The influence of body mass index obesity status on vascular surgery 30-day morbidity and mortality

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Objective: **Mild obesity may have a protective effect against some diseases, termed an "obesity paradox." This study examined the effect of body mass index (Kg/m^2 BMI) on surgical 30-day morbidity and mortality in patients undergoing vascular surgical procedures.**

Methods: **As part of the National Surgical Quality Improvement Program (NSQIP), demographic and clinical risk variables, mortality, and 22 defined complications (morbidity) were obtained over three years from vascular services at 14 medical centers. At each medical center, patients from the operative schedule were prospectively and systematically enrolled according to NSQIP protocols. Outcomes and risk variables were compared across NIH-defined obesity classes (underweight [BMI≤18.5], normal [18.5<BMI<25], overweight [25<BMI≤30], obese I [30<BMI≤35], obese II [35<BMI≤40], and obese III [BMI>40]) using analysis of variance and means comparisons. Logistic regression was used to control for other risk factors.**

Results: **Vascular procedures in 7,543 patients included lower extremity revascularization (24.6%), aneurysm repair (17.4%), cerebrovascular procedures (17.3%), amputations (9.4%), and "other" procedures (31.3%). In the entire cohort, there were 1,659 (22.0%) patients with complications and 295 (3.9%) deaths. Risk factors of hypertension and diabetes increased with BMI (analysis of variance [ANOVA] $P < .05$) as expected; smoking, disseminated cancer, and stroke decreased (ANOVA $P < .01$). Twenty other risk factors, as well as mortality and morbidity, had "U" or "J"-shaped distributions with the highest incidence in underweight and/or obese class III extremes but reduced minimums in overweight or obese I classes (ANOVA $P < .05$). After controlling for age, gender, and operation type, mortality risk remained lowest in obese class I patients (Odds ratio [OR] 0.63, $P = .023$) while morbidity risk was highest in obese class III patients (OR 1.70, $P = .0003$), due to wound infection, thromboembolism, and renal complications.**

Conclusion: **Underweight patients have poorer outcomes and class III obesity is associated with increased morbidity. Mildly obese patients have reduced co-morbid illness, surprisingly even less than normal-class patients, with correspondingly reduced mortality. Mild obesity is not a risk factor for 30-day outcomes after vascular surgery and confers an advantage. (J Vasc Surg 2009;49:140-7.)**

Obesity, which is widespread and increasing in the United States,[1] has been associated with the development of diabetes mellitus, hypertension,[2] cardiovascular disease,[3] heart failure,[4] and death from all causes.[5] Despite the association of obesity with the development of chronic disease states that lead to early mortality, a number of recent studies have described an "obesity paradox," in which an improved survival has been observed in obese patients with heart failure,[6,7] those undergoing coronary bypass,[8] and obesity was found to be a significant factor associated with smaller infarct size following myocardial infarction.[9] These reports raise the question as to what effect obesity has on short-term outcome in patients undergoing vascular surgery procedures.

To date, there are few studies that specifically address the effect of obesity on outcome in vascular surgery patients. A small study by Nicholson et al reported that obesity was not a risk factor in vascular reconstructive surgery.[10] Gurm et al likewise found no association between body mass index (Kg/m^2 BMI) and short-term outcomes after carotid stenting.[11] Chang et al found that obesity was not associated with increased infection rates after lower extremity revascularizations,[12] although Nam et al reported a higher risk of wound complications with infra-inguinal venous bypass grafting in obese patients.[13] In patients with thigh arteriovenous shunts, obesity (BMI ≥ 30) has been associated with increased access failure, and thus more operations were required in obese patients.[14] Finally, in patients with peripheral vascular disease requiring lower extremity amputation, obesity did not predict poorer prognosis.[15]

The purpose of this study was to examine the relationship between BMI obesity class as defined by National Institutes of Health (NIH) on surgical 30-day morbidity and mortality in a large cohort of patients undergoing a variety of vascular surgery procedures. This study makes use of the diverse clinical risk factors and postoperative out-

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Table I. Procedure groups used in the study with their 30-day mortality and morbidity rates

Primary procedure group	*No. of cases (% of total)*	*30-day outcomes**	
		Mortality n (%)	*Morbidity[a] n (%)*
Lower extremity revascularization	1852 (24.6%)	70 (3.8%)	573 (30.9%)
AAA – iliac aneurysm	1316 (17.4%)	55 (4.2%)	291 (22.1%)
Cerebrovascular	1307 (17.4%)	14 (1.1%)	106 (8.1%)
Amputation	712 (9.4%)	68 (9.6%)	223 (31.3%)
Mesenteric/renal revascularization	110 (1.5%)	5 (4.5%)	38 (34.6%)
Vascular access	80 (1.1%)	3 (3.8%)	11 (13.8%)
Other[b]	2166 (28.6%)	80 (3.7%)	419 (19.3%)
Total	7543 (100%)	295 (3.9%)	1661 (22.0%)

AAA, abdominal aortic aneurysm.
*30-day mortality and morbidity varied significantly by procedure group (ANOVA $P < .05$).
[a]Morbidity was defined as one or more of the 22 NSQIP defined complications.
[b]Other procedures performed on vascular surgery services at 14 academic medical centers.

comes available through the National Surgical Quality Improvement Program (NSQIP) data set gathered through the Patient Safety in Surgery Study (PSS).

METHODS

This is a sub-study of data obtained through the PSS Study. A detailed description of the PSS Study, which used NSQIP methodologies, has been reported previously[16] and is summarized here. Data from patients who underwent major vascular procedures at 14 academic medical centers participating in the PSS study from fiscal years 2002 through 2004 were analyzed. Each hospital had a risk-assessment nurse, who prospectively collected preoperative patient characteristics, clinical risk factors, intraoperative processes of care, and postoperative adverse occurrences up to 30 days after the operation. The first 40 operations in each eight-day cycle were included for data collection. Follow-up patient information was obtained from paper and electronic medical records, morbidity and mortality conference reports, as well as through communication with patients by letter or telephone after discharge. The nurses were trained on study definitions, participated in regular conference calls, and attended annual meetings. Regular site visits occurred to ensure data reliability. Multiple operations on the same patient within 30 days were not included in the analysis. If complications that required a reoperation occurred, they were recorded but the reoperation was not included as a second index case. We proposed this secondary analysis of the PSS study database to the PSS Study Publications Committee and were given the analytical results.

Measures and statistical analyses. BMI values were calculated for each patient and categorized according to the NIH obesity categories which are listed in Table I.[17] Operation complexity was measured using the maximum of the work relative value units (WRVUs)[18] associated with the procedure codes recorded for the surgery. One of the investigators (E.D.E.), a vascular surgeon, grouped the procedures based on the primary procedure by Current Procedural Terminology (CPT) code. The primary procedure codes included in each group are listed in the Appendix (online only).

Analysis of variance (ANOVA) of morbidity and mortality across obesity classes was performed. Outcome rates for each obesity class were further compared to normal-class patients using the Bonferroni test for multiple comparisons of means. Similar stratification and comparison was performed on the demographic, preoperative and perioperative variables. Complications were categorized into nine groups and similar analyses performed.

Multivariable logistic regression was used to assess the odds ratios for the 30-day outcomes with normal class used as the reference. The regressions were performed with obesity classes alone as predictor variables and then repeated with the inclusion of age, gender, procedure group, and WRVUs as controls.

RESULTS

The PSS study database included 8,706 vascular surgery patients, of which 1,163 did not have heights or weights recorded, leaving 7,543 for BMI calculation and analysis. A broad spectrum of cases performed on vascular surgery services was included in the study and significant variation in mortality and morbidity occurred between the procedure groups (ANOVA $P < .05$, Table I). Significant variation occurred in the distribution of patients by obesity class across the different procedure groups (χ^2 $P < .0001$, Table II). The median patient obesity class was overweight, and over 25% of the patients were in obese classes I through III. At the extremes, 345 (4.6%) of the patients were underweight and 285 (3.8%) were obese class III, or morbidly obese.

Patient characteristics by obesity class. The majority of underweight and obese class III patients were female (Bonferroni $P < .05$ relative to normal-class, Table III) while overweight and obese I patients were more often male (Bonferroni $P < .05$). The age at operation decreased significantly with increasing obesity (Bonferroni $P < .05$). The incidence of medically-treated diabetes and hypertension increased with obesity class as expected, as did dyspnea at rest or with mild exertion (ANOVA $P < .05$). However the relationship with cardiovascular disease (CVD, as measured by a history of congestive heart failure, myocardial infarction, angina, prior cardiac operation, or angioplasty) was less pronounced. Overweight patients had significantly higher CVD than normal class patients (Bonferroni $P < .05$). In contrast to these factors, the risk factors of smoking, pack-years smoked, history of stroke, disseminated cancer, reduced white blood cell count, and recent weight loss >10% tended to decrease with increasing BMI (ANOVA $P < .05$ except for disseminated cancer). Twelve other risk factors that varied significantly with obesity class had a "U" shaped distribution with the lowest risk in overweight or obese I

Table II. The distribution of patients by obesity class within procedure groups*

Primary procedure group (n, % of total)	*Distribution of patients within procedure group by obesity class* n (% of Group)*					
	Underweight BMI ≤ 18.5	*Normal BMI 18.6-25*	*Overweight BMI 25.1-30*	*Obese I BMI 30.1-35*	*Obese II BMI 35.1-40*	*Obese III BMI > 40*
Lower extremity revascularization (1852, 24.6%)	124 (6.7%)	677 (36.6%)	634 (34.2%)	267 (14.4%)	88 (4.8%)	62 (3.4%)
AAA – iliac aneurysm (1316, 17.4%)	43 (3.3%)	401 (30.5%)	524 (39.8%)	253 (19.2%)	67 (5.1%)	28 (2.1%)
Cerebrovascular (1307, 17.4%)	32 (2.4%)	400 (30.6%)	537 (41.1%)	220 (16.8%)	78 (6.0%)	40 (3.1%)
Amputation (712, 9.4%)	61 (8.6%)	256 (36.0%)	206 (28.9%)	106 (14.9%)	53 (7.4%)	30 (4.2%)
Mesenteric/renal revascularization (110, 1.5%)	9 (8.2%)	50 (45.5%)	30 (27.3%)	15 (13.6%)	5 (4.6%)	1 (0.9%)
Vascular access (80, 1.1%)	8 (10.0%)	25 (31.3%)	21 (26.3%)	14 (17.5%)	7 (8.8%)	5 (6.3%)
Other (2166, 28.7%)	68 (3.1%)	812 (37.5%)	679 (31.4%)	354 (16.3%)	134 (6.2%)	119 (5.5%)
Total (7543, 100%)	345 (4.6%)	2621 (34.8%)	2631 (34.9%)	1229 (16.3%)	432 (5.7%)	285 (3.8%)

*The distribution of patients across obesity classes varied significantly by procedure group (Chi-squared $P < .0001$).

Table III. Patient characteristics by obesity class

Patient characteristics	*Underweight*	*Normal (reference)*	*Overweight*	*Obese I*	*Obese II*	*Obese III*
No. of cases	345	2621	2631	1229	432	285
Demographic factors						
Male (%)*	**47.8**^{L}	56.2	**67.4**^{H}	**61.8**^{H}	51.2	**42.8**^{L}
Mean age (years)*	65.5	66.2	66.1	**63.5**^{L}	**60.8**^{L}	**57.9**^{L}
General risk factors						
ASA class 4 or 5 (%)*	21.8	15.7	14.7	13.3	13.9	18.6
Emergent (%)*	13.9	12.4	10.7	10.7	11.6	**19.3**^{H}
Medically treated diabetic (%)*	19.4	20.0	**26.5**^{H}	**35.8**^{H}	**38.4**^{H}	**48.1**^{H}
Partial or full functional dependence (%)*	**24.9**^{H}	14.7	11.7	**9.8**^{L}	17.5	16.0
Dyspnea at rest or with moderate exertion (%)*	26.1	20.0	20.6	**25.7**^{H}	**26.6**^{H}	**33.7**^{H}
Pulmonary risk factors						
COPD (%)*	**17.7**^{H}	11.6	10.6	10.8	10.4	11.9
Current smoker (%)*	**48.4**^{H}	32.2	29.4	**27.5**^{L}	28.5	27.4
Mean pack years smoked*	**34.8**^{H}	28.4	30.5	28.9	27.3	22.9
Cardiovascular risk factors						
Hypertensive req. med. (%)*	69.6	68.9	**73.9**^{H}	**78.0**^{H}	75.5	**79.3**^{H}
History of CVD[a] (%)*	31.6	33.6	**38.8**^{H}	38.2	36.6	34.0
History of PVD[b] (%)*	**60.0**^{H}	42.4	**36.6**^{L}	37.3	37.5	40.4
Central nervous system risk factor						
History of stroke[c] (%)*	23.5	21.5	21.7	19.5	17.6	15.8
Hepatic/renal/gastrointestinal risk factors						
On dialysis (%)*	**16.2**^{H}	8.6	6.5	6.1	11.6	9.8
Renal dysfunction[d] (%)	32.8	33.5	35.8	36.7	36.8	34.7
Hepatic dysfunction[e] (%)*	**50.4**^{H}	39.1	35.4	36.8	33.6	39.6
Bleeding disorder (%)*	9.6	10.4	**7.8**^{L}	8.2	8.6	8.1
Nutritional/immune/other risk factors						
Albumin (Mean)*	**3.27**^{L}	3.56	**3.66**^{H}	**3.67**^{H}	3.51	3.44
Disseminated cancer (%)	1.4	0.7	0.8	0.5	0.2	0.4
Weight loss >10% (%)*	**14.8**^{H}	4.0	**1.4**^{L}	**0.7**^{L}	**0.7**^{L}	**0.4**^{L}
WBC ≤ 4.5 (%)	3.0	5.2	4.7	4.4	3.1	2.9
Infectious risk factors						
Open wound or infection (%)*	**36.5**^{H}	22.0	19.4	20.3	24.8	28.8
Sepsis (%)*	4.7	2.6	2.3	2.2	**5.6**^{H}	4.6
WBC > 11.0 (%)*	**28.1**^{H}	17.0	15.7	17.7	18.2	**26.1**^{H}

AAA, abdominal aortic aneurysm; *COPD,* chronic obstructive pulmonary disease; *CVD,* cardiovascular disease; *PVD,* peripheral vascular disease; *WBC,* white blood cell count.

*Significant variance in risk factor across obesity classes, ANOVA $P \leq .05$.

^{H}Obesity class rate higher than normal-class based on a Bonferroni comparison of means, $P \leq .05$.

^{L}Obesity class rate lower than normal based on a Bonferroni comparison of means, $P \leq .05$.

[a]History of cardiovascular disease includes congestive heart failure, angina, myocardial infarction, prior cardiac operation, or angioplasty.

[b]History of peripheral vascular disease includes prior peripheral vascular surgery, rest pain, or gangrene.

[c]History of stroke includes transient ischemic attack or cerebrovascular accident with or without neurologic compromise.

[d]Renal dysfunction includes blood urea nitrogen (BUN) > 40 or creatinine > 1.2.

[e]Hepatic dysfunction includes alkaline phosphatase > 125, bilirubin > 1.0 or serum glutamic-oxaloacetic transaminase (SGOT) > 40.

Table IV. Intraoperative variables by obesity class

Intraoperative variable	*Underweight*	*Normal (reference)*	*Overweight*	*Obese I*	*Obese II*	*Obese III*
No. of cases	345	2621	2631	1229	432	285
Complexity (mean primary procedure work RVUs)*	18.8	18.3	18.8	18.6	17.4	**15.9**^{L}
Operation duration (mean hrs.)	3.08	2.91	3.03	3.05	2.97	2.91
Wound class contaminated or dirty/infected (%)*	**15.1**^{H}	9.2	8.3	9.1	12.5	**15.8**^{H}
Packed red blood cells transfused (mean units)	0.88	0.87	0.75	0.83	0.59	0.79

*Significant variance in variable across obesity classes, ANOVA $P \leq .05$.
^{L}Obesity class lower than normal class based on a Bonferroni comparison of means, $P \leq .05$.
^{H}Obesity class higher than normal class based on a Bonferroni comparison of means, $P \leq .05$.

patients and the highest risks at the extremes in underweight or class III obese patients. These included functional dependence, preoperative sepsis, and ASA class, the top three risk factors for vascular surgery 30-day mortality in the 2008 American College of Surgeons NSQIP report to sites.[19]

Intraoperative factors. The mean operation length of time did not vary significantly by obesity class but complexity (measured by the work RVUs of the primary procedure) and wound class did (ANOVA $P < .05$, Table IV). Obese class III patients had significantly less complex operations (Bonferroni $P < .05$) than normal class patients but similar operative durations and significantly more contaminated or dirty wounds (Bonferroni $P < .05$).

Outcomes. The 30-day mortality rates by obesity class demonstrate a reverse-"J" shape with the highest values occurring in the underweight and normal class patients (ANOVA $P < .05$, Table V). Obese I patients had less mortality than normal class patients (Bonferroni $P < .05$). The 30-day composite morbidity distribution was "U" shaped with higher levels of complications in the underweight and obese class-III extremes (ANOVA $P < .05$). The odds ratios for morbidity and mortality, without controls, follow the rate distributions; reverse–"J" for mortality and "U" shape for morbidity: both overweight and obese class-I patients have significant reductions in risk of mortality and underweight and obese class III patients have increased risk of morbidity ($P < .05$, Fig). When controlled for age, gender, procedure group, and work RVUs, overweight through obese class III patients still had reduced risk for mortality, significantly so for obese class I patients ($P < .05$). Under the same controls morbidity risks increased for obese classes I to III with obese class III patients at significantly higher risk of morbidity ($P < .05$). When the twenty-two specific complications that made up the composite morbidity definition were grouped into eight composite categories, three of the unadjusted composite rates varied significantly (ANOVA $P < 0.05$) by obesity class: respiratory complications, wound infection, and thromboembolism. When controlled for age, gender, procedure group, and work RVUs, obese class I to III patients had significantly increased risk of urinary tract complications and wound infection. Obese class III patients also had increased risk of thromboembolism. Overweight patients, however, had a significantly reduced risk for respiratory complications.

DISCUSSION

Obesity has reached epidemic proportions in the United States with far reaching adverse implications concerning the overall health status of the population.[1] In the current vascular surgery study, the majority of patients were overweight or obese, results that are in line with national trends. Additionally, most preoperative risk factors, intraoperative factors, and 30-day outcomes measured in this study varied significantly by obesity class. These findings indicate the complexity of the clinical interactions associated with a single variable, BMI.

The current study supports the well known increased risk of hypertension and diabetes as BMI increases. The incidence of cardiovascular disease, however, did not correlate linearly with increased BMI. Rather, the highest incidence was noted in overweight patients. The reason for this finding is not clear. Interestingly, most risk factors demonstrated a distribution across obesity classes following a "U" shaped curve with higher risk factors at the underweight and obese class III extremes and minimum risk in the overweight or obese I classes – not in the normal weight class. These factors include the American Society of Anesthesiologists physical status classification (ASA class), functional dependence prior to surgery, and preoperative sepsis – the top three predictors of vascular surgery 30-day mortality according to the most recent ACS NSQIP report. What is unclear is why mildly obese patients should have such reduced comorbid risk factors. The comorbid risks were not included as controls in our analysis due to uncertainty whether these factors were a result of a patient's weight status or contributed to their weight status. We controlled for age and gender because they are not caused by obesity. We also controlled for the procedure variables in an attempt to control for presentation bias in this study of patients admitted for surgery.

Under these controls, obese class I patients demonstrated a significantly reduced risk for 30-day mortality compared with normal weight patients, while morbidity risk was significantly higher in obese class III patients. The reduction in mortality in obese I patients is likely associated with the reduced comorbid risks, although again it is not clear why those risks should be lower in that group. The higher risk for morbidity in the obese class III patients appears to be primarily due to an increased rate of wound complications, renal complications, and thromboembolism. The increased rate of wound complications can be explained by the need for

Table V. Outcome rates by obesity class

Outcome	*Underweight*	*Normal (reference)*	*Overweight*	*Obese I*	*Obese II*	*Obese III*
No. of cases	345	2621	2631	1229	432	285
Mortality %*	6.96	4.81	3.42	**2.69**^{L}	3.01	3.16
Morbidity %*	28.1	22.4	19.7	22.4	23.6	28.1
Return to operating room %*	**24.1**^{H}	17.5	15.4	16.4	18.3	20.7
[a]Systemic infection %	4.1	2.4	2.1	2.6	3.0	2.8
Odds ratio with control	1.5	ref.	0.9	1.2	1.5	1.6
[b]Respiratory complication %*	13.6	9.1	**6.8**^{L}	8.5	6.7	6.7
Odds ratio with control	**1.5**^{H}	ref.	**0.8**^{L}	1.0	0.9	1.0
[c]Wound infection %*	4.1	6.3	6.7	8.1	7.9	**13.7**^{H}
Odds ratio with control	**0.5**^{L}	ref.	1.2	**1.5**^{H}	1.4	**2.5**^{H}
[d]Renal complication %	8.1	6.1	5.3	6.7	6.9	6.7
Odds ratio with control	1.2	ref.	1.0	**1.4**^{H}	**1.6**^{H}	**1.7**^{H}
[e]CNS complication %	2.0	1.8	1.6	1.8	1.4	2.1
Odds ratio with control	1.1	ref.	0.9	1.1	0.9	1.4
[f]Thromboembolism %*	1.2	1.0	1.3	1.0	1.6	**3.2**^{H}
Odds ratio with control	1.1	ref.	1.4	1.1	1.8	**3.7**^{H}
[g]Cardiac complication %	2.3	2.7	1.9	2.4	1.9	1.8
Odds ratio with control	0.8	ref.	0.7	1.0	0.8	0.8
[h]Other complication %	6.4	4.3	3.6	4.4	5.3	6.0
Odds ratio with control	1.3	ref.	0.9	1.1	1.4	1.6

CNS, central nervous system.

Complication groups include obesity class odds ratios relative to normal class controlled for age, gender, procedure group and complexity.

*Significant variance in outcome rates across obesity classes, ANOVA $P \leq .05$.

^{L}Obesity class rate lower than normal based on a Bonferroni comparison of means or odds ratio significantly less than 1.0 based on the Wald statistic, $P \leq .05$.

^{H}Obesity class rate higher than normal-class based on a Bonferroni comparison of means or odds ratio significantly higher than 1.0 based on the Wald statistic, $P \leq .05$.

[a]Systemic infections included patients with systemic inflammatory response syndrome, sepsis, or septic shock.

[b]Respiratory complications included pneumonia, failure to wean from ventilation at 48 hours postoperatively, or unplanned intubation.

[c]Wound infection included superficial and deep wound infections, organ/space infections, or wound disruptions.

[d]Renal complications included urinary tract infections, progressive renal insufficiency, and acute renal failure.

[e]Central nervous system complications included stroke, coma greater than 24 hours postoperatively, and peripheral nerve injury.

[f]Thromboembolism included pulmonary embolism and deep venous thrombosis.

[g]Cardiac complications include acute myocardial infarction and cardiac arrest requiring resuscitation.

[h]Other complications include failure of a graft, prosthesis or flap failure, and postoperative bleeding requiring transfusion.

large incisions, often in intertriginous areas, with a relatively poor blood supply to the adipose tissue.

Other studies have also investigated the effect of obesity on surgical outcome. Two studies in general surgery patients showed no increase in morbidity related to obesity.[20,21] Studies in the cardiovascular arena have largely focused on coronary artery bypass grafting (CABG) and have found mixed results.[22-35] Jin et al postulated that these mixed results were due to different BMI-class cut points and sample sizes. However, what is intriguing about Jin's study was the finding of reduced mortality in mildly obese patients.[36] Similarly, Romero-Corral, in a meta-analytical review, found that overweight CAD patients have the lowest risk of cardiovascular and total mortality.[37] These data support our findings of reduced mortality in mildly obese patients, while again not clarifying the mechanism.

In addition, while it is widely accepted that obesity increases the risk for developing heart disease, a growing number of recent reports document a significant survival benefit for obese patients once they have been diagnosed with cardiovascular diseases.[6-9] This has been termed the "obesity paradox." The current study supports this observation by demonstrating an improved mortality in overweight patients and raises the question why overweight or moderately obese patients may have an improvement in short-term surgical outcomes but be at risk for long-term illnesses that place them at increased risk for mortality at a younger age. The current study cannot directly address the causes for this paradox, but a number of hypotheses can be proposed.

One possible explanation for this paradox may be related to the metabolic activity of adipose tissue. Adipose tissue, once considered simply a lipid storage depot, is now known to produce and secrete an increasing range of factors, collectively termed adipokines.[38] For instance, recent findings have shown that the adipokine adiponectin directly affects signaling in cardiac cells and is beneficial in the

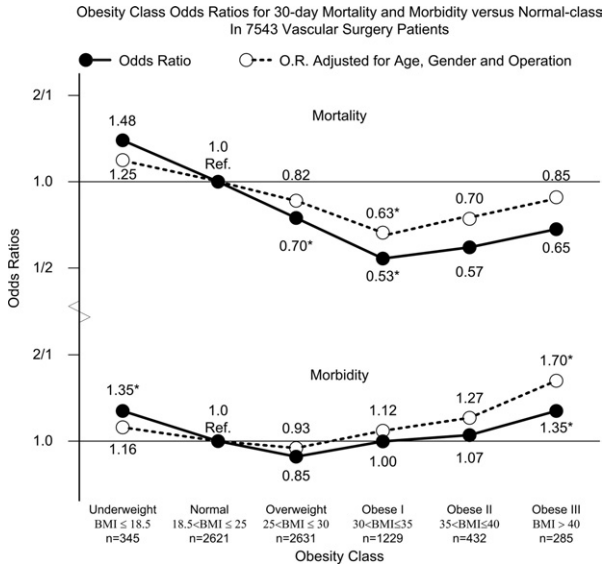

Fig. Obesity class odds ratios for thirty-day mortality and morbidity relative to normal class patients. Results shown are for obesity classes alone and with control for age, gender, and the operation. With control, obese class I patients were at reduced risk of mortality and morbidly obese patients were at increased risk of morbidity.

setting of pathological cardiac remodeling and acute cardiac injury.[39] Another cytokine produced by adipocytes that could have a protective effect is resistin.[40] Though most research has focused on its effects on glucose homeostasis,[41] resistin also induces in vitro endothelial cell proliferation and migration.[42] Such effects could aid the vascular healing process although it has been shown to cause endothelial cell dysfunction in pig coronary arteries.[43]

Another possible explanation for an obesity paradox is a nutritional component resulting in improved outcomes in patients with mild to moderate obesity. The results in the current study found that preoperative albumin levels differed significantly among the BMI groups. The highest levels were found in the obese class I patients, suggesting that these patients may have had the "best" preoperative nutritional status. These patients may, as a result, be better suited to withstand the stress of starvation and injury induced by an operation.

While the current study has demonstrated a correlation between moderately increased BMI and improved mortality, it should be emphasized that this study examined only the perioperative (30-day) outcome following a vascular surgical procedure. These results cannot and should not be compared to the long-term effects of obesity on overall health status, particularly in the relationship of obesity to the development of hypertension and diabetes. In fact, as noted, these conditions were found to increase as BMI increased.

There are obvious limitations to this observational study. While observations of relationships between risk factors, obesity class, and outcome can be made, cause and effect is difficult, if not impossible, to prove. The procedure groups also encompass many different operations. For example, treatment of aneurysm disease includes both open and endoluminal approaches. Similarly, the category of "other" is large and includes diverse vascular procedures such as thrombectomy/embolectomy, venous procedures, peripheral aneurysm repair, reoperative vascular surgery, upper extremity bypass, carotid and vertebral bypass/transposition, and endoluminal angioplasty and stenting. Additionally, while patients were included in the study in a systematic prospective fashion, it is a sampling of patients and did not include all patients undergoing vascular procedures at each institution. The study also did not identify patients with the metabolic syndrome and did not differentiate between central obesity and peripheral obesity. Such a study would require waist and hip anthropomorphic measurements.

On the other hand, there are also strengths to the study. Data collected from 14 different institutions over a three year period on several thousand patients should eliminate many sources of bias and suggests that the findings are generalizable. The use of the NSQIP methodology, definitions, and nurses also allows confidence that the data from different institutions is reproducible and comparable. Furthermore, the operations included in the study were inclusive of essentially all vascular procedures and for the patient cohort as a whole and provides an overall concept of how BMI relates to outcomes in vascular surgery patients.

Further research to isolate the specific mechanisms for these findings faces significant challenges. BMI categories interacted with numerous clinical risk factors in our study in a non-straight line fashion ("U" or "J" shaped distributions); indicating complex interdependent, or multiple independent, interactions. These risk factors included cardiovascular and peripheral vascular disease, the indication for vascular surgery, and therefore presenting selection bias in vascular surgery studies. Added to complexity and selection bias challenges, the chronicity of obesity requires evaluation, possibly starting in infancy. Effective studies will therefore need to be long term population studies including behaviors, obesity status, and clinical interventions including vascular surgery. Further basic science studies on the humoral and metabolic functions of adipose tissue should also yield clarification on the impact of obesity, if any, on the inflammatory cascade and vascular tissue repair. Lastly, we are intrigued by the potential of a randomized study of the benefits of nutritional supplementation to elective surgical patients who have the option of waiting for surgery. The well known importance of albumin as a predictor of surgical outcomes and the suggestion in our data of a relationship with mild obesity make this an intriguing study. We also postulate an interaction between BMI, nutrition, glycemic control, and 30-day outcomes that could be examined.

In summary, the current study found significant benefit in 30-day mortality in obese class I patients undergoing a vascular procedure. The mortality reduction in obese I patients is likely due to the reduced comorbid risk factors in these patients, but why they would have reduced comorbid

illness is unknown and cannot be determined from the study. These findings are consistent with other reports that have also shown improved outcome in obese patients and coined this as an "obesity paradox." We have postulated that these results could be due to differences in the metabolic makeup of obese patients and/or improved nutritional status. It also is possible that other mechanisms may be the cause of these findings and further studies will be needed to identify the precise mechanisms responsible. Significantly higher morbidity was found in obese class III patients; primarily due to the higher incidence of wound complications, thromboembolism, and renal complications in this patient group.

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Conception and design: DLD, JR, EDE
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Data collection: DLD, WGH
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Critical revision of the article: DLD, ESX, PH, JR, WGH, EDE
Final approval of the article: DLD, EDE
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REFERENCES

1. Ogden C, Yanovski S, Carroll M, Flegal K. The epidemiology of obesity. Gastroenterology 2007;123:2087-102.
2. Francischetti E, Genelhu V. Obesity-hypertension: an ongoing pandemic. Int J Clin Pract 2007;61:269-80.
3. Hubert H, Feinleib M, McNamara P, Castelli W. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968-77.
4. Kenchaiah S, Evans J, Levy D, Wilson PW, Benjamin EJ, Larson MG, et al. Obesity and the risk of heart failure. N Engl J Med 2002;347:305-13.
5. Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. N Engl J Med 2006;355:763-78.
6. Lavie CJ, Osman AF, Milani RV, Mehra M. Body composition and prognosis in chronic systolic heart failure: The obesity paradox. Am J Cardiol 2003;91:891-4.
7. Curtis JP, Selter JG, Yongfei W, Rathore SS, Jovin IS, Jadbabaie F, et al. The obesity paradox. Body mass index and outcomes in patients with heart failure. Arch Int Med 2005;265:55-61.
8. Gruber L, Mercado N, Milo S, Boersma E, Disco C, van Es G-A, et al. Impact of body mass index on the outcome of patients with multivessel disease randomized to either coronary artery bypass grafting or stentin in the ARTS trial: The obesity paradox II? Am J Cardiol 2005;95:439-44.
9. Pingitore A, DiBella G, Lombardi M, Iervasi G, Strata E, Aquaro GD, et al. The obesity paradox and myocardial infarct size. J Cardiovasc Med 2007;8:713-7.
10. Nicholson ML, Dennis MJ, Makin GS, Hopkinson BR, Wenham PW. Obesity as a risk factor in major reconstructive vascular surgery. Eur J Vasc Surg 1994;8:209-13.
11. Gurm HS, Fathi R, Kapadia SR, Abou-Chebl A, Vivek DP, Bajzer C, Yadav JS. Impact of body mass index on outcome in patients undergoing carotid stenting. Am J Cardiol 2005;96:1743-5.
12. Chang JK, Calligaro KD, Ryan S, Runyan D, Dougherty MJ, Stern JJ. Risk factors associated with infection of lower extremity revascularization: analysis of 365 procedures performed at a teaching hospital. Ann Vasc Surg 2003;17:91-6.
13. Nam JH, Gahtan V, Roberts AB, Kerstein MD. Influence of incisional complications on infrainguinal vein bypass graft outcome. Ann Vasc Surg 1999;13:77-83.
14. Cull JD, Cull DL, Taylor SM, Carsten CG 3rd, Snyder BA, Youkey JR, et al. Prosthetic thigh arteriovenous access: outcome with SVS/AAVS reporting standards. J Vasc Surg 2004;39:381-6.
15. Kalbaugh CA, Taylor SM, Kalbaugh BA, Halliday M, Daniel G, Cass AL, et al. Does obesity predict functional outcome in the dysvascular amputee? Am Surg 2006;72:707-12.
16. Khuri SF, Henderson WG, Daley J, Jonasson O, Jones RS, Campbell DA Jr, et al. The patient safety in surgery study: background, study design, and patient populations. J Am Coll Surg 2007;204:1089-102.
17. NHLBI Obesity Education Initiative Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults–The Evidence Report. National Institutes of Health. Obes Res 1998;6 Suppl 2:51S-209S.
18. CMS - Centers for Medicare and Medicaid Services. National Physician Fee Schedule Relative Value File. http://www.cms.hhs.gov/physicians/pfs. Accessed January 1, 2008.
19. American College of Surgeons National Surgical Quality Improvement Program. Semiannual Report. January 31, 2008.
20. Dindo D, Muller MK, Weber M, Clavien PA. Obesity in general elective surgery. Lancet 2003;361:2032-5.
21. Davies KE, Houghton K, Montgomery JE. Obesity and day-case surgery. Anesthesia 2001;56:1112-5.
22. Prabhakar G, Haan CK, Peterson ED, Coombs LP, Cruzzavala JL, Murray GF. The risks of moderate and extreme obesity for coronary artery bypass grafting outcomes: a study from the Society of Thoracic Surgeons' database. Ann Thorac Surg 2002;74:1125-30.
23. Engelman DT, Adams DH, Byrne JG, Aranki SF, Collins JJ Jr, Couper GS, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. J Thorac Cardiovasc Surg 1999;118:866-73.

24. Schwann TA, Habib RH, Zacharias A, Parenteau GL, Riordan CJ, Durham SJ, Engoren M. Effects of body size on operative, intermediate, and long-term outcomes after coronary artery bypass operation. Ann Thorac Surg 2001;71:521-30.
25. Reeves BC, Ascione R, Chamberlain MH, Angelini GD. Effect of body mass index on early outcomes in patients undergoing coronary artery bypass surgery. J Am Coll Cardiol 2003;42:668-76.
26. Potapov EV, Loebe M, Anker S, Stein J, Bondy S, Nasseri BA, et al. Impact of body mass index on outcome in patients after coronary artery bypass grafting with and without valve surgery. Eur Heart J 2003;24: 1933-41.
27. Uva MS, Rodrigues V, Monteiro N, Manuel Pedro A, Caria R, Mesquita A, et al. Cardiac surgery and morbid obesity. Rev Port Cardiol 2002;21:255-64.
28. Rockx MA, Fox SA, Stitt LW, Lehnhardt KR, McKenzie FN, Quantz MA, et al. Is obesity a predictor of mortality, morbidity and readmission after cardiac surgery? Can J Surg 2004;47:34-8.
29. Birkmeyer NJ, Charlesworth DC, Hernandez F, Leavitt BJ, Marrin CA, Morton JR, 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.
30. Kuduvalli M, Grayson AD, Oo AY, Fabri BM, Rashid A. Risk of morbidity and in-hospital mortality in obese patients undergoing coronary artery bypass surgery. Eur J Cardiothorac Surg 2002;22:787-93.
31. Ranucci M, Cazzaniga A, Soro G, Morricone L, Enrini R, Caviezel F. Obesity and coronary artery surgery. J Cardiothorac Vasc Anesth 1999; 13:280-4.
32. Fasol R, Schindler M, Schumacher B, Schlaudraff K, Hannes W, Seitelberger R, Schlosser V. The influence of obesity on perioperative morbidity: retrospective study of 502 aortocoronary bypass operations. Thorac Cardiovasc Surg 1992;40:126-9.
33. Moulton MJ, Creswell LL, Mackey ME, Cox JL, Rosenbloom M. Obesity is not a risk factor for significant adverse outcomes after cardiac surgery. Circulation 1996;94(Suppl):II87-92.
34. Kim J, Hammar N, Jakobsson K, Luepker RV, McGovern PG, Ivert T. Obesity and the risk of early and late mortality after coronary artery bypass graft surgery. Am Heart J 2003;146:555-60.
35. Brandt M, Harder K, Walluscheck KP, Schöttler J, Rahimi A, Möller F, Cremer J. Severe obesity does not adversely affect perioperative mortality and morbidity in coronary artery bypass surgery. Eur J Cardiothorac Surg 2001;19:662-6.
36. Jin R, Grunkemeier GL, Furnary AP, Handy JR, Jr. Is obesity a risk factor for mortality in coronary artery bypass surgery? Circulation 2005;111:3359-65.
37. Romero-Corral A, Montori VM, Somers VK, Korinek J, Thomas RJ, Allison TG, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 2006;368:666-78.
38. Odrowaz-Sypniewska G. Markers of pro-inflammatory and prothrombotic state in the diagnosis of metabolic syndrome. Adv Med Sci 2007;52:246-50.
39. Hopkins TA, Ouchi N, Shiata R, Walsh K. Adiponectin actions in the cardiovascular system. Cardiovasc Res 2007;74:11-8.
40. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. Nature 2001;409: 307-12.
41. Steppan CM, Lazar MA. The current biology of resistin. J Intern Med 2004;255:439-47.
42. Mu H, Ohashi R, Yan S, Chai H, Yang H, Lin P, et al. Adipokine resistin promotes in vitro angiogenesis of human endothelial cells. Cardiovasc Res 2006;70:146-57.
43. Kougias P, Chai H, Lin PH, Lumsden AB, Yao Q, Chen C. Adipocyte-derived cytokine resistin causes endothelial dysfunction of porcine coronary arteries. J Vasc Surg 2005;41:691-8.

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DISCUSSION

Dr Angeliki Vouyouka (*New York, NY*): The paper was very interesting, but I have a few questions.

From the data that you show us here, the obese class I and the overweight patients compared to the normal and the underweight, they appeared to be healthier. They were more likely to be diabetic and hypertensive; however, they were less likely to be smokers, they have better ASA risk class, and they were less likely to have COPD. So do you think that part of your observation reflects some selection bias among the surgeons, since they were all elective cases, and therefore when they had to operate on obese patients they chose the ones that they were in best health as compared to the rest of them?

Secondly, you have insinuated the answer of this question, but for better clarification, what percentage of the obese patients had endovascular procedures, as compared to normal weight and underweight?

And thirdly, again, in the same spirit with the first question, in this data the obese patients, obese class I, and the overweight, they did have higher albumin levels, a fact that again perhaps reflects some selection bias. Do we know patients with low preoperative serum albumin, obese or overweight, how they did compare to the ones with high levels of serum albumin?

I want again to thank the committee for the privilege to discuss this very interesting paper.

Dr Eleftherios Xenos: To answer the second question, we don't have a breakdown between endovascular versus open repair of aneurysms. There is a procedure category that was labeled other and comprised approximately 30% of the patients. It included the peripheral balloon angioplasties and stenting procedures, but I don't have an exact number of how many people had an endovascular versus open general vascular procedure.

And I agree with the observation that there might very well be a selection bias where relatively healthy obese subjects were offered an operation and very sick morbidly obese patients were denied an operation and that might be partially responsible for what we see.

Dr Martin Veller (*Johannesburg, South Africa*): Many of the individuals we treat with a low BMI have such a low BMI as a result of an underlying chronic disease. Were you in any way able to look at this in your study? For example, were the serum albumin levels helpful in differentiating those individuals with a low BMI as a result of a chronic disease from those with a low BMI without a chronic disease?

Dr Xenos: Yes, indeed, it does seem that if somebody is underweight, he's underweight for a reason. Many of our risk factors were highest in underweight patients including disseminated cancer and recent weight loss. There was also a higher incidence of patients with COPD. There was, however, no single etiology for being underweight and having chronic disease.

Dr Starros Kakkos (*Detroit, MI*): Do you think that slightly overweight people are naturally selected to be more resistant to trauma or similar conditions, like surgery?

Dr Xenos: I think it is hard to tell. In our study population, moderate overweight and obese I type patients had the least amount of risk factors.

Dr Kakkos: Probably because the definition and grades of obesity are based on survival statistics.

Dr Xenos: Yes, that is true, the patients were stratified according to their BMI, not survival statistics.

Appendix, online only. Procedure grouping by primary CPT code

Procedure group	*Primary procedure CPT codes included*
Amputation	27290, 27295, 27590, 27591, 27592, 27594, 27598, 27880, 27881, 27882, 27884, 27886, 27888, 27889, 28880, 28805, 28810, 28820, 28825
Abdominal aortic/iliac aneurysm	34800, 34802, 34803, 34804, 34805, 34808, 34825, 34900, 34808, 34812, 34813, 34820, 34826, 34833, 34834, 34830, 34831, 34832, 35081, 35082, 35091, 35092, 35102, 35103, 35131, 35132
Lower extremity revascularization	35556, 35566, 35571, 35583, 35585, 35587, 35656, 35666, 35671, 35331, 35351, 35355, 35361, 35363, 35521, 35533, 35537, 35538, 35539, 35540, 35548, 35549, 35551, 35558, 35565, 35621, 35623, 35646, 35647, 35651, 35654, 35661, 35663, 35665, 34201, 34203, 35302, 35303, 35304, 35305, 35306, 35371, 35372, 35875, 35876, 35452, 35454, 35456, 35459, 35470, 35472, 35473, 35474, 35481, 35482, 35483, 35485, 35491, 35492, 35493, 35495
Mesenteric-renal revascularization	35341, 35531, 35536, 35560, 35631, 35636, 35697, 35111, 35112, 35121, 35122, 35450, 35471, 35480, 35490
Cerebrovascular	35301, 35390, 35501, 35601, 35001, 35002, 35005, 35201, 35231, 35261, 35691, 35693, 35694, 35695
Vascular access	36825, 36830, 36818, 36819, 36820, 36821
Other	All other primary CPT codes from procedures performed on the vascular surgery service at 14 academic medical centers (197 CPT Codes).

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