

Original Contribution



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Does the obesity paradox apply to early

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Abstract

Background: There is evidence that very obese patients (body mass index [BMI] >40 kg/m²) undergoing hip replacement have longer average hospital stays, as well as higher rates of complications and readmission compared with patients with normal BMI. However, there are sparse data describing how overweight and obese patients fare in the period immediately after hip replacement surgery compared with patients with low or normal BMI. In this study, we sought to explore the association of BMI with the rate of early postoperative complications in patients undergoing total hip arthroplasty.

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http://dx.doi.org/10.1016/j.jclinane.2015.12.037 0952-8180/© 2016 Elsevier Inc. All rights reserved. **Methods:** A proprietary hospital software program, Clinical Looking Glass was used to query the Montefiore Medical Center database and create a list of patients with *International Classification of Diseases, Ninth Revision* code 81.51 (hip replacement) from the period of January 1, 2010, through December 31, 2012. The medical records of patients with length of stay 5 or more days were reviewed to evaluate the reason for the extended stay. The primary outcome studied was the association between BMI and occurrence of early complications in patients who had undergone total hip replacement surgery. Logistic regression was used to calculate adjusted odds ratio (OR) and 95% confidence interval (CI) for the association of BMI and early postoperative complications.

Results: Of the 802 patients undergoing hip replacement surgery within our time frame, 142 patient medical records were reviewed due to their length of stay of ≥ 5 days. Overall complication rate in the analyzed patients demonstrated a J-curve distribution pattern, with the highest morbidity being 23.5% in the underweight group, the second highest in the normal-weight group (17.3%), and decreasing to nadir in the overweight (8.0%) and obese class I (10.0%) and then higher again in classes II (14.3%) and III (16.7%). Adjusted ORs demonstrated the same J distribution pattern similar to the pattern observed in the univariate analysis. Of the variables studied, Charlson score (OR, 1.1; 95% CI, 1.1-1.2; P = .03), diagnosis of hip fracture (OR, 5.2; 95% CI, 2.8-9.8; P = .01), normal weight (OR, 1.9; 95% CI, 1.1-3.8; P = .04), and obese class III (OR, 2.5; 95% CI, 1.1-6.3; P = .04) were the factors associated with the highest odds of early complications after hip replacement surgery.

Conclusions: In this retrospective review of hip replacement surgery patients, BMI classification was a predictor of early postoperative complications. Although the exact underlying mechanisms are still not clear, these results are consistent with the obesity paradox, in which obesity or its correlates provide some form of protection.

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1. Introduction

The prevalence of overweight and obesity in the American population has increased steadily over the last 25 years [1]. According to the Centers for Disease Control and Prevention, 68.8% of Americans are now classified as overweight (body mass index [BMI] 25-29.9 kg/m²) [1] or obese (BMI > 30 kg/m²) [2], with more than half these patients falling into the obese category. Elevated BMI is associated with comorbidities such as ischemic heart disease [3], type 2 diabetes [4], stroke [5], and hypertension [6], and BMI is positively correlated with all-cause mortality in the general population [7]. The average BMI is increasing in many populations around the world, mounting concern about the public health effects of this obesity epidemic [8].

Recent literature, however, has shown that obesity is associated with better outcomes in certain chronic disease states. This phenomenon was initially termed "reverse epidemiology" in a 2003 review by Kalantar-Zadeh et al [9] proclaiming the protective effect of obesity on survival among dialysis patients. Furthermore, Leavey et al [10] found that in patients undergoing hemodialysis, overweight patients have a lower relative risk of mortality compared with patients with BMIs in the normal, class I obesity, and class II obesity categories. Reverse epidemiology, also known as the "obesity paradox," is seen in patients with established heart failure as well. A meta-analysis conducted by Oreopoulos et al [11] in 2007 showed that compared with normal BMI, overweight and obesity are associated with lower all-cause mortality in patients with heart failure. On the other hand, the study shows that underweight and low-normal weights compared with normal weight are associated with a higher risk of cardiovascular mortality.

The incidence of hip fracture and its surgical repair are increasing every year [12]. Studies have reported a positive correlation of postoperative complications rates and 1-year mortality rates after the hip replacement surgeries [13]. The effect of increased BMI on the rate of complications in patients undergoing surgery, specifically total hip arthroplasty, is not as well described. There is some evidence that morbidly obese patients (BMI > 40 kg/m²) undergoing hip replacement have longer average hospital stays, as well as higher rates of complications and readmission when compared with patients with normal BMI [14]. However, there are few data describing how overweight and obese patients fare in the period directly after hip replacement surgery when compared with patients with low or normal BMI. The goal of this retrospective study was to explore the association, if any, of BMI and immediate postoperative complications in patients undergoing total hip arthroplasty.

2. Methods

This retrospective study was approved by our institutional review board. Patient data included hospital records from outpatient, inpatient, and emergency department visits. All diagnostic and surgical procedures entered into these records are indexed in a computer database, allowing the retrieval of all records of interest. We queried the Montefiore Medical Center database using a patented hospital software program,



Fig. 1 Flowchart showing case selection for the study.

Clinical Looking Glass (CLG). The CLG database allows users to create lists of patients based on criteria specified by the user (eg, *International Classification of Diseases, Ninth Revision* codes, time frame, medication usage, laboratory values, etc). For the purpose of this study, a search for the *International Classification of Diseases, Ninth Revision* code 81.51 (hip replacement) from the period of January 1, 2010, through December 31, 2012, was conducted. Eight hundred two patients undergoing total hip replacement were identified (Fig. 1).

All patients included in the study were required to have BMI data available at the time of surgery. The formula used to calculate BMI was weight in kilograms divided by the square of the height in meters (kg/m²). Patients were classified as (1) underweight (BMI < 18.5 kg/m²), (2) normal weight (BMI = 18.6-24.9 kg/m²), (3) overweight (BMI = 25-29.9 kg/m²), (4) obese class I (BMI = 30-34.9 kg/m²), (5) obese class II (BMI = 35-39.9 kg/m²), and obese class III (BMI > 40 kg/m²) as specified by the National Institutes of Health (http://nhlbisupport.com/bmi/bminojs.htm; accessed November 2013). Medical records of all patients were reviewed to determine American Society of Anesthesiologist status, BMI, surgical time and length of hospital stay (LOS).

Four patients were excluded due to lack of medical records or cancelled surgery (perioperative reasons). Eight patients were excluded from the analysis because their hip fracture was sustained as a result of a comorbid condition such as seizure, stroke or abdominal aortic aneurysm. Seven hundred and ninety patients were examined for LOS. Median LOS for patients undergoing total hip replacement is 3 (3-4, 25th and 75th percentile) days at our medical center. For the purpose of this study, we deemed that patients who stayed more than 1 standard deviation above the median (\geq 5 days) had a valid reason for their extended stay. One hundred forty-two patients were identified that had hospital LOS of 5 days or more. The medical records of this subset of patients were reviewed by 2 research associates (I.K., S.N.) in order to evaluate the reason for the extended stay. Questionable medical issues were discussed with other investigators. CLG software was used to construct the Charlson comorbidity index.

Charlson comorbidity index is a validated method of classifying comorbidity to predict short-term and long-term mortality from medical records [15]. Based on occurrence of the preidentified comorbid conditions present, patients receive a score between 0 and 22, with a lower Charlson comorbidity index score indicating fewer comorbid conditions. Medical history of patients collected within 3 years prior to surgery date was used to construct Charlson score. CLG was also used to identify patients who were readmitted to our hospital within 30 days after surgery and the patients who died within a month of surgery. Reasons for the readmissions were identified from medical records.

The primary outcome studied was the association between BMI and occurrence of early complications in patients who had undergone total hip replacement surgery. Early postoperative complications were defined as a hospital LOS of 5 or more days for which there was a valid medical reason. Early complications included acute blood loss requiring transfusion, wound infections, and systematic complications including pulmonary embolism, electrolyte imbalance, elevated troponin level, pneumonia, genitourinary tract related complications, and gastrointestinal complications. Discharge summaries were also examined for the above-mentioned complications.

Patients who remained in the hospital for nonmedical reasons such as nonavailability of a rehabilitation bed or social issues were considered noncomplication patients, as were patients with no adverse conditions reported on their charts.

Basic descriptive statistics including median (25th percentile, 75th percentile) for continuous variables and percentages for categorical variables were calculated for baseline demographics and other operative characteristics. Prevalence of overweight and obesity was described as simple proportions. Pearson χ^2 for categorical variables and Kruskal-Wallis test for continuous variables were used to assess bivariate associations of the baseline clinical and perioperative differences with BMI categories.

Multivariable analysis was performed using forward stepwise logistic regression to calculate the adjusted odds ratio (OR) for the occurrence of complication in the BMI categories with the overweight group (BMI 25-29.9 kg/m²) as reference. Overweight was chosen as reference because it exhibited the fewest complications in bivariate analysis. Variables were entered into the model on the basis of statistical significance and clinical relevance. Model fit was assessed with the Hosmer-Lemeshow goodness-of-fit test. All reported *P* values were 2 sided, and a *P* value <.05 was

considered statistically significant. Analysis of data was performed using SPSS version 21.0 (SPSS Inc, Chicago, IL).

3. Results

In total, 142 charts were reviewed. Of these, 46 patients were further excluded from the final analysis, as the only reason for extended stay was receiving blood transfusions and no other medical issues were identified. Demographic data and medical information for all the patients entered into the analysis are listed in Table 1. Age, American Society of Anesthesiologist Physical Status Classification System, length of surgery, and hematocrit before and after surgery were not similar among the groups. The median number of perioperative blood transfusions was greater in patients with the lowest BMI group. The number of transfusions was negatively correlated with the BMI groups and also with the preoperative hematocrit level ($\rho = -0.20$ and -0.40; both P <.001). The mortality rate of the initial 802 patients included in the study was 0.4% within the first 30 postoperative days. One patient died of complications from hip surgery, and 2 others died of multiorgan failure related to cancer and HIV. Readmission within 30 days, LOS, number of transfusions, and patient deaths are depicted in Table 2.

The overall complication rate in the analyzed patients demonstrated a J-curve distribution pattern, with the highest morbidity being 23.5% in the underweight group, the second highest in the normal-weight group (17.3%), and decreasing to nadir in the overweight (8.0%) and obese class I (10.0%) and then higher again in groups II (14.3%) and III (16.7%; P = .028; Fig. 2). Complications occurred in each BMI group is depicted in Table 3. LOS for these patients demonstrated the same trend. Although the median LOS was not statistically significantly different among the groups, patients in the lowest BMI and normal-weight group remained in the hospital longer when compared with other higher BMI groups. The incidence of pulmonary embolism was 0.8% and did not demonstrate any statistical difference among the groups (data not shown). The

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	<18.5 (n = 17)	18.6-24.9 (n = 168)	25-29.9 (n = 249)	30-34.9 (n = 211)	35-39.9 (n = 91)	>40 (n = 54)	Р
Age (y)	57 (46-69)	64 (53-75)	65 (55-76)	62 (52-70)	60 (51-64)	60 (53-66)	.02
Charlson score	0 (0-2)	1 (0-4)	1 (0-2)	1 (0-3)	1 (0-3)	1 (0-2)	.05
Age-related Charlson risk score	2 (0-3)	4 (1-3)	3 (1-3)	3 (1-3)	2.50 (1-2)	3 (1-2)	.03
Sex (female)	58.8%	57.9%	51.6%	60.6%	60%	60%	.37
ASA score	2 (2-3)	2 (2-3)	2 (2-3)	2 (2-3)	2 (2-3)	3 (2-3)	.08
Length of surgery	116 (102-156)	113 (93-145)	114 (95-137)	123 (96-150)	122 (103-155)	135 (105-191)	.02
HCT before	36.5 (30-43)	37.8 (34-41)	39.3 (37-43)	40.1 (38-43)	39.7 (37-43)	40.1 (38-44)	<.001
Diagnosis of hip fracture	35.3%	15.7%	8.8%	2.4%	3.2%	1.9%	<.001
Any malignancy	5.9%	13.1%	6.4%	12.3%	13.2%	5.6%	.11

 Table 1
 Preoperative characteristic of 790 hip replacement surgery patients

ASA = American Society of Anesthesiologist; HCT = hematocrit.

Data presented as median (25%-75%) and percentage unless stated otherwise.

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	<18.5	18.6-24.9	25-29.9	30-34.9	35-39.9	>40	Р
Length of hospital stay (d)	4 (3-7)	3 (3-5)	3 (3-4)	3 (3-4)	3 (3-4)	3 (3-4)	.09
No. of transfusions	2 (0-2)	2 (0-2)	0 (0-2)	0 (0-2)	0 (0-2)	0 (0-2)	<.001
Readmission within 30 d	5.9%	4.9%	4.9%	3.8%	6.7%	7.4%	.87
Died	0.0%	0.0%	0.4%	0.9%	0.0%	0.0%	
Determined as modifier (250/ 750/) and assessed as males at the string							

 Table 2
 Thirty-day readmission, length of hospital stay, number of transfusions, and patient deaths

Data presented as median (25%-75%) and percentage unless stated otherwise.

combined postoperative infection rates which include wound infections, urinary tract infections, and pneumonia was highest in the underweight group and also demonstrated the J-shaped distribution pattern (data not shown), without statistical difference.

Adjusted ORs demonstrated the same J-shaped distribution pattern similar to the pattern observed in the univariate analysis (Fig. 3). Age, Charlson score, length of surgery, hip fracture, and the 5 BMI classes were entered into the logistic regression model with overweight, which has the lowest complication rate, considered as the reference group. Of these variables, Charlson score (OR, 1.1; 95% confidence interval [CI], 1.1-1.2; P = .03), diagnosis of hip fracture (OR, 5.2; 95% CI, 2.8-9.8; P = .01), normal weight (OR, 1.9; 95% CI, 1.1-3.8; P = .04), and obese class III (OR, 2.5; 95% CI, 1.1-6.3; P = .04) were the factors associated with the highest odds of early complications after hip replacement surgery. The ORs for other variables in the final model are shown in Table 4.

4. Discussion

In this retrospective review of hip replacement surgery patients, BMI classification was a predictor of early postoperative complications. However, the predictions did not follow a linear pattern. The poorest outcomes were found to be in the underweight, normal, and morbidly obese groups. The phenomenon in which overweight and obese patients exhibit decreased morbidity and mortality rates compared with normal-weight and underweight patients has been termed the "obesity paradox" [16–23].

As seen in other studies that assessed obesity as a predictor of morbidity and mortality, the highest complication rate (23.5%) was in the group with the lowest BMI, <18.5 (16-23) kg/m². One of the possible reasons for this high complications rate in the underweight group could be preexisting comorbid conditions and the higher occurrence of hip fractures in this group. Preexisting medical comorbidites were adjusted using the Charlson comorbidity index. The Charlson comorbidity index score for the underweight group was the lowest of all the groups, which indicates better health condition when compared with all the other BMI class. However, this group did have more hip fractures (35.3%). One possible reason for the increase in hip fracture could be the increased incidence of osteoporosis in underweight patients compared with heavier patients [24]. Underweight BMI status may also reflect poor nutritional status, thus impacting postoperative healing and response to the stresses of surgery [25-27]. Sullivan et al [28] found that elderly patients who were malnourished, as evident by low



Fig. 2 Bar graph showing BMI class and the incidence of early complication rates in 790 hip replacement surgery patients. Value labels percentage of complication rate. BMI = body mass index.

BMI1	BMI2	BMI3	BMI4	BMI5	BMI6
UTI, gluteal	hemorrhage, delayed drain removal, increased pain	Excessive blood loss, pneumonia, sepsis, sacral ulcer, postoperative electrolyte imbalance, intraoperative cardiac arrest, hematuria, atrial flutter, AKI, new onset of seizure, pulmonary embolism, postoperative bradycardia, cognitive decline	Atrial fibrillation, postoperative bleeding, delayed drain removal, UTI, postoperative electrolyte imbalance, postoperative delirium, atrial flutter, pulmonary embolism, reoperation, renal failure, hematuria	Postoperative ileus, acute blood loss, postoperative electrolyte imbalance, CHF, postoperative delirium, angina, compartment syndrome, intraoperative fracture, cognitive decline, respiratory distress, postoperative tachycardia, urinary retention	Fever, delayed drain removal, postoperative electrolyte imbalance, postoperative ileus, postoperative hypotension, cognitive decline, acute blood loss, increased pain
Prolonged	intubation, electrolyte imbalance, arrhythmia, postoperative ileus, delayed Foley removal, UTI				

Table 3Complications in each BMI group

AKI = acute kidney injury; BMI = body mass index; CHF = congestive heart failure; UTI = urinary tract infection.

BMI, lean and fat mass depletion, and weight loss during hospitalization, have increased rates of life-threatening complications during hospitalization. It is possible that these elderly malnourished patients were at an increased risk for complications during their hospitalization, even prior to undergoing surgery.

The next highest complication rate (17.3%) was in the normal-weight group with BMI 18.6-24.9 kg/m². The Charlson comorbidity index was similar to other groups, except from the underweight class which was the lowest.

This normal-weight group had the second highest fracture diagnosis for hip replacement surgery (15.7%). When examined, the diagnosis of fracture and the occurrence of complication events within the BMI 18.6-24.9 kg/m² group were found to be evenly distributed. Meanwhile, the overweight group (BMI 25-29.9 kg/m²) in this study had the lowest morbidity rate (8%). As a patient gets older, it becomes more difficult to maintain normal weight as metabolism decreases and the ratio of lean muscle mass to body fat naturally decreases [29]. In this study, the Charlson



Fig. 3 Adjusted odds ratio for early complication rates according to BMI categories (overweight as the reference category). The J-shape relationship is maintained with highest odds of early complication is in the underweight and in the overweight class III categories. Value labels represent odds ratio and 95% confidence interval. BMI = body mass index.

Table 4 Predictors of early postoperative complications

Variables in the model	Р	OR	95% C	I
BM1 (kg/m ²)				
<18.5	.20	2.3	0.62	8.5
8.6-24.9	.04	1.9	1.1	3.8
25-29.9 ^a		1.00		
30-34.9	.29	1.4	0.73	2.8
35-39.9	.05	2.1	0.98	4.6
>40	.04	2.5	1.1	6.3
Age	.82	1.00	0.99	1.0
Charlson score	.02	1.1	1.1	1.2
Length of surgery	.07	1.00	1.0	1.0
Diagnosis of hip fracture	<.001	5.2	2.8	9.8

BMI = body mass index; CI = confidence interval; OR = odds ratio. Statistical comparison derived from logistic regression model.

^a Reference category.

comorbidity index is relatively low for the overweight group. One possible explanation for decreased complication rate is described by the "fat but fit" or "healthy obesity" theories [30,31]. These theories support the concept that there is no further increased risk for overweight or obese patients if they have a normal cardiometabolic risk profile.

Complication rates for patients in the class I obesity (10%), class II obesity (14.3%), and class III obesity (16.7%)categories were less than the complication rate for the underweight and normal-weight groups. Although the exact underlying mechanisms are still unclear, these results are consistent with obesity or its correlates providing some form of protection. Explanations offered include lipoprotein protection against endotoxins, inflammatory cytokines, and other inflammatory mediators [32,33]. These lipoproteins may also serve to protect patients from inflammation associated with surgery, particularly in the overweight, class I obesity, and class II obesity categories. However, as patients' weight surpassed a BMI of 40 kg/m² into the class III obesity category, complication rates and ORs again were observed to be higher, although in this small sample, the differences are not statistically significant (2.5 compared with 2.3 for the >18.5 kg/m² BMI groups). Several studies have identified class III obesity as an independent predictor for postoperative complications [34,35], and in our study, the risk of class III obesity seems to outweigh any protective effects.

The combined incidence of early complication in this study sample was 12.2%, which is consistent with the national average of 1-month morbidity after hip surgery [36]. However, patients that fell into the overweight, class I obesity, class II obesity, and class III obesity categories had fewer complications than did patients that fell into the underweight and normal-weight categories. The complication rates by obesity classification exhibits a J-shaped curve, which is consistent with some epidemiologic studies [9,37] but differs from other surgical studies that showed a reverse J-shaped curve relationship [38].

There are several differences between this study and other studies that looked into postoperative morbidity. Our study looked only into early complications that prolonged the hospital stay of the patients. It is possible that if this study had a longer follow-up period, a reverse J-shaped curve might have been observed. In addition, the other studies also found the most pronounced reverse J-shaped curve for all-cause mortality. It is important to note that this study had no deaths in the operating room or in the immediate postoperative period that was reviewed (however, as noted earlier, 3 deaths did occur after hospital discharge and within 30 days).

Our study has several limitations. One of the primary limitations is the retrospective nature and the limited sample size of our sample population. Also, this sample population is all from a single center and surgeries were performed by different surgeons. Although a multivariable regression analysis was used to show the association between BMI and the incidence of early complications, causality cannot be determined. We adjusted for potentially confounding risk factors shown in similar studies as well as clinically important variables; however, there may be other variables such as difference in mental status, cognitive capacity, and surgeon's expertise which we were unable to capture that could have confounded the results. In addition, we did not consider functional issues-who was weight bearing quickly and, moreover, what type of reconstruction was performed. The retrospective character of the study could also introduce bias despite our best efforts. Therefore, without a better understanding of the mechanism, it cannot be known for certain whether the early complications seen were due to increased BMI or as a result of an unaccounted specific patient character.

As demonstrated in our study and studies from other subspecialties, the 2 extreme ends of the BMI groups, the underweight and the morbidly obese are at the highest risk for the occurrence of perioperative complications. One of the possible ways to address this issue is to give special attention to this group of patient population and enhance their preoperative evaluation. For underweight patients, nutrition screening tools can be used to identify patients who may benefit from additional parenteral nutritional supplements. There are published studies reporting the association of the use of nutritional supplements and reduction of surgical complications [39,40]. On the other hand, the morbidly obese patient population may benefit from an in-depth screening of all possible health concerns, such as cardiopulmonary function and status of obstructive sleep apnea, in reducing adverse events [41].

In summary, our study suggests the possibility that hip replacement patients characterized as overweight may be at lower risk for postoperative complications than either their lighter or heavier counterparts. Future studies should attempt to replicate these results in other patient populations and determine whether higher incidence of complications is a result of the weight itself or due to other related factors.

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