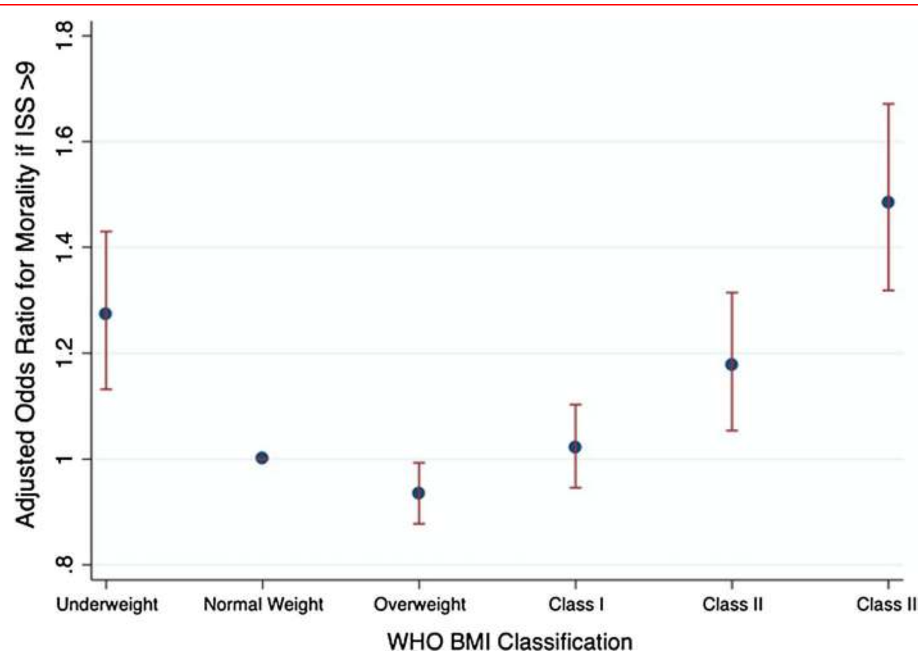

Fig. 3 Relationship between BMI category and adjusted mortality for ISS >9

Table 3 Subgroup analysis of primary outcome by BMI stratum compared to normal BMI for patients with ISS ≤9

BMI	Mortality (OR 95% CI)	*p*
BMI <18.5	1.601 (1.364–1.880)	<0.001
BMI 18.5–24.9	1.000	–
BMI 25.0–29.9	0.892 (0.795–1.001)	0.052
BMI 30.0–34.9	1.033 (0.894–1.194)	0.658
BMI 35.5–39.9	1.271 (1.039–1.554)	0.020
BMI >40.0	1.635 (1.340–1.995)	<0.001

Table 4 Subgroup analysis of primary outcome by BMI stratum compared to normal BMI for patients with ISS >9

BMI	Mortality (OR 95% CI)	*p*
BMI <18.5	1.251 (1.113–1.406)	<0.001
BMI 18.5–24.9	1.000	–
BMI 25.0–29.9	0.935 (0.879–0.995)	0.035
BMI 30.0–34.9	1.023 (1.948–1.105)	0.552
BMI 35.5–39.9	1.181 (1.057–1.319)	0.003
BMI >40.0	1.510 (1.342–1.699)	<0.001

Discussion

When assessing the impact of BMI on trauma mortality, a *U*-shaped curve is seen in which underweight patients as well as Class II and Class III obese patients have increased odds of mortality, while overweight and Class I obese patients appear to benefit from some protective effect. This relationship remains when subgroup analysis is performed for those with above and below average injury severity scores. Increasing BMI categories are, however, associated with increased morbidity, as reflected by longer hospital and ICU LOS and ventilator days. These findings are consistent with the results of studies in non-trauma patient populations which have demonstrated the existence of an "obesity paradox" [4–12].

Previous studies assessing the association between obesity and trauma mortality have had inconsistent findings. A 2007 study by Newell et al. [16] found no association between obesity and mortality in critically injured blunt trauma patients, while studies by Neville et al. [25] and Brown et al. [21] found that obesity did have an association with increased mortality. Examining Class III obesity, studies by Diaz et al. [15] and Ditillo et al. [24] found increased mortality in trauma patients with BMI ≥40. The inconsistencies in the results between previous works are likely secondary to single-institution retrospective designs, leading to small sample sizes. Additionally, obesity was often a binary variable in previous studies, limiting the ability to assess the association of each BMI category with mortality and ignoring the nonlinear relationship between increasing BMI and death. By examining all BMI categories, we were able to demonstrate the presence of an obesity paradox in trauma patients.

There are several proposed mechanisms to explain the obesity paradox. Adipose tissue has cytokines which impact immune function. One of those cytokines is leptin, which is found in increased levels in overweight and obese patients. Leptin deficiency has been associated with increased susceptibility to viral and bacterial infections, as well as increased susceptibility to the toxicity of proinflammatory stimuli [26]. Patients with increased leptin levels may have an advantage in fighting infection, which may benefit critically ill trauma patients at increased risk of infection. Another possible explanation is the presence of increased metabolic and energy reserves in obese patients [27]. Admission to the ICU is often associated with malnutrition [28], and obese patients might better tolerate a temporary state of malnutrition given their increased energy stores.

The presence of the obesity paradox across multiple disease states may illuminate the limitations of BMI as a metric. BMI does not differentiate muscle mass from fat mass and is thus not able to differentiate fitness from adiposity [29]. This has been demonstrated when other measures of obesity are used to examine the association

Table 5 Secondary outcomes by BMI stratum compared to normal BMI

BMI	Hospital LOS (IRR 95% CI)	ICU LOS (IRR 95% CI)	Ventilator days (IRR 95% CI)
BMI <18.5	1.070 (1.056–1.083)	1.070 (1.035–1.106)	1.111 (1.039–1.189)
BMI 18.5–24.9	1.000	1.000	1.000
BMI 25.0–29.9	1.009 (1.003–1.015)	1.031 (1.015–1.047)	1.031 (0.999–1.064)*
BMI 30.0–34.9	1.055 (1.050–1.063)	1.146 (1.124–1.169)	1.217 (1.171–1.263)
BMI 35.5–39.9	1.117 (1.105–1.129)	1.225 (1.191–1.259)	1.295 (1.228–1.366)
BMI >40.0	1.220 (1.206–1.234)	1.388 (1.347–1.431)	1.536 (1.450–1.627)

Unless otherwise indicated, all *p* values <0.05

* $p = 0.054$

between obesity and mortality in patients with heart failure. When waist-to-hip ratio or waist circumference is used as a measure of obesity, rather than BMI, the obesity paradox in patients with heart failure disappears [29, 30]. If BMI is in fact a useful metric, this study brings into question the categorization of BMI. As opposed to the presence of an actual paradox, the presence of the obesity paradox across many different disease states may reflect too narrow or a skewed definition of what a normal BMI is.

While overweight and Class I obesity was associated with decreased odds of mortality, increasing BMI categories above normal had a linear relationship with the secondary outcomes of LOS, ICU LOS and ventilator days, as seen by sequential increases in IRR for those categories with each successive BMI category. The association between increased BMI and increased LOS, ICU LOS and ventilator days is congruent with other publications examining the impact of obesity on trauma [16, 21, 22, 24]. Obesity is associated with reduced lung volumes, decreased lung compliance and reduced gas exchange, leading to difficulty weaning from mechanical ventilation [31]. Furthermore, it is associated with increased ICU resource utilization, as well increased nursing-care burden [32, 33]. Some combination of these factors likely explains the demonstrated increase in LOS and ventilator days among all BMI categories above normal, despite overweight and Class I obesity having a protective effect on mortality.

This study must be interpreted within the limitations of its design. Firstly, its retrospective database-driven design suffers from the disadvantages inherent to all such studies. We were not able to account for missing data points in the NTDB and had to remove pts with aberrant weights and heights. Additionally, while we adjusted for multiple comorbidities, given the data limitations, it is not possible to know which patients had do not resuscitate (DNR) orders, or end-stage diseases that likely influenced survival, such as advanced metastatic cancer. Despite these limitations, the large study cohort likely minimizes the impact of outliers on this study.

Conclusion

Overweight patients have improved odds of trauma survival, while patients classified as underweight and Class II and Class III obese have higher risk of mortality. This finding is consistent with studies in non-trauma populations and reveals the existence of an Obesity Paradox for trauma survival, despite increases in length of stay and ICU resource use. Furthermore, it challenges the definition of what we consider a "normal" BMI, and BMI as a metric. Due to the rising obesity epidemic, research expanding the understanding of the impact of obesity on trauma outcomes is increasingly relevant, and may guide future therapy and prevent mortality.

Compliance with ethical standards

Conflict of interest These authors disclose no conflicts of interest.

Appendix

See Table 6.

Table 6 WHO BMI categories

BMI	Classification
<18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Overweight
30.0–34.9	Class I obesity
35.0–39.9	Class II obesity
≥ 40.0	Class III obesity

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