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ORIGINAL ARTICLE – HEALTHCARE POLICY AND OUTCOMES

Body Mass Index and Major Cancer Surgery Outcomes: Lack of Association or Need for Alternative Measurements of Obesity?

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ABSTRACT

Background. Although surgical studies have reported inconsistent associations between increased body mass index (BMI) and operative outcomes, the accuracy of BMI for measuring obesity has been questioned in previous epidemiologic studies. Simultaneously, BMI has known comorbidities, which may mediate the effect of BMI if included in multivariable models. We sought to examine the effect of BMI on operative outcomes after adjusting for preoperative factors.

Methods. We identified 8858 patients who underwent major thoracic, abdominal, and pelvic surgery for solid organ tumors in American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) centers from 2005 to 2007. We used multivariable analyses to assess the effect of BMI on short-term operative outcomes after controlling for covariates.

Results. Increased BMI was not associated with worse short-term operative outcomes in our bivariable analyses. However, patients with BMI $\geq$35 had higher American Society of Anesthesiologists scores, longer operative times, and an increased number of postoperative complications ($P < 0.0001$). After adjusting for pre- and intraoperative factors, BMI did not predict any short-term operative outcome except for an increased total number of complications in BMI $\geq$35. These results persisted after removing potential mediators from the multivariable analysis.

Conclusions. In ACS NSQIP, BMI has minimal association with short-term operative outcomes after major cancer surgery. Although these findings may suggest a lack of association between obesity and cancer surgery outcomes, it confirms the previously examined limitations of BMI. Because of the rising incidence of obesity in the United States and its challenging effect on surgeon's practice, ACS NSQIP should consider exploring alternative measures of general and abdominal obesity.

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Since 1990, the prevalence of obesity has doubled in the United States. Obesity has been associated with an increased risk for many health problems including cancer, heart disease, and excess mortality, thus posing a significant health care concern.[1–4] Today, surgeons are faced with the unavoidable reality of obesity in their practice, which complicates caring for patients with solid organ malignant cancers. Specifically, surgeons are compelled to address several competing challenges, including the rising incidence of obesity in the United States, the unequivocal need for surgical resection to treat most solid organ tumors, and the compromise in patient's oncologic outcomes in treatment delays to benefit from weight reduction programs.

The association between body mass index (BMI) and operative outcomes has been investigated by several surgical studies showing mixed results from no difference in operative outcomes to high BMI strongly predictive of worse operative outcomes.[5–12] In these studies, obesity was measured by BMI, the standard method recognized by the World Health Organization and the National Institutes of Health.[13,14] Emerging surgical literature from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) reports a negative association

between obesity and adverse operative outcomes after major abdominal procedures. More specifically, increased BMI was not found to be a significant predictor of most short-term operative outcomes after major intra-abdominal resections for cancer in these studies.[10] Other investigators, however, have reported that BMI was predictive of surgical-site infections, renal failure, and pulmonary embolism after colorectal or hepatic resections in ACS NSQIP.[6,9] The conflicting results of the BMI-operative outcomes relationship and outcomes have also been observed in several previous single-hospital and region-based studies.[7,11]

The accuracy of BMI in measuring obesity has been raised by several epidemiologic studies from the United States and Europe.[15–21] In these studies, investigators argue that BMI does not differentiate between general versus abdominal obesity. Additionally, the accuracy of BMI has been shown to vary greatly by race, as it becomes less accurate in other ethnicities.[22–24] Although BMI was associated with several comorbidities such as diabetes, cardiac diseases, and death, these large epidemiologic studies have shown that BMI is less accurate than waist circumference or waist-to-hip ratio in predicting the development of these outcomes. Additionally, others have proposed that effect of BMI on disease may be mediated by its known comorbidities if included in multivariable modeling.[17,18] As a result, including such comorbidites in multivariable analyses could diminish the true causal effect as a result of overadjustment for factors that lie on the causal pathway between BMI and operative outcomes.

In light of the above evidence, we postulate that the effect of obesity on operative outcomes by using the measure of BMI will be minimal, thus potentially underestimating its effect on cancer surgery outcomes. Additionally, we postulate that the effects of obesity-related comorbidities (e.g., diabetes, cardiac diseases) lie on the causal pathway between BMI and operative outcomes (e.g., 30-operative mortality, postoperative complications), thus potentially mediating the effect of BMI on operative outcomes. By means of the ACS NSQIP database, we examined whether BMI affects short-term operative outcomes after major oncologic resections, controlling for other independent risk factors. Additionally, we sought to assess this association after removing potential mediators of BMI from our multivariable analyses.

METHODS

Data Source

For our study, we used the 2005 to 2007 Participant Use File of the ACS NSQIP, a large, prospective, multihospital, risk-adjusted database that is based on the experience of the Veterans Affairs NSQIP. In 2002, the ACS became interested in the NSQIP after the demonstrated success of the Veterans Administration NSQIP in reducing mortality and improving patient safety at Veterans Affairs Medical Centers as well as private sector hospitals.[25–29] The ACS NSQIP collects detailed data from patients undergoing inpatient and outpatient surgical procedures from >190 participating university and private sector medical centers. ACS NSQIP captures information on preoperative risk factors and laboratory values, intraoperative variables, and 30-day postoperative mortality and morbidity outcomes, thereby providing participating institutions with practical feedback and supporting continuous quality improvement at these centers. Approval to conduct our study was obtained from both of the University of Minnesota Institutional Review Board and ACS NSQIP. The ACS NSQIP is not responsible for the statistical validity of the data analysis or the conclusions derived by users of the data.

Patients

Between 2005 and 2007, the ACS NSQIP database has recorded information from a total of 9323 patients who underwent a major thoracic, abdominal, or pelvic resection for solid organ neoplasia. For our case definition, we used the assigned International Classification of Diseases (9th edition) codes for neoplasia and matched cases with those who had undergone cancer surgery by Current Procedure Terminology codes. Patients were excluded from our study if they had missing values for BMI calculations (i.e., height [n = 107] and weight [n = 24]). Patients were additionally excluded if they weighed <90 pounds (n = 36) or were under 60 inches in height (n = 298) because we thought these values were unrealistic for our patient population. Our final cohort consisted of 8858 patients.

BMI Definition

BMI was calculated by dividing weight in pounds by height in inches squared and multiplying by a conversion factor of 703.[30] Our final cohort of 8858 patients was then categorized into BMI ranges according to the World Health Organization definitions: <18.5 (underweight), 18.5 to 24.9 (normal weight), 25 to 29.9 (overweight), 30 to 34.9 (obese, class I), and ≥35 (obese, class II).[14]

Outcome Definitions

For short-term operative outcomes, we examined 30-day mortality, length of stay (LOS) in days, proportion of patients with prolonged LOS, number of postoperative complications, and types of postoperative complications (major vs. minor).

LOS was defined as the number of days from operation to hospital discharge. We analyzed only patients who were discharged alive from the hospital after postoperative day 4 because 96% of patients fell within this range and a shorter LOS (i.e., <4 days) would be unrealistic (or potentially miscoded). However, given the potential bias that this may introduce to our "prolonged LOS" multivariable analyses, we performed additional analyses using the following criteria: (1) LOS of <4 days with deaths included, (2) LOS of <4 days with deaths excluded, (3) LOS of <1 day with deaths included, and (4) LOS of <1 day with deaths excluded. Our estimates remained unchanged. Additionally, to be consistent with previous work with NSQIP, we defined prolonged LOS for our study as a LOS beyond the 75th percentile.[31,32] In our study, 75% of the cohort was discharged before postoperative day 11.

The total number of complications consisted of the sum of the major and minor complications within 30 days of the operation, with the potential for multiple complications within each category.

Postoperative complications were classified as major or minor. Major complications included sequelae of deep incisional, organ/space surgical site infection, wound disruptions, pneumonia, the need for reintubation, pulmonary embolism, progressive renal insufficiency, acute renal failure, cerebrovascular accidents, coma, peripheral nerve injury, cardiac arrest, myocardial infarction, graft/flap failure, sepsis, septic shock, the need for return to the operating room, or >48 hours on a ventilator. Minor complications included sequelae of superficial surgical site infections, urinary tract infections, and deep vein thrombosis/thrombophlebitis.

Statistical Analyses

For our unadjusted analysis, we compared demographics, preoperative factors, preoperative laboratory values, intraoperative data, 30-day operative mortality, postoperative complications, and LOS by BMI groups by χ^2 tests for categorical variables and ANOVA test for continuous variables. Finally, we conducted a Cochrane-Armitage test for trend to examine the relationship between BMI and an increased total number of complications.

To confirm these observations, we performed a multivariable logistic regression analyses to predict the association between BMI and four categories of short-term operative outcomes, after adjusting for covariates. These categories consisted of 30-day operative mortality, the likelihood of developing major (vs. no) postoperative complications, and prolonged LOS. To predict the effect of BMI on the increased total number of postoperative complications (major or minor), we used ordinal logistic regression analysis. Because of the relationship between BMI and other comorbidities, we repeated our multivariable logistic regression analyses after removing potential mediators of BMI (e.g., diabetes and cardiac disease). We controlled for potential confounders of this relationship, including demographics, preoperative factors, laboratory values, intraoperative variables, and types of operative resection. Operative resections were divided into two categories: major or complex. Complex surgeries included pancreaticoduodenectomy, total pancreatectomy, total pneumonectomy, lobectomy, or esophagectomy. Major surgeries included total or distal gastrectomy, open distal pancreatectomy, hepatic or bile duct resection, abdominoperineal resection, pelvic exenteration, proctectomy, radical nephrectomy, urinary cystectomy, or pelvic exenteration. Patients with missing values for the potential confounders including comorbidities, preoperative laboratory values, and intraoperative variables were excluded from the final regression analysis. However, to confirm whether our estimates were influenced by including only patients with no missing values, we repeated all our multivariable analyses after including those with missing values. Finally, we evaluated the interaction between BMI and all other variables in the model to identify whether the effect of BMI was modified by additional factors in our model.

RESULTS

Of the 8858 patients we identified who underwent major resections for thoracic, abdominal, or pelvic neoplasms, 339 (3.8%) underwent total pneumonectomy or lobectomy; 535 (6.0%) esophagectomy; 979 (11.1%) total or distal gastrectomy; 2463 (27.8%) pancreaticoduodenectomy or total pancreatectomy; 954 (10.8%) open distal pancreatectomy; 2102 (23.7%) hepatic or bile duct resection; 836 (9.4%) abdominoperineal resection or pelvic exenteration; 519 (5.9%) proctectomy with or without total abdominal colectomy; and 131 (1.5%) radical nephrectomy, urinary cystectomy, or pelvic exenteration. The median age at diagnosis was 62 years (range, 17–90 years).

In our cohort, patients with a higher BMI were also more likely to be white ($P = 0.0001$), younger ($P < 0.0001$), and never smokers ($P < 0.001$); further, they had higher proportions of comorbidities and had higher American Society of Anesthesiologists (ASA) scores ($P < 0.0001$) (Table 1). Risk factors for worse surgical outcomes were more common in patients with higher BMI. For example, these risk factors included lesser rates of nondiabetes (92.1% in BMI 18.5 to 24.9 vs. 67.8% in BMI ≥35, $P < 0.001$) and increased rates of orally treated hypertension (32.3% in BMI 18.5 to 24.9 vs. 63.9% in BMI ≥35, $P = 0.0019$) with increase BMI (Table 1). Higher BMI was also associated with significant variations

TABLE 1 Preoperative and intraoperative factor profile stratified by BMI[a]

Characteristic	BMI					*P*
	<18.5 (n = 265)	18.5–24.9 (n = 3178)	25–29.9 (n = 3145)	30–34.9 (n = 1432)	≥35 (n = 838)	
Sex						0.0001
Female	58.50%	48.80%	37.20%	44.30%	51.30%	
Male	41.50%	51.20%	62.80%	55.70%	48.70%	
Race						0.0001
White	72.45%	75.24%	77.58%	78.21%	77.92%	
Black	9.81%	7.08%	7.34%	8.87%	9.55%	
Hispanic	2.64%	4.37%	3.85%	3.91%	4.06%	
Other	9.06%	6.10%	3.08%	1.19%	1.07%	
Unknown	6.04%	7.21%	8.14%	7.82%	7.40%	
Age						<0.0001
<50 years	22.26%	20.52%	16.72%	18.72%	25.78%	
51–60 years	23.77%	22.09%	22.38%	27.51%	29.36%	
61–70 years	21.89%	22.56%	24.96%	25.91%	27.09%	
≥70 years	32.08%	34.83%	35.93%	27.86%	17.78%	
Admitted from home	97.36%	96.70%	97.90%	98.18%	97.85%	0.0084
Smoking status						<0.0001
Current	37.70%	24.40%	17.90%	16.90%	16.23%	
Previous	13.20%	19.30%	28.50%	25.10%	24.30%	
Never	49.10%	56.30%	58.50%	58.00%	59.40%	
Independent functional status	96.60%	98.27%	98.47%	98.53%	97.97%	0.1862
ASA classification						<0.0001
1 + 2	32.83%	38.67%	37.57%	34.57%	26.13%	
3 + 4	67.17%	61.33%	62.16%	65.43%	73.87%	
>10% weight loss	34.72%	17.85%	9..83%	7.82%	4.65%	<0.0001
Presence of cardiac comorbidities	7.55%	9.47%	12.10%	12.10%	10%	0.0019
Orally treated hypertension	32.08%	40.25%	50.90%	61.17%	63.96%	<0.0001
Pulmonary comorbidities	17.70%	12.80%	11.96%	15.80%	19.50%	<0.0001
Preoperative cerebrovascular events	6.42%	4.50%	4.96%	4.68%	4.53%	0.65
Diabetes mellitus, none	92.08%	88.58%	83.75%	77.16%	67.78%	<0.0001
Sodium (mmol/L)						<0.0001
<135	13.96%	10.95%	8.27%	8.59%	5.01%	
136 < Sodium < 144	82.26%	81.94%	83.40%	84.40%	86.28%	
>145	0.75%	2.52%	3.12%	2.79%	2.98%	
Missing	3.02%	4.59%	5.21%	4.19%	5.73%	
Albumin (g/dL)						<0.0001
>2.6	78.87%	77.88%	76.88%	80.03%	74.94%	
<2.5	4.91%	3.87%	2.38%	1.54%	2.39%	
Missing	16.23%	18.25%	20.73%	18.44%	22.67%	
Wound class						0.0001
Clean	6.79%	7.77%	7.76%	11.03%	11.81%	
Clean/contaminated	86.42%	85.21%	85.12%	83.38%	82.10%	
Contaminated/infected	6.79%	7.02%	7.12%	5.59%	6.09%	
PRBC units transfused						0.09
0	70.94%	73.90%	75.50%	74.70%	73.27%	
1–2	17.36%	16.70%	14.70%	14.20%	14.32%	
3+	11.70%	9.30%	9.70%	11.10%	12.41%	

TABLE 1 continued

Characteristic	BMI					*P*
	<18.5 (n = 265)	18.5–24.9 (n = 3178)	25–29.9 (n = 3145)	30–34.9 (n = 1432)	≥35 (n = 838)	
Duration of anesthesia (mean ± SD)	338.6 ± 143	356.3 ± 336	367.7 ± 143	372.65 ± 146	375.6 ± 150	<0.0001
Total operation time (mean ± SD)	262.3 (±240)	279.3 (±134.3)	290 (±133.1)	294.6 (±136)	292.3 (±276)	<0.0001

BMI body mass index, *ASA* American Society of Anesthesiologists, *PRBC* packed red blood cells, *SD* standard deviation

[a] Other factors included "do not resuscitate" code status, >2 alcoholic drinks per day, corticosteroid use for chronic conditions, preoperative chemoradiotherapy, preoperative renal failure, esophageal varices, bleeding disorders, preoperative transfusion of >4 units of PRBCs, preoperative sepsis, and prior operation within 30 days were also assessed and were nonsignificant ($P > 0.05$)

in preoperative laboratory values and longer total operative ($P < 0.0001$) and anesthesia times ($P = 0.009$) (Table. 1). However, the number of packed red blood cell units transfused ($P = 0.09$) and intraoperative occurrences ($P = 0.83$) did not vary significantly by BMI groups.

Short-Term Operative Outcomes

The overall 30-day mortality rate for all patients was 2.5%, with a major postoperative complication rate of 26.01% (Table 2). Patients with a higher BMI did not experience higher rates of 30-day operative mortality (2.49% for BMI 18.5 to 24.9 vs. 1.67% for BMI ≥35, $P = 0.51$), or significantly higher rates of major postoperative complications (25.7% for BMI 18.5 to 24.9 vs. 28.3% for BMI ≥35, $P = 0.086$), or prolonged LOS (28.36% for BMI 18.5 to 24.9 vs. 31.32% for BMI ≥5, $P = 0.76$) (Table. 2). However, those with BMI ≥35 experienced a significantly higher total number of operative complications (17.2% with more than two complications for BMI ≥35 vs. 14.3% for BMI 18.5 to 24.9, $P = 0.028$). Specifically, patients with BMI ≥35 had higher rates of surgical-site infections (23.39% for BMI ≥35 vs. 15.54% for BMI 18.4 to 24.9, $P = 0.001$)

Multivariable Analysis of BMI and Short-Term Operative Outcomes

The minimal effect of higher BMI on short-term operative outcomes persisted in our multivariable logistic regression analysis (Figs. 1, 2, 3). That is, BMI was not associated with a higher 30-day operative mortality (for BMI ≥35 vs. BMI 18.5 to 24.9, odds ratio [OR] = 1.13 [0.58, 2.20], $P = 0.71$), an increased likelihood of developing major complications within 30 days of surgery (OR = 1.18 [0.94, 1.47], $P = 0.14$) (data not shown), or having a prolonged LOS (OR = 0.99 [0.78, 1.26], $P = 0.92$) after adjusting for potential covariates or after removing mediators of BMI from our multivariable models. However, BMI was associated with an increased total number of postoperative complications in morbidly obese patients (i.e., those with BMI ≥35) compared with normal-weight patients with BMI 18.5 to 24.9 (OR = 1.40 [1.14, 1.71], $P = 0.005$) after adjusting for potential covariates including comorbidities, preoperative laboratory values, intraoperative variables, and type of operative resection (selected variables shown in Figs. 1, 2, 3).

We conducted additional analyses to examine whether the observed associations were due to adjustment for

TABLE 2 Short-term outcomes by BMI

Outcome	BMI					*P*
	<18.5 (n = 265)	18.5–24.9 (n = 3178)	25–29.9 (n = 3145)	30–34.9 (n = 1432)	≥35 (n = 838)	
30-day mortality	2.26%	2.49%	2.58%	2.86%	1.67%	0.511
Total number of complications						
0	72.83%	71.74%	71.38%	69.69%	64.9%	0.012
1	13.58%	13.97%	14.98%	14.66%	17.9%	
≥2	13.58%	14.29%	13.64%	15.64%	17.2%	
Major complications	26.0%	25.7%	23.9%	26.1%	28.3%	0.086
LOS (d) (mean ± SD)	11.7 ± 12.2	10.5 ± 9.2	10.5 ± 9.9	10.1 ± 9.1	10.4 ± 11	0.15
Proportions of patients with prolonged LOS	29.07%	28.36%	28.49%	27.57%	31.32%	0.76

LOS length of stay, *SD* standard deviation

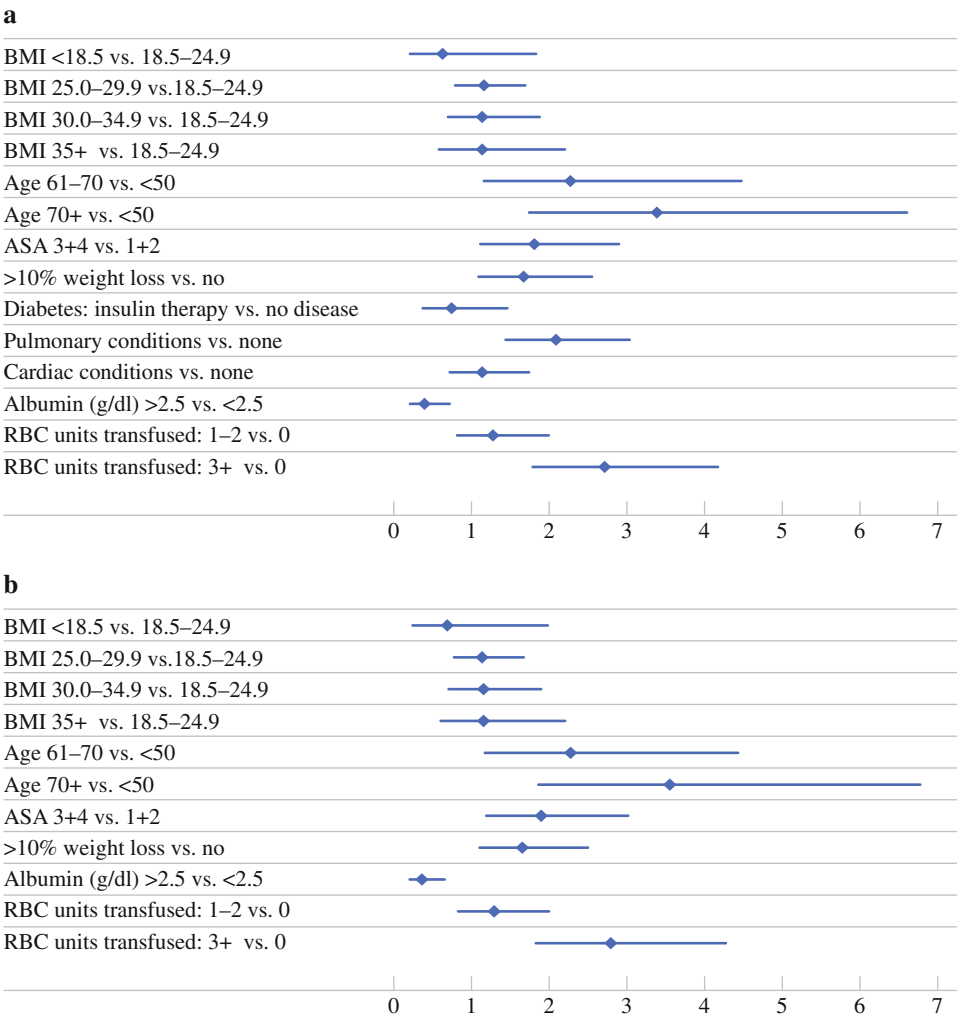

FIG. 1 **a** Odds ratios with 95% CI for selected factors significantly predictive of 30-day mortality after major cancer surgery (mediators of BMI included). * $P < 0.05$ for selected predictors. Additionally adjusted for type of surgical resection, race, sex, smoking status, operative year, and creatinine level, white blood cell count, bilirubin levels, and platelet count. **b** Odds ratios with 95% CI, for selected factors significantly predictive of mortality after major cancer surgery (potential mediators of BMI removed). * $P < 0.05$ for selected predictors. Additionally adjusted for type of surgical resection, race, sex, smoking status, operative year, and creatinine level, white blood cell count, bilirubin levels, and platelet count. *95% CI* 95% confidence interval, *BMI* body mass index, *ASA* American Society of Anesthesiology score, *PRBC* packed red blood cells

factors that may be causally associated with high BMI such as diabetes and cardiac and pulmonary comorbidities. When included in each model, these factors either significantly predicted worse short-term operative outcomes or improved the predictive ability of the model. Models with and without these potential mediators of BMI are presented in Figs. 1, 2, and 3. With no model do we see evidence of an association between BMI and worse outcomes, expect for total number of postoperative complications. Other factors previously shown to affect short-term operative outcomes, including ASA score, age, preoperative weight loss of >10% of body weight, and the receipt of red blood cells intraoperatively, were unaffected by the insertion or removal of BMI.

We performed additional sensitivity analyses to confirm that our findings were not the result of our modeling decisions. We found no change regardless of whether we modeled BMI as a continuous or categorical variable (data not shown). We also repeated our analyses after removing underweight patients because of the potential for miscoding, and our conclusions were unaffected (data not shown). We also found no difference when dividing types of resections into abdominopelvic versus thoracic resections (data not shown). We also repeated our analyses including patients with missing data (using "missing" as a category), and our point estimates remained unchanged (data not shown). Finally, we removed BMI from the analysis altogether. Neither estimates of other predictors nor the model fit significantly changed (data not shown).

DISCUSSION

In ACS NSQIP, BMI (as one established measure of obesity) was not found to be predictive of worse short-term operative outcomes after major operative resections for solid organ tumors except for BMI ≥35, where it predicted an increased total number of operative complications. The current study is consistent with epidemiologic investigations that question the use of BMI alone as an accurate measure of obesity. Our study does not demonstrate that obesity has little effect on operative outcome after major oncologic resection surgery; rather, it shows that high BMI

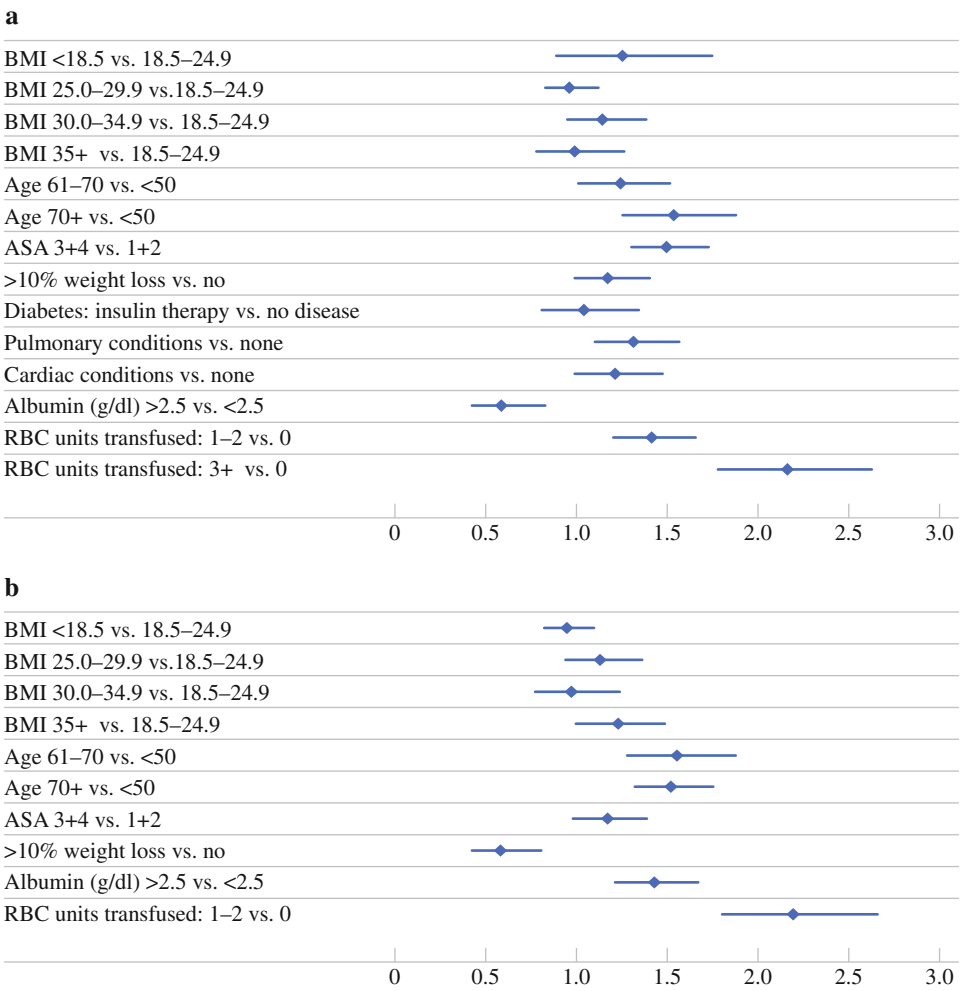

FIG. 2 **a** Odds ratios with 95% CI, for selected factors significantly predictive of prolonged length of stay (mediators of BMI included). * $P < 0.05$ for selected predictors. Additionally adjusted for type of surgical resection, race, sex, smoking status, operative year, and creatinine level, white blood cell count, bilirubin levels, and platelet count. **b** Odds ratios with 95% CI, for selected factors significantly predictive of prolonged length of stay (potential mediators of BMI removed). * $P < 0.05$ for selected predictors. Additionally adjusted for type of surgical resection, race, sex, smoking status, operative year, and creatinine level, white blood cell count, bilirubin levels, and platelet count. *95% CI* 95% confidence interval, *BMI* body mass index, *ASA* American Society of Anesthesiology score, *PRBC* packed red blood cells

has little association with operative outcomes. This distinction is important in highlighting the limitations of the use of BMI as a sole measure of obesity. To our knowledge, the present study is one of the first surgical studies that highlights this previously mentioned distinction.

The observed lack of association between high BMI and worse operative outcomes was also observed in several other surgical studies.[7,10,33] By using the Patient Safety in Surgery Study of 14 NSQIP hospitals, we found that increased BMI did not predict higher operative mortality or major complications after major intra-abdominal resections for cancer.[10] Indeed, only BMI <18 predicted worse short-term operative outcomes after major oncologic resection. However, the variability of these estimates was large, especially in those patients who were underweight (BMI <18.5) (OR = 5.24; 95% confidence interval [95% CI], 1.7–16.2). This variance is possibly explained as a result of the small sample size of underweight patients in their study (2.4%), or it is suggestive of the presence of large unobserved confounders. The lack of association between obesity and operative outcomes was also found in a large prospective single-hospital study of >6000 patients who underwent elective surgical procedures.[33] Furthermore, although it did not predict worse surgical outcomes in 1300 common surgical procedures (cholecystectomy, unilateral mastectomy, and colectomy), increased BMI was associated with increased operative resource use. However, these results can not be generalized to other major operative resections. Because of the observed correlation between increased BMI and other comorbidities in these studies, the effect of BMI on operative outcomes after removing its mediators (e.g., diabetes, higher ASA score) was not examined. As such, many investigators were led to conclude that obesity has a minimal effect on surgical outcomes. However, in our study, we performed a robust set of multivariable analyses to show that BMI has a minimal effect on operative outcomes. We performed our multivariable analyses with and without the potential mediators of BMI. With no model do we see evidence of an association between increased BMI and worse outcomes except for BMI ≥35, which predicted increased number of total operative complications.

Conversely, the adverse effect of obesity (measured according to BMI) on short-term operative outcomes has

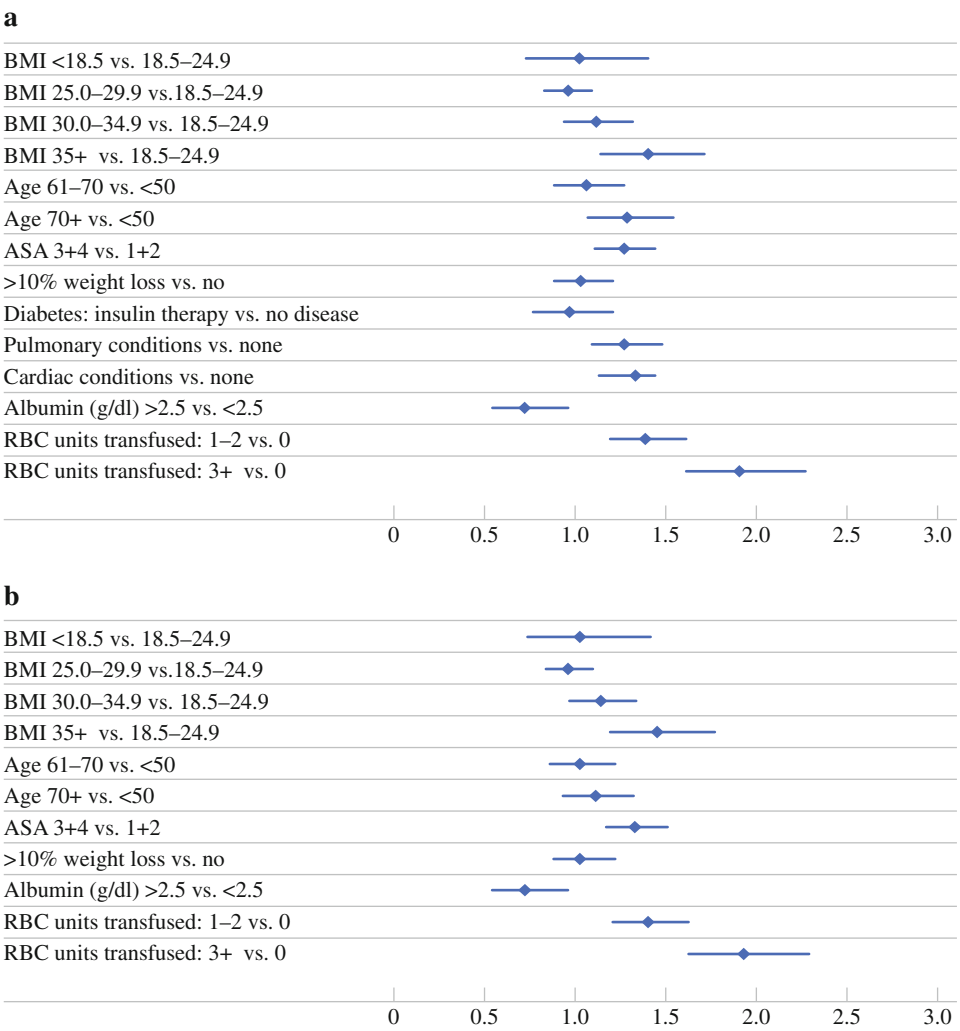

FIG. 3 **a** Odds ratios with 95% CI, for selected factors significantly predictive of postoperative complications (mediators of BMI included). * $P < 0.05$ for selected predictors. Additionally adjusted for type of surgical resection, race, sex, smoking status, operative year, and creatinine level, white blood cell count, bilirubin levels and platelet count. **b** Odds ratios with 95% CI, for selected factors significantly predictive of increased total number of complications (potential mediators of BMI removed) * $P < 0.05$ for selected predictors. Additionally, we adjusted for type of surgical resection, race, sex, smoking status, operative year, and creatinine level, white blood cell count, bilirubin levels, and platelet count. *95% CI* 95% confidence interval, *BMI* body mass index, *ASA* American Society of Anesthesiology score, *PRBC* packed red blood cells

been observed in other surgical studies.[5,6,8,9,11] In patients who underwent colectomies for cancer at ACS NSQIP hospitals, increased BMI was associated with higher rates of surgical site infections (OR = 2.66, 95% CI, 1.91–3.73), renal failure (OR = 2.75, 95% CI, 1.21–6.26), and pulmonary embolism (OR = 6.98, 95% CI, 1.62–30.06).[9] Additional studies of patients undergoing hepatic resections in ACS NSQIP showed that increased BMI was predictive of delayed weaning off the ventilator (OR = 4.5, 95% CI, 1.20–16.1).[6] Other investigators have observed similar findings when large databases are used.[11,12] For example, in a study of 18,000 orthotopic liver transplantations, mortality rates of the morbidly obese were significantly higher up to 2 years after surgery (33% vs. 24% to 26%; $P < 0.05$). Further, the authors found that morbid obesity predicted worse 30-day and 2-year survival.[11] Most recently, the adverse effect of higher preoperative BMI on surgical complications was demonstrated in a cohort of patients enrolled in the Japan Clinical Oncology Group Trial (JCOG 9501).[12] In particular, patients with BMI >25 who underwent D2 lymphadenectomy for resectable gastric adenocarcinoma were at far higher risks of surgical complications and blood loss. As such, these studies continue to demonstrate that obesity has an effect on operative outcomes, which is perhaps limited by the sole use of BMI.

In the epidemiologic literature, obesity has been associated with increased risk for cardiovascular disease and mortality.[15,34] BMI is one of the most easily measured proxies for obesity, but increasing evidence suggests that other measures of abdominal obesity better predict outcomes. In a large case-control study of the risk factors for myocardial infarction measured by four different proxies for obesity (BMI, waist-to-hip ratio, waist measure, and hip measure), waist-to-hip ratio was found to be the best predictor of myocardial infarction among all ethnic groups.[34] The authors found a modest association between BMI and myocardial infarction (OR = 1.44, 95% CI, 1.32–1.57) comparing the highest to lowest quartiles of BMI, which disappeared after adjustment for other risk factors. At the same time, waist-to-hip ratio and hip circumference were closely associated (OR = 1.75; $P = 0.0001$) with risk of

myocardial infarction, even after adjustment for other risk factors. Additionally, Folsom and colleagues conducted studies on the predictive ability of obesity measures on several outcomes.[15] In a prospective cohort study of 31,702 Iowa women, the authors found waist-to-hip ratio to be the best predictor of total mortality. Additionally, they concluded that waist-to-hip ratio offers additional prognostic information beyond BMI, showing positive associations with mortality from cardiovascular diseases, cancer, and other causes. Although our study suggests that a BMI-based measure of obesity is inadequate to predict surgical risk, additional studies are needed to examine whether alternate measures of obesity, such as waist-to-hip ratio, might be more useful for surgeons wishing to predict surgical outcomes.

Perhaps one of the interesting aspects of our results is the persistence of a minimal relationship between BMI and surgical outcomes even after performing a robust set of sensitivity analyses and carefully addressing those patients with missing values. These findings continue to suggest that alternate measures of obesity may provide a more realistic understanding of the obesity-surgical outcomes relationship especially, in those with BMI $\geq$35. Additionally, the present study highlights that our point estimates for BMI remained unchanged even after removing patients with missing data.

Our study is unique in several respects. First, our patients come from a nationally recognized multihospital database that was established to safeguard patient safety and promote quality improvement by measuring operative outcomes in a risk-adjusted manner. These data are prospectively gathered by trained nurses who follow strict definitions of all the pre-, intra-, and postoperative variables entered into the ACS NSQIP. Furthermore, our study contained a larger cohort of patients than previous studies of the ACS NSQIP.

Our results have the following limitations: <10% of our patients had BMI $\geq$35. Therefore, it is possible that we underestimated the adverse effect of morbid obesity on operative outcomes in morbidly obese patients. Second, ACS NSQIP does not collect information on waist-to-hip ratio, waist measure, or hip measure to allow us to examine the effect of various measures of obesity on operative outcomes after major resection of solid organ tumors. However, we acknowledge that although BMI may not be the best surrogate marker for obesity, it is the most widely available and used measure in surgical practice. Third, because ACS NSQIP does not provide results on postoperative events specific to certain procedures (e.g., delayed gastric emptying after pancreatectomy, anastomotic leak after esophagectomy), the association between BMI and postoperative events were not included in our analysis. It is possible that increased BMI has an additional effect of procedure specific events such as leaks after pancreatectomy. ACS NSQIP is currently assessing expanding its current format to include specialty- or procedure-specific events. Finally, hospitals participating in the ACS NSQIP may not be representative of U.S. hospitals as a whole. However, the finding that >50% of our surgeries were performed in 2007 is in line with the recently published blueprint for a new ACS NSQIP and is predictive that this program is expected to grow and evolve to be the most representative and important tool to measure and improve surgical quality in the United States.[5]

The current study provides important insights for surgeons caring for obese patients who are in need of major operative resections. Our study also opens up several avenues to explore the relationship between obesity and cancer care. First, our results come from a cohort of persons with a predominantly independent functional capacity and few comorbidities. Future validations should investigate our findings in other settings. With the current strained economic circumstances, future assessment of the effect of obesity on a hospital's resource use will continue to be a sobering reality. Second, the routine preoperative use of waist circumference and waist-to-hip ratios among bariatric surgeons should be investigated in major general and oncologic surgery procedures. For example, although BMI may underestimate those patients with central obesity, alternative measures of obesity may be particularly relevant to surgeons performing pelvic surgeries where there is a higher risk for retained foreign objects and lithotomy position-related nerve injuries. Third, emerging evidence suggests that obesity is linked to worse oncologic outcomes, including nodal involvement after pancreatectomy for cancer. As such, investigators should carefully assess the effect of obesity on the quality of oncologic resections and the delivery of cancer care.[8,12,35] It is possible that the effect of obesity may have been underestimated in previous studies assessing the efficacy of cancer treatment in obese cancer patients. Finally, several National Cancer Institute–sponsored cancer trials currently use BMI as a measure of obesity to stratify the selection of enrollees into their protocols and evaluate outcomes. If our current findings are validated, future considerations should be made to include other measurements of obesity in the assessments and stratification measures of current clinical cancer trials.

In ACS NSQIP, BMI (as one established measure of obesity) did not predict short-term operative outcomes after major cancer surgery. However, BMI $\geq$35 predicted an increased total number of operative complications. Although these findings may suggest a lack of association between obesity and cancer surgery outcomes, it may also confirm the previously examined limitation of BMI as a sole measure of obesity. Because of the rising incidence of obesity in the United States and its challenging effect on a

surgeon's practice, ACS NSQIP should consider exploring alternative measures of general and abdominal obesity.

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REFERENCES

1. Mokdad AH, Serdula MK, Dietz WH, et al. The spread of the obesity epidemic in the United States, 1991–1998. *JAMA.* 1999;282:1519–22.
2. Mokdad AH, Serdula MK, Dietz WH, et al. The continuing epidemic of obesity in the United States. *JAMA.* 2000;284:1650–1.
3. Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. *JAMA.* 2001;286:1195–200.
4. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA.* 2003;289:76–9.
5. Birkmeyer NJ, Charlesworth DC, Hernandez F, et al. Obesity and risk of adverse outcomes associated with coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. *Circulation.* 1998;97:1689–94.
6. Gedaly R, McHugh PP, Johnston TD, et al. Obesity, diabetes, and smoking are important determinants of resource utilization in liver resection: a multicenter analysis of 1029 patients. *Ann Surg.* 2009;249:414–9.
7. Hawn MT, Bian J, Leeth RR, et al. Impact of obesity on resource utilization for general surgical procedures. *Ann Surg.* 2005;241:821–6.
8. Kodera Y, Ito S, Yamamura Y, et al. Obesity and outcome of distal gastrectomy with D2 lymphadenectomy for carcinoma. *Hepatogastroenterology.* 2004;51:1225–8.
9. Merkow RP, Bilimoria KY, McCarter MD, et al. Effect of body mass index on short-term outcomes after colectomy for cancer. *J Am Coll Surg.* 2009;208:53–61.
10. Mullen JT, Davenport DL, Hutter MM, et al. Impact of body mass index on perioperative outcomes in patients undergoing major intra-abdominal cancer surgery. *Ann Surg Oncol.* 2008;15:2164–72.
11. Nair S, Verma S, Thuluvath PJ. Obesity and its effect on survival in patients undergoing orthotopic liver transplantation in the United States. *Hepatology.* 2002;35:105–9.
12. Tsujinaka T, Sasako M, Yamamoto S, et al. Influence of overweight on surgical complications for gastric cancer: results from a randomized control trial comparing D2 and extended para-aortic D3 lymphadenectomy (JCOG9501). *Ann Surg Oncol.* 2007;14:355–61.
13. National Institutes of Health. National Heart, Lung, and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. NIH Publication 98-4083. Rockville, MD: National Institutes of Health; 1998. http://www.nhlbi.nih.gov/guidelines/obesity/ob_gdlns.pdf. Accessed 8 June 2009.
14. Body mass index classification. http://apps.who.int/bmi/index.jsp?introPage=intro_3.html. Accessed 5 January 2009.
15. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. *Arch Intern Med.* 2000;160:2117–28.
16. Freedman DS, Wang J, Thornton JC, et al. Racial/ethnic differences in body fatness among children and adolescents. *Obesity (Silver Spring).* 2008;16:1105–11.
17. Kurth T, Gaziano JM, Berger K, et al. Body mass index and the risk of stroke in men. *Arch Intern Med.* 2002;162:2557–62.
18. Kurth T, Gaziano JM, Rexrode KM, et al. Prospective study of body mass index and risk of stroke in apparently healthy women. *Circulation.* 2005;111:1992–8.
19. Romero-Corral A, Montori VM, Somers VK, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet.* 2006;368(9536):666–78.
20. Romero-Corral A, Somers VK, Sierra-Johnson J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. *Int J Obes (Lond).* 2008;32:959–66.
21. Schneider HJ, Glaesmer H, Klotsche J, et al. Accuracy of anthropometric indicators of obesity to predict cardiovascular risk. *J Clin Endocrinol Metab.* 2007;92:589–94.
22. Dudeja V, Misra A, Pandey RM, et al. BMI does not accurately predict overweight in Asian Indians in northern India. *Br J Nutr.* 2001;86:105–12.
23. Misra A, Vikram NK, Gupta R, et al. Waist circumference cutoff points and action levels for Asian Indians for identification of abdominal obesity. *Int J Obes (Lond).* 2006;30:106–11.
24. Vikram NK, Pandey RM, Misra A, et al. Non-obese (body mass index <25 kg/m^2) Asian Indians with normal waist circumference have high cardiovascular risk. *Nutrition.* 2003;19:503–9.
25. Fink AS, Campbell DA Jr, Mentzer RM Jr, et al. The National Surgical Quality Improvement Program in non-veterans administration hospitals: initial demonstration of feasibility. *Ann Surg.* 2002;236:344–53.
26. Khuri SF. The NSQIP: a new frontier in surgery. *Surgery.* 2005;138:837–43.
27. Khuri SF, Daley J, Henderson W, et al. The National Veterans Administration Surgical Risk Study: risk adjustment for the comparative assessment of the quality of surgical care. *J Am Coll Surg.* 1995;180:519–31.
28. Khuri SF, Daley J, Henderson W, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. *Ann Surg.* 1998;228:491–507.
29. Khuri SF, Daley J, Henderson W, et al. Risk adjustment of the postoperative mortality rate for the comparative assessment of the quality of surgical care: results of the National Veterans Affairs Surgical Risk Study. *J Am Coll Surg.* 1997;185:315–27.
30. National Heart, Lung, and Blood Institute. Obesity education initiative. http://www.nhlbi.nih.gov/about/oei/. Accessed 9 January 2009.
31. Collins TC, Daley J, Henderson WH, et al. Risk factors for prolonged length of stay after major elective surgery. *Ann Surg.* 1999;230:251–9.
32. Wright CD, Gaissert HA, Grab JD, et al. Predictors of prolonged length of stay after lobectomy for lung cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk-adjustment model. *Ann Thorac Surg.* 2008;85:1857–65.
33. Dindo D, Muller MK, Weber M, et al. Obesity in general elective surgery. *Lancet.* 2003;361(9374):2032–5.
34. Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet.* 2005;366(9497):1640–9.
35. Fleming JB, Gonzalez RJ, Petzel MQ, et al. Influence of obesity on cancer-related outcomes after pancreatectomy to treat pancreatic adenocarcinoma. *Arch Surg.* 2009;144:216–21.