ORIGINAL RESEARCH

Obesity, Treatment Times, and Cardiovascular Outcomes After ST-Elevation Myocardial Infarction: Findings From Mission: Lifeline North Texas

Tiffany Champagne-Langabeer, PhD, RD; Junghyun Kim, PhD; Julie K. Bower, PhD; Angela Gardner, MD; Raymond Fowler, MD; James R. Langabeer, II, EdD, PhD

***Background*—**With increasing rates of obesity and its link with cardiovascular disease, there is a need for better understanding of the obesity-outcome relationship. This study explores the association between categories of obesity with treatment times and mortality for patients experiencing ST-segment elevation myocardial infarction.

***Methods and Results*—**We examined 8725 patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention and used regression models to analyze the relationship between 6 categories of body mass index with key door-to-balloon time, total ischemic time, and in-hospital mortality. We relied on data from the Mission: Lifeline North Texas program, consisting of 33 percutaneous coronary intervention–capable hospitals in 6 counties surrounding Dallas, Texas. Data were extracted from the National Cardiovascular Data Registry for each participating hospital. Of the samples, 76% were overweight or obese. Comparing the univariate differences between the normal-weight group and the pooled sample, we observed a U-shaped association between body mass index and both mortality and door-to-balloon times. The most underweight and severely obese had the highest mortality and median door-to-balloon time, respectively. These differences persisted after multivariate adjustments for door-to-balloon time, but not for mortality.

***Conclusions*—**Extremely obese patients have longer treatment time delays than other body mass index categories. However, this did not extend to significant differences in mortality in the multivariate models. We conclude that clinicians should incorporate body mass assessments into their diagnosis and treatment plans to mitigate observed disparities. **(*J Am Heart Assoc*. 2017;6: e005827. DOI: 10.1161/JAHA.117.005827.)**

Key Words: body mass index • obesity • quality of care • ST-segment elevation myocardial infarction

Nearly one third of US adults are considered obese.[1,2] Body mass index (BMI) is frequently used as a screening tool for obesity and to estimate the health of an individual. Although there are more direct measures of body composition and adiposity, BMI is the most widely used in the clinical setting because measures of height and weight can be easily obtained without specialized training or equipment.[3] Clinically, BMI is strongly correlated with known risk factors for cardiovascular disease across all population subgroups.[4–6]

The National Institutes of Health classifies BMI into the following 6 categories: underweight (BMI, <18.5 kg/m^2), normal weight (BMI, 18.5–24.9 kg/m^2), overweight (BMI, 25–29.9 kg/m^2), obesity class 1 (BMI, 30–34.9 kg/m^2), obesity class 2 (BMI, 35–39.9 kg/m^2), and extreme obesity class 3 (BMI, $\geq$40 kg/m^2).[7] According to the National Health and Nutrition Examination Survey,[8] $\approx$68.8% of the US population has a BMI >25 kg/m^2 and is considered overweight to extremely obese.

There is a growing epidemic of obesity in the United States, fueled partially by lifestyle choices and genetics.[9] There has been some evidence pointing to an "obesity paradox"—a reverse epidemiologic phenomenon in which a protective effect is experienced by overweight and mildly obese patients after a cardiovascular event. These patients tend to have a better prognosis when compared with normal-weight patients and often have lower mortality rates.[5,10–12] This shielding effect may extend to patients with hypertension. The findings to date have been

From The University of Texas Health Science Center, Houston, TX (T.C.-L., J.K., J.R.L.); The Ohio State University, Columbus, OH (J.K.B.); and The University of Texas Southwestern Medical Center, Dallas, TX (A.G., R.F.).

Correspondence to: James Langabeer, EdD, PhD, School of Biomedical Informatics, The University of Texas Health Science Center, 7000 Fannin St, Ste 600, Houston, TX 77030. E-mail: James.R.Langabeer@uth.tmc.edu

Received February 10, 2017; accepted August 18, 2017.

Clinical Perspective

What Is New?

- Our study comes from 1 of the largest regional systems of care in the United States, and provides evidence from 8725 patients on the relationship between varying levels of body mass and cardiovascular outcomes.
- Our findings signify that body mass is associated with longer treatment times and, to some extent, mortality, although the differences do not persist after multivariate adjustments. The extremely obese category had the highest observed delays in treatment after arrival at the hospital, suggesting potential clinical difficulties in diagnosis for those patients.

What Are the Clinical Implications?

- The relationship between a patient's weight (especially both the extremely underweight and extremely obese) should be taken into consideration for screening and short-term management in ST-elevation myocardial infarction.
- Given the high rates of women in certain weight categories, we suggest that sex should be a higher priority for consideration in patient treatment decisions.

inconsistent and focused exclusively on the mortality-BMI relationship.[13–15]

Treatment times are also important, given their relationship with long-term health status and mortality. Specifically, door-to-balloon (D2B) time has predicted survival in patients with ST-segment elevation myocardial infarction (STEMI).[16,17] Total ischemic time (measured as symptom onset to balloon time) has also had a direct association with myocardial salvage, future patient health status, and overall mortality.[18] Consequently, treatment times have become a major focus for cardiovascular guidelines and contemporary systems of care. However, little obesity research has focused on the impact of obesity on D2B and total ischemic times.

We propose that body mass matters in treatment delays, because time affects longer-term health status. The precise explanatory mechanisms for why prolonged delays affect mortality and myocardial salvage are uncertain; however, most theories suggest that systolic and diastolic irregularities produce left ventricular dysfunction. Therefore, greater treatment times result in lower left ventricular function.[19] Cardiovascular function could be dependent on levels of body mass. For example, extremely obese individuals especially have had a high likelihood for acute coronary syndrome, heart failure, and mortality. We sought to explore if disparities exist in key outcomes for patients within established body mass profile categories.

In this study, we explore the relationship between categories of obesity and 3 cardiovascular outcomes (D2B time, total ischemic time, and in-hospital mortality) in a large population of patients with STEMI undergoing primary percutaneous coronary intervention (PCI).

Methods

Data Source

Data for this study came from a regional cardiovascular system of care (American Heart Association Mission: Lifeline North Texas). The system consists of 33 nonaffiliated hospitals in 6 counties of northeast Texas surrounding the Dallas, Texas, metropolitan area. Data were extracted from each hospital's entry into the National Cardiovascular Data Registry ACTION Registry, a standardized comprehensive registry for patients with myocardial infarction across hospitals with PCI capabilities. Registry data included demographic information, interventions, medications, discharge status, and outcomes. Six years of data were examined (January 1, 2010 through December 31, 2015). Because data were retrospectively collected in this observational study, it was not a requirement for patients to provide informed consent. Institutional review board approval was obtained by The University of Texas Health Sciences Center at Houston.

Obesity, Outcome, and Control Variables

BMI values were calculated from the recorded patients' height and weight data at PCI admission. We categorize patients according to the National Institutes of Health classification system described earlier, involving 6 categories for body mass: underweight (1; BMI, <18.5 kg/m^2), normal weight (2; BMI, 18.5–24.9 kg/m^2), overweight (3; BMI, 25.0–29.9 kg/m^2), obesity class 1 (4; BMI, 30.0–34.9 kg/m^2), obesity class 2 (5; BMI, 35.0–39.9 kg/m^2), and extreme obesity class 3 (6; BMI, $\geq$40 kg/m^2).[7] This classification structure was developed by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

We chose to include only patients with STEMI to control for the pathophysiological, treatment, and outcome differences that exist with non-STEMI. The primary dependent variables included D2B time, total ischemic time, and in-hospital mortality. Treatment times were measured in minutes. Total ischemic time was expressed as the difference in minutes between the time a patient reported his or her first symptom onset to the time the artery was opened and the first device was inserted in the catheterization laboratory. D2B time was calculated as the difference in minutes between when the patient arrived at the hospital door to the time of first device placement. In-hospital mortality was defined as binary (alive or dead) at the time of discharge.

We adjusted for multiple control variables. Sex was classified as either male or female, with male being the reference group for comparison in the statistical models. Patient age was defined in years. We incorporated an additional variable for age and sex to account for the interaction effect between these variables. To control for risks, comorbidities, and condition on arrival at the hospital, we included multiple controls: the presence of shock at first medical contact, the presence of heart failure on first medical contact, indicators for diabetes mellitus and smoking, history of cardiovascular disease and prior stroke, and presence of shock and heart failure. To account for institutional and geographic differences, we further adjusted for the hospital that performed the procedure and the county the patient originated from.

Statistical Analysis

Analyses were stratified across the 6 categories of body mass to present baseline characteristics and presence of outcomes, and regression models used a pooled sample to assess nonlinear BMI-related differences in outcomes, including treatment times and mortality. Both D2B and total ischemic time data were highly skewed; therefore, we present medians and interquartile ranges and used a logarithmic transformation of both for multivariable analyses. Other continuous data are presented as means (SDs). Both χ^2 and analysis of variance were used for initial univariate comparisons for continuous data, and Kruskal-Wallis tests were used for nonparametric data.

Univariate tests were first used to explore differences in outcomes (D2B time, total ischemic time, and mortality) across all 6 BMI categories. On the basis of the univariate statistical results, we then conducted both linear regression and logistic regression models controlling for age, sex, hospital, county, and important patient comorbidities (diabetes mellitus, history of cardiovascular disease, presence of heart failure and shock, smoking, and prior myocardial infarction). Logistic regression was used for mortality, and linear regression (using a logarithmic transformation of D2B time) was applied for D2B time. A 2-tailed $P<0.05$ was considered statistically significant. All analyses were performed using SAS Version 9.4.

Results

We analyzed 8725 patient records with STEMI and subsequent PCI. The median BMI was 28.3 kg/m^2 (overweight), and the mean age was 60.7 years. Approximately 21.8% of the sample was considered "normal" weight, and 76% were in one of the overweight or obese categories. There was a significantly higher proportion of men than women, with 6306 men (72.3%) and 2419 women (27.7%). Table 1 summarizes the patient characteristics of the study sample stratified by BMI category.

As Table 1 illustrates, there are statistically significant differences based on BMI categories. Patients with a higher BMI were more likely to have diabetes mellitus. The underweight category, although small, was composed primarily of older female patients (nearly 3.5 years older and nearly twice the ratio of women than the normal-weight group). Patients who were underweight were more likely to have a history of cardiovascular disease and previous stroke and were more likely to have shock and heart failure before PCI.

Table 2 shows the differences among level of BMI for quality outcomes in the univariate analyses. On average, the underweight group had the highest D2B median minutes and mortality rates. There was not a significant difference in the median total ischemic times by category. Underweight patients, thus, had greater delays in initial diagnosis in the hospital to treatment (D2B time), relative to the overall median (61 versus 55 minutes; 10.9% difference; $P<0.001$). Mortality was also significantly higher for those who were underweight (12.6 % versus 4.7% for obesity class 2; $P<0.001$). The extreme obesity class 3 group had the second longest D2B time and the third worst mortality rate. The Figure summarizes the curvilinear relationships between both D2B time and mortality outcomes with BMI category. There is a significantly higher mortality in both the high and especially the low BMI ranges (8.4% and 12.6%; $P<0.001$) compared with the rest of the BMI groups, respectively.

Both D2B time and mortality had significant statistical differences between categories of BMI; therefore, we developed regression models to see if differences persisted with multivariable adjustments for these 2 outcomes. We also observed interaction effects between age and sex, which were incorporated into our models. After controlling for patient and institutional covariates, BMI category remained statistically significantly associated with D2B time. Obesity class 3 had the highest D2B times after adjustments. Mortality, however, was no longer significantly different between categories of body mass. Obesity class 3 had the highest overall odds ratio for mortality, but was just outside the statistically significant range ($P=0.052$) after controlling for covariates. Table 3 presents the linear and logistic regression model results.

The underweight group had the longest median D2B time, of nearly 61 minutes, 10.9% higher than the overall median. The extremely obese (class 3) group had the second highest median D2B times. After multivariate adjustments, D2B time continues to be significantly longer in all other categories than the normal BMI group, indicating that mass is statistically significant in its association with treatment times. Mortality differences, although observed in univariate tests, did not persist after other adjustments. However, we cannot draw any conclusions from this; we can only infer that we need more

DOI: 10.1161/JAHA.117.005827

Table 1. Baseline Patient Demographics and Comorbidities by BMI Category

Demographics	Total	Underweight	Normal Weight	Overweight	Obesity Class 1	Obesity Class 2	Obesity Class 3	*P* Value
Cases, n (%)	8725	127 (1.5)	1904 (21.8)	3258 (37.3)	2083 (23.9)	845 (9.7)	467 (5.4)	
Age, mean (SD), y	60.7 (12.8)	68.4 (14.0)	64.9 (13.7)	62.5 (13.0)	58.6 (11.6)	56.2 (12.2)	55.8 (11.7)	<0.001
Sex, n (%)								
Male	6306 (72.3)	51 (40.2)	1271 (66.8)	3774 (73.1)	1576 (75.7)	597 (70.7)	281 (60.2)	<0.001
Female	2419 (27.7)	76 (59.8)	633 (33.3)	1388 (26.9)	507 (24.3)	248 (29.4)	186 (39.8)	
Race, n (%)								
White	6264 (71.8)	91 (71.7)	1334 (70.1)	2376 (72.9)	1494 (71.7)	606 (71.7)	330 (10.7)	<0.0001
Black	993 (11.4)	20 (15.8)	218 (11.5)	316 (9.7)	249 (12.0)	100 (11.8)	88 (18.8)	
Asian	272 (3.1)	2 (1.6)	111 (5.8)	113 (3.5)	30 (1.4)	11 (1.3)	4 (0.9)	
Hispanic	1049 (12.0)	14 (11.0)	202 (10.6)	398 (12.2)	280 (13.4)	109 (12.9)	41 (8.9)	
Other	147 (1.7)	-	39 (2.1)	55 (1.7)	30 (1.4)	19 (2.3)	4 (0.9)	
Comorbidities, n (%)								
Smoking	3372 (38.7)	61 (48.0)	803 (42.2)	1246 (38.3)	747 (35.9)	323 (38.2)	181 (38.8)	<0.001
Diabetes mellitus	2465 (28.3)	13 (10.2)	401 (21.1)	822 (25.3)	684 (32.9)	322 (38.1)	213 (45.6)	<0.001
History of CVD	656 (7.5)	16 (12.6)	179 (9.4)	240 (7.4)	131 (6.3)	53 (6.3)	36 (7.7)	<0.001
History of stroke	466 (5.3)	8 (6.3)	122 (6.4)	173 (5.3)	94 (4.5)	45 (5.3)	23 (4.9)	<0.001
Cardiogenic shock before PCI	631 (7.2)	17 (13.4)	186 (9.8)	196 (6.0)	135 (6.5)	52 (6.2)	34 (7.3)	<0.001
Heart failure before PCI	660 (7.6)	12 (9.5)	158 (8.3)	228 (7.0)	155 (7.5)	56 (6.6)	45 (9.6)	<0.001
Signs and symptoms of presentation								
Heart rate, mean (SD), beats/min	81.0 (24.7)	84.1 (22.9)	79.9 (24.9)	79.5 (24.8)	82.1 (24.4)	84.5 (24.4)	84.3 (23.3)	0.888
Systolic blood pressure, mean (SD), mm Hg	142.8 (38.5)	133.0 (36.0)	137.2 (38.3)	142.8 (38.5)	146.1 (37.3)	147.6 (38.5)	145.4 (41.1)	0.0002
Initial creatinine, mean (SD), mg/dL	1.2 (0.9)	1.1 (0.7)	1.2 (1.0)	1.2 (0.8)	1.2 (1.1)	1.2 (0.8)	1.3 (1.1)	0.002
Lowest hemoglobin, mean (SD), g/dL	12.1 (2.3)	10.8 (2.2)	11.5 (2.3)	12.2 (2.3)	12.4 (2.3)	12.5 (2.3)	12.1 (2.4)	<0.0001
Initial troponin, mean (SD), ng/mL	7.9 (33.9)	12.0 (87.5)	8.8 (36.5)	7.6 (30.3)	8.2 (36.3)	6.3 (26.3)	5.9 (21.4)	0.742
Medications, n (%)								
Aspirin	7606 (87.2)	98 (77.2)	1592 (83.6)	2904 (89.1)	1845 (88.6)	753 (89.1)	389 (83.3)	<0.0001
Clopidogrel	4446 (51.0)	68 (53.5)	1007 (52.9)	1698 (52.1)	1021 (49.0)	414 (49.0)	225 (48.2)	<0.0001
β Blocker	7331 (84.0)	91 (71.7)	1498 (68.7)	2787 (85.5)	1808 (86.8)	732 (86.6)	392 (83.9)	<0.0001
Angiotensin receptor blocker	645 (7.4)	7 (5.5)	98 (5.2)	233 (7.2)	186 (8.9)	83 (9.8)	38 (8.1)	<0.0001
ACE inhibitor	5324 (61.0)	71 (55.9)	1060 (55.7)	2041 (62.7)	1295 (62.2)	550 (65.1)	292 (62.5)	<0.0001
Statin	7443 (85.3)	96 (75.6)	1543 (81.0)	2834 (87.0)	1814 (87.1)	743 (87.9)	389 (83.3)	<0.0001

BMI categories: underweight (1; BMI, <18.5 kg/m^2), normal weight (2; BMI, 18.5–24.9 kg/m^2), overweight (3; BMI, 25.0–29.9 kg/m^2), obesity class 1 (4; BMI, 30.0–34.9 kg/m^2), obesity class 2 (5; BMI, 35.0–39.9 kg/m^2), and extreme obesity class 3 (6; BMI, ≥40 kg/m^2). ACE indicates angiotensin-converting enzyme; BMI, body mass index; CVD, cardiovascular disease; and PCI, percutaneous coronary intervention.

Table 2. Quality Outcomes by BMI Category

Outcomes	Total	Underweight	Normal Weight	Overweight	Obesity Class 1	Obesity Class 2	Obesity Class 3	*P* Value
Door-to-balloon time, median (IQR), min	55.0 (46)	61.0 (42)	56.0 (44.0)	52.0 (44.0)	55.0 (45.0)	54.0 (45.0)	57.0 (46.0)	<0.001
Total ischemic time, median (IQR), min	185.0 (253)	187.0 (459)	183.8 (277)	181.4 (241)	186.3 (244)	194.5 (279)	188.5 (207)	0.192
Mortality, n (%)	576 (6.6)	16 (12.60)	172 (9.03)	182 (5.59)	114 (5.47)	40 (4.73)	39 (8.35)	<0.001

BMI categories: underweight (1; BMI, <18.5 kg/m^2), normal weight (2; BMI, 18.5–24.9 kg/m^2), overweight (3; BMI, 25.0–29.9 kg/m^2), obesity class 1 (4; BMI, 30.0–34.9 kg/m^2), obesity class 2 (5; BMI, 35.0–39.9 kg/m^2), and extreme obesity class 3 (6; BMI, ≥40 kg/m^2). BMI indicates body mass index; and IQR, interquartile range.

evidence to explore that there are significant differences between the groups.

Discussion

This large study of 8725 patients with STEMI who underwent primary PCI points to a curvilinear relationship for obesity, with 2 key cardiovascular outcomes. Specifically, we found that the most obese categories have the highest D2B times and mortality rates. These differences remained after covariate adjustments for D2B time, but did not persist with mortality. We did not observe significant differences in total ischemic time between categories of BMI in either univariate or multivariate models.

Although there has been a hypothesized obesity paradox for some time, prior studies have largely focused only on the association between mortality and BMI; these findings have been widely conflicted. Some studies have found a survival advantage with increased BMI,[20,21] but others report no significant relationships.[13,22] Other studies suggest moderating effects, such as sex or patient risk and severity.[23–27] One study showed overweight and mildly obese patients with hypertension to have better outcomes when compared with their similar hypertensive counterparts with a lower BMI.[28]

Our study extends the literature to assess body mass relationships with time-based outcomes as well, including D2B and total ischemic times. D2B times vary significantly by body mass categories, with the longest D2B times in the severely obese. We observed no significant differences in total ischemic time, measured by symptom onset to arterial reperfusion. On the basis of prior research, the impact of left ventricular dysfunction might be most significant in these

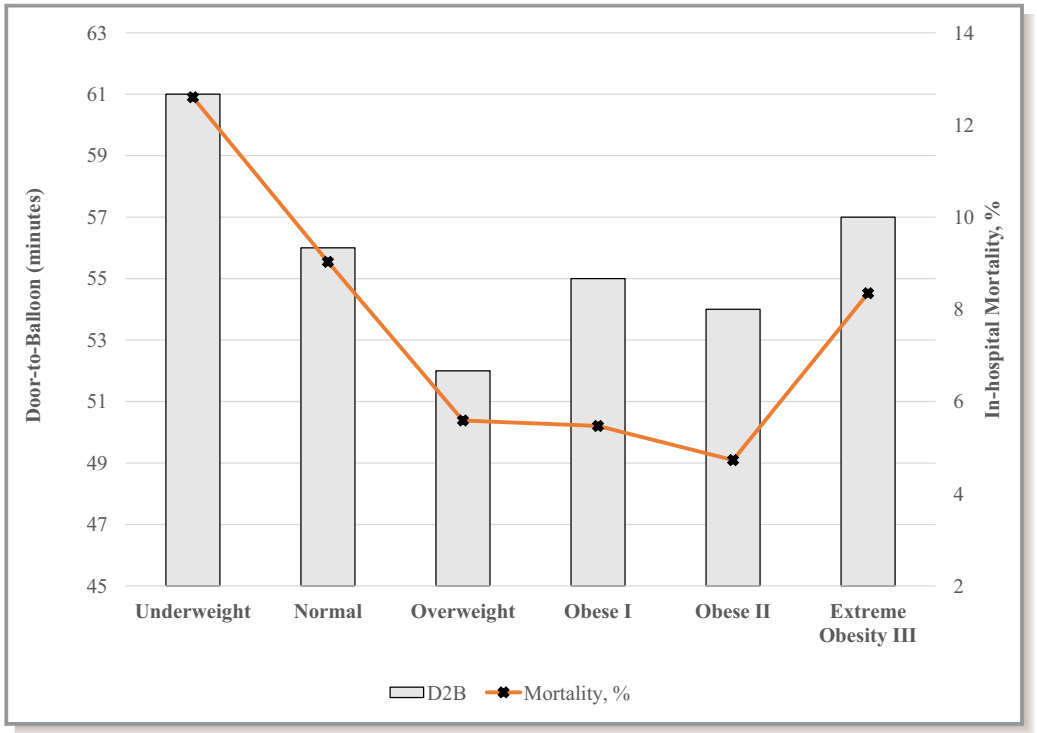

Figure. Mortality and door-to-balloon (D2B) time by body mass index category.

Table 3. Regression Model Results

Variables	D2B Time		Mortality	
	β (95% CI)	*P* Value	OR (95% CI)	*P* Value
BMI category				
Underweight	1.28 (1.04–1.52)*	<0.0001	2.39 (0.56–10.15)	0.391
Normal weight (reference)				
Overweight	1.34 (1.12–1.55)*	<0.0001	1.15 (0.53–2.49)	0.463
Obesity class 1	1.32 (1.11–1.53)*	<0.0001	1.20 (0.46–3.11)	0.637
Obesity class 2	1.33 (1.12–1.55)*	<0.0001	0.65 (0.14–3.06)	0.213
Obesity class 3	1.35 (1.14–1.57)*	<0.0001	3.83 (1.02–14.41)	0.052

BMI categories: underweight (1; BMI, <18.5 kg/m^2), normal weight (2; BMI, 18.5–24.9 kg/m^2), overweight (3; BMI, 25.0–29.9 kg/m^2), obesity class 1 (4; BMI, 30.0–34.9 kg/m^2), obesity class 2 (5; BMI, 35.0–39.9 kg/m^2), and extreme obesity class 3 (6; BMI, ≥40 kg/m^2). Estimates adjusted for sex, age, sex×age, smoking status, diabetes mellitus status, prior cardiovascular disease, prior stroke, shock before percutaneous coronary intervention, heart failure, hospital, and county. BMI indicates body mass index; CI, confidence interval; D2B, door-to-balloon; and OR, odds ratio.
*P<0.0001.

extreme BMI categories. Although early coronary reperfusion is necessary for all patients, it is especially vital for certain groups of individuals in the extreme weight categories, both low and high. In the underweight especially, cardiac cachexia has been noted in prior studies, representing a lack of functional reserve by those with less body mass.[11] No prior studies have assessed the impact on BMI and delays for presentation and prognosis (through time-to-treatment outcome metrics) for patients with STEMI undergoing primary PCI.

Although other studies have suggested a protective effect of obesity, this may reflect differential risk profiles at baseline. In this study, after adjustments for major comorbidities and institutional effects, we did not observe a protective effect of added obesity. Although differences in mortality existed (with the extremely obese and underweight extremes having the highest rates of mortality), these differences were not statistically significant in the final model.

Observed delays in treatment from arrival at the hospital could potentially be based on clinical difficulties in diagnosis for the generally older female population. We incorporated both variables, and the interaction effect between them, and all were significantly associated with mortality after other patient risk adjustments. Sex-based differences have been known to complicate initial diagnosis and treatment.[29] This study concludes that significantly greater research should focus on sex-related diagnostic and treatment differences in cardiovascular outcomes for women.

Limitations and Future Research

There are strengths and limitations to this study. The primary strength is that this study is the first to determine the impact of treatment delays by body mass. We found a curvilinear effect extends beyond mortality to treatment times (D2B times) in univariate tests, and these were confirmed in multivariate analyses for D2B times. In addition, the robustness of the data set provides another strength. Our present study represents a contemporary analysis involving >8700 patients in a large urban region.

There are limitations to our findings. First, this is a retrospective observational analysis of secondary data. The data are derived from the regional subset of the National Cardiovascular Data Registry ACTION Registry, which has been established as comprehensive and valid in multiple studies. Second, we did not have access to more direct measures of obesity, such as metabolic insulin measurements or waist and hip circumference. We relied on BMI as a proxy for adiposity. BMI has been examined extensively, however, and has been shown to be a reliable indicator for obesity. Third, there are small sample sizes in certain categories (eg, extreme underweight), which might affect lack of significance in the mortality results. Greater distribution and size of the sample across all categories would be beneficial for future research. Finally, the data are derived from 1 large urban region and may not be representative or generalizable to other populations.

Given our findings and limitations, future research should focus on the role of nutrition and physical activity counseling in the postdischarge process. Given the extreme lack of overall body mass on the underweight and obesity at the highest levels, nutritional and dietetic counseling and follow-up should be included for patients in these categories to improve proper weight management. We also suggest guideline and protocol enhancements for physicians to incorporate body mass into diagnoses, noting the outcomes found in the extremes. In addition, sex was shown to be significant in the obesity-outcome relationship. Disparities for diagnosis and treatment need to be more carefully examined. We recommend large-scale studies to prospectively confirm findings

and further identify the relationships between sex, obesity, and outcomes for patients with acute coronary disease.

Conclusions

In summary, we observed that the key time-to-treatment metric, D2B time, is associated with BMI. There are significant disparities in treatment delays by category of BMI, and the extremely obese are most vulnerable to longer treatment times. This is the first study to measure the impact of obesity on patient treatment delays, and the effect of this relationship persisted even after multivariable adjustments. We recommend future research should focus on sex disparities, identify mechanisms for reducing system delays, and improve nutritional counseling within cardiac rehabilitation after reperfusion.

Sources of Funding

This work was partially supported by a grant from the American Heart Association.

Disclosures

None.

References

1. Ogden CL, Carroll MD, Bit BK, Flegal KM. Prevalence of obesity in the United States, 2009–2010. *NCDS Data Brief*. 2012;82:1–8.
2. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA*. 2012;307:491–497.
3. Flegal KM, Graubard BI. Estimates of excess deaths associated with body mass index and other anthropometric variables. *Am J Clin Nutr*. 2009;89:1213–1219.
4. Willett K, Jiang R, Lenart E, Spiegelman D, Willett W. Comparison of bioelectrical impedance and BMI in predicting obesity-related medical conditions. *Obesity (Silver Spring)*. 2006;14:480–490.
5. Lavie CJ, McAuley PA, Church TS, Milani RV, Blair SN. Obesity and cardiovascular diseases: implications regarding fitness, fatness, and severity in the obesity paradox. *J Am Coll Cardiol*. 2014;63:1345–1354.
6. Westerman S, Wenger NK. Women and heart disease, the underrecognized burden: sex differences, biases, and unmet clinical and research challenges. *Clin Sci (Lond)*. 2016;130:551–563. DOI: 10.1042/CS20150586.
7. National Institutes of Health (NIH). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report [published correction appears in *Obes Res*. 1998;6:464]. *Obes Res*. 1998;6(suppl 2):51S–209S.
8. NHANES. National Health and Nutrition Examination Survey. US Centers for Disease Control and Prevention. Survey instrument and data. https://www.cdc.gov/nchs/nhane. Published 2017. Accessed January 4, 2017.
9. Apovian C. The obesity epidemic: understanding the disease and the treatment. *N Engl J Med*. 2016;374:177–179. https://doi.org/10.1056/nejme1514957.
10. Curtis JP, Selter JG, Wang Y, Rathore SS, Jovin IS, Jadbabaie F, Kosiborod M, Portnay E, Sokol S, Bader F, Krumholz HM. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med*. 2005;165:55–61.
11. Bucholz EM, Rathore S, Reid K, Jones P, Chan P, Rich M, Spertus J, Krumholz H. Body mass index and mortality in acute myocardial infarction patients. *Am J Med*. 2012;125:796–803.
12. Buschur ME, Smith D, Share D, Campbell W, Mattichak S, Sharma M, Gurm H. The burgeoning epidemic of morbid obesity in patients undergoing percutaneous coronary intervention: insight from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium. *J Am Coll Cardiol*. 2013;62:685–691.
13. Akin I, Schneider H, Nienaber C, Jung W, Lubke M, Rillig A, Ansari U, Wunderlich N, Birkemeyer R. Lack of "obesity paradox" in patients presenting with ST-segment elevation myocardial infarction including cardiogenic shock: a multicenter German network registry analysis. *BMC Cardiovasc Disord*. 2015;15:67.
14. Angerås O, Albertsson P, Karason K, Ramunddal T, Matejka G, James S, Lagerqvist B, Rosengren A, Omerovic E. Evidence for obesity paradox in patients with acute coronary syndromes: a report from the Swedish Coronary Angiography and Angioplasty Registry. *Eur Heart J*. 2013;34:345–353.
15. Hastie C, Padmanabhan S, Slack R, Pell A, Oldroyd K, Flapan A, Jennings K, Irving J, Eteiba H, Dominiczak A, Pell J. Obesity paradox in a cohort of 4880 consecutive patients undergoing percutaneous coronary intervention. *Eur Heart J*. 2010;31:222–226.
16. Nallamothu BK, Bradley EH, Krumholz HM. Time to treatment in primary percutaneous coronary intervention. *N Engl J Med*. 2007;357:1631–1638.
17. Nallamothu BK, Normand S, Wang Y, Hofer TP, Brush JE, Messenger JC, Bradley E, Rumsfeld J, Krumholz HM. Relation between door-to-balloon times and mortality after primary percutaneous coronary intervention over time: a retrospective study. *Lancet*. 2015;385:1114–1122.
18. Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ, Gore JM, Weaver WD, Rogers WJ, Tiefenbrunn AJ. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA*. 2000;283:2941–2947.
19. Møller JE, Pellikka P, Hillis G, Oh J. Prognostic importance of diastolic function and filling pressure in patients with acute myocardial infarction. *Circulation*. 2006;114:438–444.
20. De Schutter A, Lavie CJ, Milani RV. The impact of obesity on risk factors and prevalence and prognosis of coronary heart disease: the obesity paradox. *Prog Cardiovasc Dis*. 2014;56:401–408.
21. Wienbergen H, Gitt AK, Juenger C, Schiele R, Heer T, Towae F, Gohlke H, Senges J. Impact of body mass index on occurrence and outcome of acute ST-elevation myocardial infarction. *Clin Res Cardiol*. 2008;97:83–88.
22. Wells B, Gentry M, Ruiz-Arango A, Dias J, Landolfo C. Relation between body mass index and clinical outcome in acute myocardial infarction. *Am J Cardiol*. 2006;98:474–477.
23. Cepeda-Valery BK, Chaudhry K, Slipczuk L, Pressman GS, Figueredo V, Lavie CJ, Morris D, Romero-Corral A. Association between obesity and severity of coronary artery disease at the time of acute myocardial infarction: another piece of the puzzle in the "obesity paradox." *Int J Cardiol*. 2014;176:247–249.
24. Dooley J, Chang A, Salhi R, Hollander J. Relationship between body mass index and prognosis of patients presenting with potential acute coronary syndromes. *Acad Emerg Med*. 2013;20:904–910.
25. Dhoot J, Tariq S, Erande A, Amin A, Patel P, Malik S. Effect of morbid obesity on in-hospital mortality and coronary revascularization outcomes after acute myocardial infarction in the United States. *Am J Cardiol*. 2013;111:1104–1110.
26. Niraj AJ, Pradhan J, Fakhry H, Veeranna V, Afonso L. Severity of coronary artery disease in obese patients undergoing coronary angiography: "obesity paradox" revisited. *Clin Cardiol*. 2007;30:391–396.
27. Payvar S, Kim S, Rao S, Krone R, Neely M, Paladugu N, Daggubati R. In-hospital outcomes of percutaneous coronary interventions in extremely obese and normal-weight patients: findings from the NCDR (National Cardiovascular Data Registry). *J Am Coll Cardiol*. 2013;62:692–696.
28. Uretsky S, Messerli FH, Bangalore S, Champion A, Cooper-Dehoff RM, Zhou Q, Pepine CJ. Obesity paradox in patients with hypertension and coronary artery disease. *Am J Med*. 2007;120:863–870.
29. Khera S, Kolte D, Gupta T, Subramanian KS, Khanna N, Aronow WS, Ahn C, Timmermans RJ, Cooper HA, Fonarow GC, Frishman WH, Panza JA, Bhatt DL. Temporal trends and sex differences in revascularization and outcomes of ST-segment elevation myocardial infarction in younger adults in the United States. *J Am Coll Cardiol*. 2015;66:1961–1972.