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Association of Body Mass Index and Postoperative Acute Kidney Injury in Patients Undergoing Laparoscopic Surgery

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Background: Whether the deleterious effects of carbon dioxide pneumoperitoneum on the kidneys are exacerbated in the obese population remains unknown. We hypothesized that increased body mass index (BMI) is associated with an increased incidence of postoperative acute kidney injury (AKI) in patients undergoing noncardiac laparoscopic surgery.

Methods: Following institutional review board approval, we analyzed data on 8,543 adult patients with American Society of Anesthesiologists physical status scores of I-IV who had inpatient noncardiac laparoscopic surgery from 2005-2014. Because the exposure (current BMI) is a chronic condition, we a priori assumed that diabetes mellitus, hypertension, coronary artery disease, and chronic obstructive pulmonary disease might mediate the effect of obesity on outcome. Our primary analysis was a proportional odds logistic regression model with current BMI as a predictor and AKI as an ordinal outcome.

Results: After controlling for potential confounding variables, the odds of developing a more serious level of AKI was 7% (95% CI 0%, 15%) greater with a 5-unit increase in BMI (P=0.05). When the analysis was adjusted for the a priori mediators in an attempt to estimate the pure effect of BMI on AKI, the result was no longer significant (Wald test P=0.35), with the residual effect of BMI of 3% (95% CI –4%, 11%).

Conclusion: We found a marginal association between BMI and an increased risk of developing AKI in adult patients after having noncardiac laparoscopic surgery. The BMI effect became insignificant when potential mediator variables were considered. The association of BMI and AKI after noncardiac laparoscopic surgery is likely mediated through components of the metabolic syndrome.

Keywords: *Acute kidney injury, body mass index, laparoscopy*

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INTRODUCTION

Insufflation of the abdominal cavity with carbon dioxide (CO_2) during laparoscopic abdominal surgery can have deleterious effects on the kidneys.[1-4] Increased intraabdominal pressure can cause reductions in renal blood flow, renal cortical perfusion (through renal vasoconstriction), and glomerular filtration rate (GFR).[2-8] In addition, compression of the renal vein and the renal parenchyma has been reported.[2,9] Various etiologies have been identified for this pneumoperitoneum-induced renal injury.[9] Some of the reported etiologies include baseline abnormal renal function, baseline fluid status (hypovolemia), perioperative hemodynamic fluctuations, high arterial CO_2 levels, and the degree of intraabdominal pressure elevation caused by CO_2 insufflation.[5,7,9,10] Pneumoperitoneum can also cause renal injury indirectly through release of various hormones, including catecholamines, angiotensin II, endothelin, and vasopressin.[10-12]

Whether the deleterious effects of CO_2 pneumoperitoneum on the kidneys are exacerbated in the obese population remains in question. In the obese population, CO_2 pneumoperitoneum is postulated to exacerbate the occurrence of kidney injury through further triggering of an activated renin-angiotensin-aldosterone system (RAAS).[13] Activation of the RAAS, coupled with increased sympathetic nervous system activity, results in an increase in the renal tubular reabsorption of sodium with resultant hypertension.[13,14] Obesity is also known to be accompanied by an increase in GFR, renal plasma flow, and urinary albumin excretion, ultimately resulting in glomerulosclerotic damage.[14-16] Serra et al studied the glomerular architecture in renal biopsies of morbidly obese patients with normal renal function and

determined that glomerular lesions in the form of increased mesangial matrix, mesangial cell proliferation, podocyte hypertrophy, and glomerulomegaly occurred more frequently in obese patients than in the comparison (nonobese) group.[17]

We hypothesized that an increased body mass index (BMI) is associated with an increased incidence of postoperative acute kidney injury (AKI) in patients undergoing noncardiac intraabdominal laparoscopic surgery.

METHODS

Ethical approval for this study was provided by the Cleveland Clinic Institutional Review Board (IRB) on May 5, 2015. After IRB approval, we obtained data on noncardiac laparoscopic inpatient surgeries on adult patients at the Cleveland Clinic main campus between May 2005 and December 2014 from our Perioperative Health Documentation System (PHDS). The PHDS (IRB-8167) contains data on all patients who had noncardiac surgery since May 2005 at the Cleveland Clinic main campus and integrates preoperative variables (demographics, conditions, etc), intraoperative variables (via the anesthesia record-keeping system), and postoperative outcomes (by linking to the larger Cleveland Clinic billing data systems). The IRB waived the requirement for written informed consent.

We did not consider patients with preoperative chronic kidney disease (stage III and above), patients undergoing outpatient surgery, and patients with American Society of Anesthesiologists (ASA) physical status scores above IV. We excluded open and urologic surgeries. Cases missing BMI and baseline and postoperative creatinine measurements were excluded as well.

Sex, race, ASA physical status, history of congestive heart failure, ascites, renal insufficiency, and emergency surgery were considered for confounding adjustment and coded as categorical or binary variables. Age, preoperative serum creatinine, and duration of surgery were considered for confounding adjustment and were coded as continuous variables. Because of the large number of surgical procedure categories, we adjusted for type of surgery in terms of risk of AKI as follows. First, we characterized each patient's primary procedure using the US Agency for Healthcare Research and Quality single-level Clinical Classifications Software (CCS) for International Classification of Diseases, 9th Revision, Clinical Modification procedure codes. The single-level CCS is a tool for aggregating individual procedure codes into clinically meaningful procedure categories. We then adjusted for a procedure as a continuous covariable by using the incidence of AKI for each CCS category.

Because the exposure (current BMI) is a chronic condition, the research question and analyses are complex and require certain assumptions about the temporality of other chronic health conditions that might mediate or confound the outcome. We distinguished the potential confounders (ie, variables potentially affecting both BMI and outcome, such as age and sex) from potential mediator variables (ie, variables such as diabetes mellitus that might be caused by obesity and thus mediate the effect of being obese on the outcome). The following variables were identified a priori to potentially mediate part of the effect of obesity on outcome: history of diabetes mellitus, hypertension, coronary artery disease, and history of chronic obstructive pulmonary disease (COPD). By not considering these variables as confounding variables but rather as potential mediators, we made the unverifiable assumption that the conditions developed after the patient developed his/her current BMI status. While this assumption may be true for some patients, it is most likely not true for others. We therefore performed 2 primary analyses: not adjusting for the potential mediators and adjusting for them.

For reporting purposes, we used the World Health Organization (WHO) BMI classification to define BMI categories (kg/m^2): underweight ($BMI<18.5$), normal ($18.5\leq BMI<25$), overweight ($25\leq BMI<30$), obese grade 1 ($30\leq BMI<35$), obese grade 2 ($35\leq BMI<40$), or obese grade 3 ($BMI\geq 40$).[18]

The primary outcome was the occurrence of AKI as defined by the Acute Kidney Injury Network (AKIN) classification.[19] Urine output was not considered. The AKIN defines 3 stages of AKI based on maximum elevations in serum creatinine. As per Walsh et al,[20] we extended the normal 48-hour creatinine window used by the AKIN to 7 days to better characterize the postoperative period.

- Stage 1: Serum creatinine increase $\geq$26.4 μmol/L ($\geq$0.3 mg/dL) OR increase to 1.5- to 2.0-fold from baseline
- Stage 2: Serum creatinine increase $>$2.0- to 3.0-fold from baseline
- Stage 3: Serum creatinine increase $>$3.0-fold from baseline OR serum creatinine $\geq$354 μmol/L ($\geq$4.0 mg/dL)

The secondary postoperative outcomes were in-hospital mortality and the occurrence of end-stage renal disease as evidenced by the need for hemodialysis.

Statistical Analysis

Descriptive summary statistics are reported for the potential confounding, mediator, and outcome variables.

We assessed the association between BMI and AKI, adjusting for the confounding variables and not adjusting for the potential mediators. We fit a proportional odds logistic regression model that takes into account the ordinal nature of the response variable (ie, no AKI, better than stage I AKI, better than stage II AKI, better than stage III AKI). The resulting odds ratio estimates the relative odds of developing a more serious level of AKI for a 5-unit increase in BMI. The model assumption of the odds proportionality was assessed graphically. The lack of collinearity among covariates included in the model was checked.

The confounder-adjusted analysis estimated the overall relationship between obesity and outcome and includes any effect that might be mediated by the potential mediators.

As a second analysis, we adjusted for potential mediators as well as confounders, attempting to estimate the direct or pure effect of BMI on AKI (assuming that all true confounding and mediator variables had been adjusted for).

We recognized that the risk of AKI depending on BMI might be nonlinear: the risk might be higher for underweight patients, lower for normal-weight patients, and then increase again for overweight and obese patients. However, we only expected a small percentage of underweight patients. Therefore, for the purpose of the primary analysis, we ignored this nonlinearity. As a sensitivity analysis, we

assessed the association between BMI and AKI, excluding underweight patients and adjusting for the potential confounders.

For the secondary outcomes, we assessed the association between BMI and in-hospital mortality using a logistic regression model with adjustment for the potential confounders. The incidence of end-stage renal disease (defined as the need for hemodialysis) was reported; however, formal analysis was not possible because of the very low incidence.

Model-based Wald chi-square tests were used to test all hypotheses involving proportional odds model coefficients. We kept the Type I error rate at the 5% level for both the primary and the secondary hypotheses.

Given a total sample size of 8,543 and approximately 3% of patients experiencing any stage of AKI, we had approximately 90% power to detect an odds ratio of developing a more serious level AKI of 1.10 or greater for a 5-unit increase in BMI at the 0.05 significance level and assuming a normal distribution for BMI with a mean of 36 kg/m^2 and standard deviation of 11 kg/m^2.

SAS statistical software v.9.3 (SAS Institute) was used for all statistical analyses.

RESULTS

The query of the PHDS revealed 121,745 unique noncardiac surgeries on adult inpatients who did not have chronic kidney disease and had ASA physical status scores of I-IV at the Cleveland Clinic main campus between May 2005 and December 2014. After eliminating patients who underwent open and urologic surgeries and patients with missing BMI and creatinine records, 8,543 patients remained in the study (Figure). Table 1 shows the patients' baseline characteristics and surgical factors overall and by BMI category. Sixty-two percent of the study population was obese according to the WHO BMI classification, with 34% of patients in the grade 3 obesity category. As seen in Table 1, most of the potential confounding factors, including number of patients and surgical characteristics, changed with change in BMI; therefore, it was important to adjust for all the potential confounders in the analyses. Table 2 lists the surgeries considered in the study. Results for the primary and secondary outcomes are summarized in Table 3.

BMI was associated with an increased level of AKI after adjusting for the potential confounding variables and not adjusting for the potential mediators (Wald test P=0.05), with an adjusted proportional odds ratio of 1.07 (95% confidence interval [CI] 1.00, 1.15) for a 5-unit increase in BMI. In other words, after controlling for the potential confounding variables, the odds of developing a more serious level of AKI were 7% (95% CI 0%, 15%) greater for a patient who was 5 BMI units heavier. The proportional odds logistic regression model demonstrated reasonable predictive accuracy with a C-statistic of 0.76.[21]

After additional adjustment for the potential mediators (diabetes mellitus, hypertension, coronary artery disease, and history of COPD), the result was not significant (Wald test P=0.35). The residual pure effect of BMI expressed via the adjusted proportional odds ratio of developing a more advanced stage of AKI was 1.03 (95% CI 0.96, 1.11). In other words, after controlling for the potential confounding variables and potential mediators, the odds of developing a more serious level of AKI were 3% (95% CI −4%, 11%) greater for a patient who was 5 BMI units heavier.

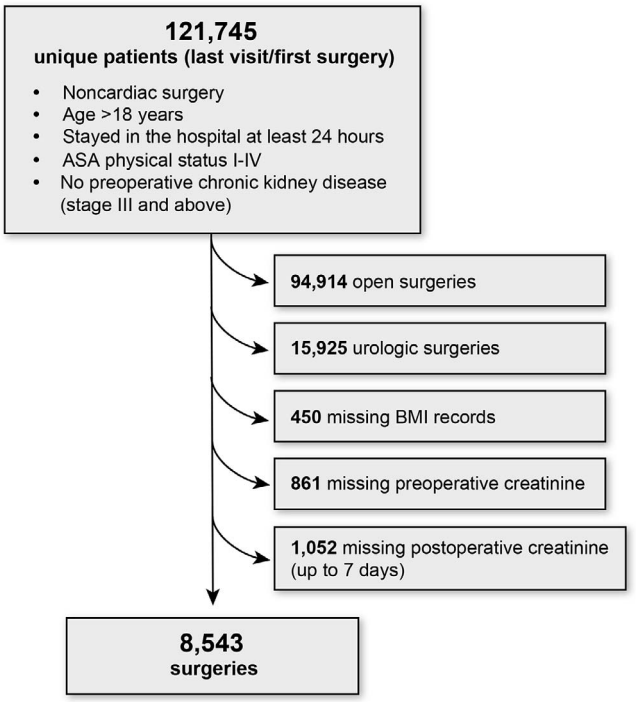

Figure. Flow chart of patient selection. ASA, American Society of Anesthesiologists; BMI, body mass index.

The difference of 4% (7%–3%=4%) in the BMI effect between the 2 primary analyses might be attributable to the potential mediators; the BMI effect was reduced by 4% once we adjusted for these potential mediators. However, we did not do a full mediation analysis and therefore do not have strong evidence for the mediation of diabetes, hypertension, coronary artery disease, and COPD in the relationship between BMI and postoperative AKI.

A sensitivity analysis excluding underweight patients showed a stronger association between BMI and increased risk of AKI (Wald test P=0.02) with an adjusted proportional odds ratio of 1.08 (95% CI 1.01, 1.16) for a 5-unit increase in BMI.

The number of in-hospital mortalities was 36 (0.4%). We found a negative association between in-hospital mortality and BMI (P<0.001), with an odds ratio of 0.991 (95% CI 0.990, 0.992) for a 5-unit increase in BMI. The strong predictive accuracy of this logistic regression model was confirmed by a C-statistic of 0.80.

Only one case of end-stage renal disease was observed after surgery; therefore, formal statistical analysis was not feasible.

DISCUSSION

The results of this study show that obesity per se is not associated with an increased risk of AKI after noncardiac laparoscopic surgery, but comorbidities that are frequently associated with obesity, namely diabetes mellitus, hypertension, coronary artery disease (components of the metabolic syndrome), and COPD, might significantly increase the odds of developing a more serious level of AKI by 7% (95% CI 0%, 15%) for each 5-unit increase in BMI

Table 1. Baseline and Surgery Characteristics for Patients Undergoing Laparoscopic Noncardiac Surgeries

Factor	Total n=8,543 (100%)	Underweight (BMI<18.5) n=100 (1%)	Normal (18.5≤BMI<25) n=1,500 (18%)	Overweight (25≤BMI<30) n=1,672 (20%)	Obese Grade 1 (30≤BMI<35) n=1,255 (15%)	Obese Grade 2 (35≤BMI<40) n=1,118 (13%)	Obese Grade 3 (BMI≥40) n=2,898 (34%)	*P* Value[a]
Potential Confounders								
Age, years	52 ± 15	49 ± 17	54 ± 17	57 ± 15	56 ± 14	52 ± 13	47 ± 12	<0.001
Male	2,368 (28)	20 (20)	391 (26)	644 (39)	394 (31)	252 (23)	667 (23)	<0.001
Body mass index, kg/m^2	36 ± 11	17.3 ± 1	22.4 ± 2	27 .4 ± 1	32.4 ± 1	37.6 ± 2	48.8 ± 8	<0.001
Race								
White	6,837 (80)	90 (90)	1,298 (87)	1,405 (84)	997 (79)	883 (79)	2,164 (75)	<0.001
Black	1,394 (16)	6 (6)	128 (9)	199 (12)	213 (17)	210 (19)	638 (22)	
Other	312 (4)	4 (4)	74 (5)	68 (4)	45 (4)	25 (2)	96 (3)	
ASA physical status								
I	178 (2)	2 (2)	80 (5)	52 (3)	32 (3)	6 (1)	6 (0)	<0.001
II	2,872 (34)	41 (41)	715 (48)	749 (45)	497 (40)	354 (32)	516 (18)	
III	5,042 (59)	51 (51)	641 (43)	791 (47)	668 (53)	712 (64)	2,179 (75)	
IV	451 (5)	6 (6)	64 (4)	80 (5)	58 (5)	46 (4)	197 (7)	
Congestive heart failure	358 (4)	3 (3)	66 (4)	72 (4)	46 (4)	40 (4)	131 (5)	0.66
Ascites	6 (0)	0 (0)	2 (0)	3 (0)	0 (0)	1 (0)	0 (0)	0.12
Renal insufficiency[b]	22 (0)	0 (0)	4 (0)	4 (0)	1 (0)	4 (0)	9 (0)	0.76
Preoperative serum creatinine, mg/dL	0.83 ± 0.24	0.70 ± 0.20	0.79 ± 0.23	0.86 ± 0.24	0.85 ± 0.22	0.83 ± 0.32	0.83 ± 0.21	<0.001
Emergency surgery	284 (3)	5 (5)	69 (5)	82 (5)	45 (4)	37 (3)	46 (2)	<0.001
Duration of surgery, minutes	190 ± 75	175 ± 97	176 ± 79	183 ± 81	191 ± 82	195 ± 76	199 ± 64	<0.001
Potential Mediators								
Diabetes mellitus	2,035 (24)	2 (2)	107 (7)	243 (15)	253 (20)	358 (32)	1,072 (37)	<0.001
Hypertension	4,557 (53)	21 (21)	467 (31)	734 (44)	700 (56)	689 (62)	1,946 (67)	<0.001
Coronary artery disease	829 (10)	5 (5)	133 (9)	201 (12)	128 (10)	120 (11)	242 (8)	<0.001
Chronic obstructive pulmonary disease	1,539 (18)	11 (11)	198 (13)	221 (13)	187 (15)	245 (22)	677 (23)	<0.001

ASA, American Society for Anesthesiologists.

Note: Data are presented as mean ± standard deviation for normally distributed variables or n (%) for proportions.

[a]*P* value represents analysis of variance test for continuous variables and Pearson chi-square/Fisher exact test for categorical variables.

[b]Corresponds to International Classification of Diseases, 9th Revision, codes 585.1-585.2, chronic kidney disease stage I and II; the patients with preoperative chronic kidney disease of stage III and above were excluded from the analysis as per the exclusion criteria.

Table 2. Study Surgical Procedures Classified With Clinical Classifications Software (CCS) Procedure Category Type and International Classification of Diseases, 9th Revision (ICD-9) Procedure Codes (n=8,543)

CCS Procedure Category	ICD-9 Procedure Code	ICD-9 Procedure Description	n (%)
Other OR upper GI therapeutic procedures	4438	LAP gastroenterostomy (begin 2004)	2,259 (26.4)
	4467	LAP creat esoph sphinct (begin 2004)	281 (3.3)
	4495	LAP gastric restric proc (begin 2004)	213 (2.5)
	4468	LAP gastroplasty (begin 2004)	37 (0.4)
	4497	LAP rem gast restric dev (begin 2004)	33 (0.4)
	4496	LAP rev gast restri proc (begin 2004)	14 (0.2)
Hysterectomy, abdominal and vaginal	6841	LAP total abdominal hyst (begin 2006)	726 (8.5)
	6851	LAP assist vag hys (begin 1996)	541 (6.3)
	6861	LAP radical abdomnl hyst (begin 2006)	103 (1.2)
	6831	LAP supracervical hysterecto	90 (1.1)
	6871	LAP radical vaginal hyst (begin 2006)	40 (0.5)
	686	Radical abd hysterectomy	14 (0.2)
Colorectal resection	1733	LAP right hemicolectomy (begin 2008)	404 (4.7)
	1736	LAP sigmoidectomy (begin 2008)	350 (4.1)
	4581	LAP tot intr-ab colectmy (begin 2008)	218 (2.6)
	1732	LAP cecectomy (begin 2008)	61 (0.7)
	1735	LAP left hemicolectomy (begin 2008)	59 (0.7)
	4851	LAP abdperneal resc rec (begin 2008)	44 (0.5)
	1739	LAP pt ex lrg intest nec (begin 2008)	16 (0.2)
	1734	LAP res transverse colon (begin 2008)	8 (0.1)
	1731	LAP mul seg res lg intes (begin 2008)	4 (0.0)
Cholecystectomy and common duct exploration	5123	LAP cholecystec (begin 1991)	699 (8.2)
	5124	Laparoscop part chole (begin 1996)	7 (0.1)
Gastrectomy, partial and total	4382	LAP vertical gastrectomy (begin 2011)	422 (4.9)
Other hernia repair	5362	LAP incis hern repr-grft (begin 2008)	185 (2.2)
	5371	LAP abd rep-diaphr hern (begin 2008)	135 (1.6)
	5363	LAP hern ant abd-gft nec (begin 2008)	29 (0.3)
	5342	LAP umbil hernia-graft (begin 2008)	23 (0.3)
	5383	LAP thorc app-diaph hern (begin 2008)	4 (0.0)
	5343	LAP umbilical hernia nec (begin 2008)	2 (0.0)
Insertion, replacement, or removal of extracranial ventricular shunt	234	Ventricl shunt-abdomen	294 (3.4)
Excision, lysis peritoneal adhesions	5451	LAP lysis abd adhes (begin 1996)	282 (3.3)
Appendectomy	4701	Laparoscop appendect (begin 1996)	207 (2.4)
	4709	Other appendect (begin 1996)	51 (0.6)
Other OR gastrointestinal therapeutic procedures	5025	LAP abltn liver les/tiss (begin 2006)	214 (2.5)
Oophorectomy, unilateral and bilateral	6563	Lapar remov salp ov bil (begin 1996)	118 (1.4)
	6541	Lapar salp ooph uni (begin 1996)	60 (0.7)
	6531	Laparsc oophectomy uni (begin 1996)	9 (0.1)
	6539	Oth laparsc oophect uni (begin 1996)	9 (0.1)
	6564	Lapar remv salp ov rem (begin 1996)	8 (0.1)
	6553	Lapar bil ooph (begin 1996)	2 (0.0)
Laparoscopy	5421	Laparoscopy	100 (1.2)

Table 2. Continued

CCS Procedure Category	ICD-9 Procedure Code	ICD-9 Procedure Description	n (%)
Other gastrointestinal diagnostic procedures	5014	LAP liver bx (begin 2007)	46 (0.5)
Gastrostomy, temporary and permanent	4311	Percu endosc gastrostomy (begin 1989)	43 (0.5)
	4432	Percutaneous gastrojejunostomy (begin 1989)	1 (0.0)
Other operations on ovary	6525	Oth lapar excis ov (begin 1996)	27 (0.3)
	6581	Lapar lysis adhes ov (begin 1996)	9 (0.1)
Inguinal and femoral hernia repair	1711	LAP dir ing hern-graft (begin 2008)	7 (0.1)
	1712	LAP indir ing hern-graft (begin 2008)	6 (0.1)
	1722	LAP bi indir ing hrn-grf (begin 2008)	4 (0.0)
	1721	LAP bil dir ing hrn-grft (begin 2008)	3 (0.0)
	1723	LAP bi dr/ind ing hrn-gr (begin 2008)	3 (0.0)
	1724	LAP bil ing hern-grf nos (begin 2008)	2 (0.0)
Ileostomy and other enterostomy	4632	Percu endosc jejunostomy (begin 1989)	7 (0.1)
Other therapeutic procedures	1742	LAP robotic assist proc (begin 2008)	6 (0.1)
	1749	Robotic ast proc nec/nos (begin 2008)	1 (0.0)
Other bowel diagnostic procedures	4512	Endosc sm bowel thru st	2 (0.0)
	4511	Transab sm bowel endosc	1 (0.0)

GI, gastrointestinal; LAP, laparoscopic; OR, operating room.

(Wald test P=0.05). Glance et al identified a 3- to 7-fold increased risk of renal complications in patients with modified metabolic syndrome who underwent noncardiac surgery.[22] However, their study population was not confined to patients undergoing laparoscopic surgery. The inclusion of patients undergoing open (nonlaparoscopic) surgeries in their study also explains their findings of a 1.5- to 3-fold increase of renal complications in morbidly obese patients without modified metabolic syndrome and further highlights a potential beneficial effect of laparoscopy surgery on the reduction of the incidence of AKI when compared with open surgery.[23]

The incidence of postoperative AKI in our study population was 2.9%. This finding is in contrast to a 2013 report of an overall incidence of AKI of 6.1% in patients undergoing noncardiac surgery.[24] The difference in the incidence of AKI is the result of the exclusion criteria applied in the current study (patients undergoing open procedures and urologic procedures, as well as those with chronic kidney disease stage III and higher, were excluded in the current study) and the result of the different definitions used in the studies (AKIN criteria used in the current study vs the RIFLE [Risk, Injury, Failure, Loss of renal function, End-stage renal disease] criteria[25] used in the previous report). In addition, the previous report[24] included patients undergoing vascular procedures, a patient population at higher risk of developing postoperative AKI as a result of more pronounced fluid shifts, contrast dye exposure, and major vessel clamping and a higher incidence of preoperative chronic kidney disease.

The reduction in fluid shifts in patients undergoing laparoscopic surgery, as well as the reduction in proinflammatory cytokine release, may have also contributed to a reduction in renal injury in the current study.[26]

Furthermore, reduced hemodynamic fluctuations with laparoscopic surgery could also have contributed to the reduction in postoperative AKI, especially with studies identifying reduction in blood pressure (hypotension) as an independent predictor of the occurrence of AKI in the hospital setting.[27,28]

It is important to note that preoperative chronic renal disease is one of the most important predictors of postoperative AKI.[29] Therefore, a study that only included patients undergoing noncardiac surgery who had normal preoperative renal function reported an incidence of postoperative acute renal failure as low as 0.8%.[30]

Our study results indicate an association between increased BMI and a reduction of in-hospital mortality. This protective effect has been termed the obesity paradox in prior studies.[31,32] The metabolically triggered low-grade inflammatory state in the obese population may augment the adaptive response to surgical injury and promote tissue repair while reducing infectious complications.[33] In addition, the adipocyte-derived hormone leptin has been shown to exert immunomodulating effects and increased bacterial clearance and survival in animal experiments.[34,35]

LIMITATIONS

As with all retrospective studies, our ability to adjust for potential confounding is limited to available data. Although we accounted for the potential confounding effects of 11 factors, residual bias attributable to uncontrolled confounding variables may remain and cannot be determined. Consequently, the associations we report should not be considered evidence of a causal relationship. We did not do a full mediation analysis; thus, 2 reported primary associations should not be considered as evidence for the mediation effect of diabetes, hypertension, coronary artery

Table 3. Raw Incidences of Primary and Secondary Outcomes by Body Mass Index Category

Factor	Total n=8,543 (100%)	Underweight (BMI<18.5) n=100 (1%)	Normal (18.5≤BMI<25) n=1,500 (18%)	Overweight (25≤BMI<30) n=1,672 (20%)	Obese Grade 1 (30≤BMI<35) n=1,255 (15%)	Obese Grade 2 (35≤BMI<40) n=1,118 (13%)	Obese Grade 3 (BMI≥40) n=2,898 (34%)	Adjusted OR (95% CI) with 5-unit increase in BMI	*P* Value[a]
Primary Outcome									
BMI effect on AKI, including possible mediation via diabetes mellitus, hypertension, CAD, and COPD								1.07 (1.00, 1.15)[b]	0.05
Pure[c] BMI effect on AKI								1.03 (0.96, 1.11)[b,c]	0.35
No AKI	8,297 (97.1)	96 (96.0)	1,466 (97.7)	1,619 (96.8)	1,218 (97.1)	1,079 (96.5)	2,819 (97.3)		
Any AKI	246 (2.9)	4 (4.0)	34 (2.3)	53 (3.2)	37 (2.9)	39 (3.5)	79 (2.7)		
Stage I	182 (2.1)	3 (3.0)	27 (1.8)	42 (2.5)	28 (2.2)	29 (2.6)	53 (1.8)		
Stage II	41 (0.5)	1 (1.0)	5 (0.3)	8 (0.5)	5 (0.4)	2 (0.2)	21 (0.7)		
Stage III	23 (0.3)	0 (0)	2 (0.1)	3 (0.2)	4 (0.3)	8 (0.7)	5 (0.2)		
Secondary Outcomes									
In-hospital mortality	36 (0.4)	1 (1.0)	9 (0.6)	9 (0.5)	5 (0.4)	4 (0.4)	8 (0.3)	0.991 (0.990, 0.992)[b]	<0.001
End-stage renal disease[d]	1 (0)		1 (0)						

AKI, acute kidney injury; BMI, body mass index (kg/m^2); CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio.
Note: Observed raw incidences are reported as n (%).
[a]*P* value corresponds to model-based Wald chi-square tests; significant *P* value is <0.05 for the primary and secondary outcomes.
[b]Multivariable proportional odds model was used, and the odds ratio was reported; results were adjusted for age, sex, race, American Society of Anesthesiologists physical status, history of congestive heart failure, ascites, renal insufficiency, preoperative serum creatinine level, emergency surgery, and type and duration of surgery.
[c]To eliminate possible mediation of diabetes mellitus, hypertension, CAD, and COPD in the relationship between BMI and AKI, we did additional adjustment for these variables in the described multivariable proportional odds model.
[d]We were not able to formally assess the association between BMI and end-stage renal disease (defined by the need for hemodialysis) because of the very low incidence.

disease, and COPD in the relationship between BMI and postoperative AKI.

We also had missing data, principally because postoperative serum creatinine measurements are not routinely performed but also because some preoperative serum creatinine and height measurements were missing (the missing height measurements precluded the calculation of BMI). The exclusion of patients with missing preoperative or postoperative creatinine levels may have potentially biased the reported association between BMI and AKI.

CONCLUSION

In conclusion, we found a marginal association between BMI and an increased risk of developing AKI in adult patients after having noncardiac laparoscopic surgery. However, this BMI effect diminished to statistical insignificance once diabetes mellitus, hypertension, coronary artery disease, and history of COPD were considered as potential confounding factors.

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