Safety of Hepatic Resections in Obese Veterans

John K. Saunders, MD; Alan S. Rosman, MD; Dena Neihaus, RN, MPA; Thomas H. Gouge, MD; Marcovalerio Melis, MD

Objective: To determine the effects of body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) on outcomes after liver resection performed at Veterans Affairs medical centers.

Design, Setting, and Patients: We queried the Veterans Affairs Surgical Quality Improvement Program database for liver resections (2005-2008) and grouped the patients into 5 BMI categories: normal weight (BMI 18.5-24.9), overweight (BMI 25.0-29.9), obese class 1 (BMI 30.0-34.9), obese class 2 (BMI 35.0-39.9), and obese class 3 (BMI ≥40.0). Differences in risk factors and perioperative complications across groups were analyzed in univariate and multivariate analyses.

Results: Of 403 patients who underwent hepatectomy, 106 (26%) were normal weight, 161 (40%) were overweight, 94 (23%) were obese class 1, 31 (8%) were obese class 2, and 11 (3%) were obese class 3. Among these groups, higher BMI was associated with increased rates of hypertension (52%, 61%, 77%, 77%, and 73%, respectively; \( P = .002 \)) and diabetes (18%, 27%, 36%, 39%, and 45%, respectively; \( P = .04 \)) and lower incidence of smokers (33%, 35%, 30%, 16%, and 9%, respectively; \( P < .001 \)). The BMI groups were similar in demographic characteristics and metrics correlating with preexisting liver disease. There were no differences across BMI groups in overall and specific morbidity or in length of stay. Compared with the other groups, obese class 3 patients received more blood transfusions (mean [SD], 4.3 [2.7] in obese class 3 patients vs 1.1 [0.2] in normal-weight patients; \( P = .02 \)) and had a higher 30-day mortality (27% in obese class 3 patients vs 6% in normal-weight patients; \( P = .05 \)). Multivariate analyses confirmed obese class 3 as an independent predictor of postoperative mortality.

Conclusions: Obesity did not increase postoperative complications after liver resection in veterans. After adjusting for other clinical factors, extreme obesity (BMI ≥40.0) was an independent risk factor for increased mortality.


See Invited Critique at end of article

The strong association of obesity with cardiovascular disease, dyslipidemia, diabetes mellitus, and other comorbidities has led many surgeons to investigate the influence of an elevated BMI on postoperative morbidity and mortality following major surgery. Those studies have generated contradicting results, and currently the impact of obesity on perioperative outcomes remains poorly defined in the surgical literature. One of the reasons for those apparently conflicting results is that most studies have compared outcomes of obese patients as a whole with outcomes of overweight and normal-weight patients. This approach does not consider that different degrees of obesity might be associated with different outcomes. Some studies in fact have suggested that while mild obesity may not significantly impair surgical outcomes, extreme obesity (BMI ≥40.0) might increase risks of complications.

For a number of reasons, surgeons will increasingly be performing hepatic surgery for obese patients. Indications for liver resection are expanding, the prevalence of obesity is on the rise, and patients with a high BMI are at increased risk for developing hepatocellular carcinoma and colorectal liver metastases.
ing use of hepatobiliary surgical procedures in a more obese patient population demands that surgeons recognize the complex relationship between obesity and surgical outcomes.18-21

The VA Surgical Quality Improvement Program (VASQIP) offers a unique opportunity to study the relationship between obesity and surgical outcomes following hepatic surgery. Each year, the VASQIP prospectively collects detailed data regarding perioperative risk and outcomes for more than 127,000 surgical procedures performed across 124 VA medical centers.

Since its inception in 1994, the VASQIP has been the gold standard for analysis of surgery outcomes. Initially started as a tool to monitor quality within the many VA medical centers throughout the nation, it has since been implemented in many sectors as a tool to improve the quality of the surgical care delivered.22 The VASQIP has been repeatedly validated. It compares favorably to administrative data for predicting adverse outcomes based on preoperative factors.23 It has also bested other administrative data collections in predicting mortality based on risk assessment.24

In this study, we used the VASQIP database specifically to examine whether different degrees of obesity are associated with increased complication rates after liver resection in a population of veterans.

METHODS

Data are prospectively collected in the VASQIP from several VA medical centers by trained surgical clinical reviewers at each site and are submitted to the central registry. Data collection includes 13 demographic variables, 28 clinical variables, 13 intraoperative variables, and information on postoperative morbidity and mortality. The BMI was recorded in the VASQIP database for those patients undergoing surgery after 2004. The VA National Surgical Quality Improvement Program database was queried for patients undergoing elective hepatic resection (Current Procedural Terminology Fourth Edition codes 47120, 47122, 47125, 47130) between January 1, 2005, and December 31, 2008. Patients with the primary procedure listed as liver biopsy or wedge biopsy of the liver (Current Procedural Terminology codes 47000, 47001, 47100) were excluded. We grouped patients into 5 BMI groups according to the World Health Organization’s BMI categories25: normal weight was defined as a BMI of 18.5 to 24.9; overweight, a BMI of 25.0 to 29.9; obese class 1, a BMI of 30.0 to 34.9; obese class 2, a BMI of 35.0 to 39.9; and obese class 3, a BMI of 40.0 or greater. Underweight (BMI 16.0-18.4) and severely underweight (BMI <16.0) were excluded from the current analysis. The BMI groups were otherwise similar in terms of age, race, sex, underlying pathology, underlying comorbidities, and institution where the procedure was performed. Notably, there were no significant differences across groups with regard to the various metrics that could be attributed to preexisting liver disease, such as rates of alcohol abuse, ascites, or esophageal varices. Liver resection was performed for liver malignant neoplasms in 90% of patients, and rates of preoperative administration of chemotherapy and radiation therapy were similar across groups.

The only significant difference in preoperative laboratory analysis was that the obese class 3 group had a significantly higher level of alkaline phosphatase (Table 2).

There were no differences in type of resection performed (segmentectomy vs lobectomy vs trisegmentectomy), number of blood units transfused intraoperatively, operative time, and work relative value units (Table 3).

Postoperatively, there were no significant differences in overall and specific morbidity across BMI groups (Table 4). Postoperative cardiac arrest and mortality were higher in obese class 3 patients. When controlling for obesity category, age, sex, functional status, smoking history, underlying diabetes and hypertension, prior percutaneous coronary interventions, and preoperative levels of alkaline phosphatase, a BMI of 40.0 or greater remained a significant predictor of postoperative mortality.

RESULTS

The VASQIP query yielded 386 men and 17 women who fit inclusion criteria. The BMI breakdown was as follows: 106 patients (26%) were normal weight, 161 (40%) were overweight, 94 (23%) were obese class 1, 31 (8%) were obese class 2, and 11 (3%) were obese class 3. Eight underweight patients (BMI <18.4) were excluded from the current analysis. Table 1 shows baseline characteristics of patients in the 5 BMI groups. There was a higher incidence of smokers in normal-weight patients. There were significantly higher rates of hypertension in the obese class 1 and obese class 2 groups and significantly higher rates of diabetes among the obese class 2 and obese class 3 groups. Patients in the extreme obesity group (obese class 3) had undergone more percutaneous coronary interventions. Obese class 3 patients also had worse functional status compared with the normal-weight group (independent functional status, 91% vs 98%, respectively; P < .01). The BMI groups were otherwise similar in terms of age, race, sex, underlying pathology, underlying comorbidities, and institution where the procedure was performed. Notably, there were no significant differences across groups with regard to the various metrics that could be attributed to preexisting liver disease, such as rates of alcohol abuse, ascites, or esophageal varices. Liver resection was performed for liver malignant neoplasms in 90% of patients, and rates of preoperative administration of chemotherapy and radiation therapy were similar across groups.

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In the United States, approximately two-thirds of all adults are overweight or obese, and nearly half of the US population (45%) is expected to be obese by 2020.26,27 In line with recent epidemiologic data, most patients in our study were overweight or obese (40% and 34%, respectively).

Despite current obesity trends, the surgical community has only recently started investigating effects of high BMI on outcomes after various surgical procedures. However, data have so far provided inconsistent results. Some investigators have found that an elevated BMI is an independent predictor of morbidity, whereas others have argued that rates of complications in obese patients are directly attributable to clustered risk factors such as smoking.
or diabetes and that high BMI is not a risk factor for major postoperative complications (perhaps aside from an increased incidence of minor wound complications) or death.\(^3\)\(^-\)\(^12\)\(^-\)\(^28\)\(^-\)\(^31\) Interestingly, some researchers claim an advantage in postoperative survival for moderately obese patients (the “obesity paradox”). For instance, in a National Surgical Quality Improvement Program–based report of 118,707 patients undergoing nonbariatric general surgery, Mullen et al\(^32\) found that overweight, obese class 1, obese class 2, and obese class 3 patients had lower 30-day mortality than their underweight and normal-weight counterparts.

Some of these discrepancies across studies could be explained by the use of different definitions of perioperative complications and obesity (especially in reports from eastern Asia), inclusion of heterogeneous surgical procedures, and lack of statistical power (especially for groups in the highest BMI categories).

Few studies have specifically looked at the influence of BMI on outcomes after liver resection.\(^33\)\(^-\)\(^36\) Unfortunately, these have also generated heterogeneous results.

In 2008, Utsunomiya et al\(^33\) found that obesity did not affect outcomes in 388 patients undergoing liver resection for hepatocellular carcinoma. However, because of lower prevalence of obesity in Japan, patients in this single-institution retrospective review were categorized as obese if their BMI was greater than 25.

In 2010, Balzan et al\(^34\) evaluated postoperative outcomes in 684 patients undergoing liver resection at a single institution. They also found that being overweight (n=228 [34%]) or obese (n=87 [14%]) did not affect overall morbidity and mortality. However, both being overweight and being obese were associated with increased risk of major complications (odds ratio=1.9 [95% CI, 1.2-3.2] and odds ratio=2.6 [95% CI, 1.2-5.8], respectively). Obese patients were also at higher risk for blood transfusions (odds ratio=3.3 [95% CI, 1.4-7.9]) and had longer intensive care unit and hospital stays.\(^34\)

In 2010, Mathur et al\(^35\) described 279 patients undergoing liver resection for malignant neoplasms. Outcomes of obese patients (BMI >30) were compared with those of nonobese patients (ie, normal-weight and over-

### Table 2. Baseline Laboratory Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal Weight (n = 106)</th>
<th>Overweight (n = 161)</th>
<th>Obese Class 1 (n = 94)</th>
<th>Obese Class 2 (n = 31)</th>
<th>Obese Class 3 (n = 11)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit, %</td>
<td>39.6 (0.5)</td>
<td>39.9 (0.4)</td>
<td>40.5 (0.5)</td>
<td>39.8 (1.0)</td>
<td>39.2 (2.0)</td>
<td>.87</td>
</tr>
<tr>
<td>Platelet count, x10^9/μL</td>
<td>244.9 (10.3)</td>
<td>211.4 (7.1)</td>
<td>203.5 (8.8)</td>
<td>223.7 (15.2)</td>
<td>261.4 (29.1)</td>
<td>.15</td>
</tr>
<tr>
<td>INR</td>
<td>1.08 (0.02)</td>
<td>1.08 (0.01)</td>
<td>1.06 (0.01)</td>
<td>1.06 (0.02)</td>
<td>1.08 (0.06)</td>
<td>.80</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.75 (0.05)</td>
<td>3.80 (0.05)</td>
<td>3.82 (0.06)</td>
<td>3.84 (0.11)</td>
<td>3.90 (0.09)</td>
<td>.89</td>
</tr>
<tr>
<td>Alkaline phosphatase, U/L</td>
<td>111.5 (7.6)</td>
<td>111.4 (5.4)</td>
<td>102.3 (5.4)</td>
<td>79.4 (4.8)</td>
<td>192.9 (73.0)</td>
<td>.002</td>
</tr>
<tr>
<td>Bilirubin, mg/dL</td>
<td>0.8 (0.05)</td>
<td>0.8 (0.06)</td>
<td>0.8 (0.04)</td>
<td>0.7 (0.08)</td>
<td>0.7 (0.08)</td>
<td>.37</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>14.9 (0.7)</td>
<td>15.4 (0.5)</td>
<td>15.1 (0.6)</td>
<td>15.4 (1.1)</td>
<td>14.7 (1.7)</td>
<td>.95</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.0 (0.06)</td>
<td>1.0 (0.03)</td>
<td>1.0 (0.02)</td>
<td>1.1 (0.05)</td>
<td>1.1 (0.09)</td>
<td>.94</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BUN, blood urea nitrogen; INR, international normalized ratio.

SI conversion factors: To convert hematocrit to proportion of 1.0, multiply by 0.01; to convert platelet count to x10^9 per liter, multiply by 1.0; to convert albumin to grams per liter, multiply by 10; to convert alkaline phosphatase to microkatal per liter, multiply by 0.0167; to convert bilirubin to micromoles per liter, multiply by 17.104; to convert BUN to millimoles per liter, multiply by 0.357; and to convert creatinine to micromoles per liter, multiply by 88.4.

\(^a\) The BMIs for each group are as follows: normal weight, 18.5 to 24.9; overweight, 25.0 to 29.9; obese class 1, 30.0 to 34.9; obese class 2, 35.0 to 39.9; and obese class 3, 40.0 or greater.

### Table 3. Operative Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal Weight (n = 106)</th>
<th>Overweight (n = 161)</th>
<th>Obese Class 1 (n = 94)</th>
<th>Obese Class 2 (n = 31)</th>
<th>Obese Class 3 (n = 11)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of resection, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.20</td>
</tr>
<tr>
<td>Partial lobectomy</td>
<td>62</td>
<td>60</td>
<td>70</td>
<td>81</td>
<td>55</td>
<td>.55</td>
</tr>
<tr>
<td>Right lobectomy</td>
<td>18</td>
<td>24</td>
<td>18</td>
<td>16</td>
<td>27</td>
<td>.27</td>
</tr>
<tr>
<td>Left lobectomy</td>
<td>14</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>9</td>
<td>.9</td>
</tr>
<tr>
<td>Trisegmentectomy</td>
<td>6</td>
<td>7</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>.9</td>
</tr>
<tr>
<td>Units of blood transfused, mean (SEM), No.</td>
<td>1.1 (0.2)</td>
<td>1.7 (0.3)</td>
<td>2.5 (0.5)</td>
<td>0.9 (0.3)</td>
<td>4.3 (2.7)</td>
<td>.02</td>
</tr>
<tr>
<td>Operative time, mean (SEM), h</td>
<td>5.1 (0.2)</td>
<td>5.1 (0.2)</td>
<td>5.4 (0.3)</td>
<td>4.5 (0.4)</td>
<td>6.7 (0.8)</td>
<td>.28</td>
</tr>
<tr>
<td>Work RVUs, mean (SEM)</td>
<td>43.7 (0.8)</td>
<td>44.4 (0.7)</td>
<td>42.6 (0.8)</td>
<td>40.8 (1.3)</td>
<td>44.3 (2.8)</td>
<td>.25</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); RVUs, relative value units.

\(^a\) The BMIs for each group are as follows: normal weight, 18.5 to 24.9; overweight, 25.0 to 29.9; obese class 1, 30.0 to 34.9; obese class 2, 35.0 to 39.9; and obese class 3, 40.0 or greater.
Compared with nonobese patients, the obese patients (n = 97 [35%]) had similar perioperative mortality but increased perioperative morbidity, which included higher rates of bile leak (9.9% vs 18.6%, respectively), urosepsis (7.7% vs 16.5%, respectively), pneumonia (2.2% vs 9.3%, respectively), acute renal failure (1.7% vs 7.2%, respectively), and deep surgical site infections (1.7% vs 7.2%, respectively).35 Mathur et al36 also published in 2010 a retrospective analysis of American College of Surgeons National Surgical Quality Improvement Program data. There were 3960 patients undergoing liver resection, of whom 33.4% were overweight and 31.7% were obese. The mortality rate was 2.5% and the complication rate was 23.3%. After adjusting for underlying conditions and other clinical factors, degree of obesity was independently associated with a slightly increased complication rate (odds ratio = 1.24 [95% CI, 1.01-1.55]) but not increased mortality.

None of those studies analyzed the effect of different degrees of obesity on complications. Furthermore, to our knowledge, no investigators have looked at the influence of BMI specifically in a population of veterans undergoing liver resection.

In our study, we found that despite a morbidity rate similar to that of the other BMI groups, extreme obesity (BMI $\geq$40.0) was independently associated with increased mortality after liver resection. Taken together, our results suggest that when complications do develop in extremely obese patients, they are likely to be severe and potentially life threatening. Patients with BMI of 40.0 or greater probably have limited functional reserve as a result of underlying obesity-associated conditions. Diabetes was more common among patients with higher BMI but was not a significant independent risk factor for postoperative mortality in our multivariate analysis. Available literature is actually conflicting on the role of diabetes in immediate outcomes after liver resection.37-39 Nevertheless, diabetes is usually associated with a significant increase in postoperative morbidity after a major surgical procedure.34,38

Levels of alkaline phosphatase were significantly higher in obese class 3 patients. However, these were not associated with increased mortality in logistic regression.

We also found that amounts of blood transfusions were higher in obese patients. The reasons for bleeding in obese patients are not clear; however, others have reported the same observation.34 It is a common experience that patients with increased BMI require higher intraoperative ventilation pressure.34 This could impair hepatic venous outflow and increase the pressure in the hepatic veins, causing troublesome bleeding not stopped by partial triad clamping.34,40,41

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Our study has few limitations, which should be acknowledged.

The group of patients with BMI of 40.0 or greater represented a small percentage of our study population.
the low prevalence of specific morbidities, our study was likely underpowered to detect differences between the obese class 3 group and other groups. Increased morbidity in patients with BMI of 40.0 or greater might become apparent in larger-scale studies.

With a sufficient number of extremely obese subjects, a propensity score–matching method could be performed to match obese and control subjects for other variables. A comparison of matched subjects would better estimate the effect of obesity on mortality.

The VASQIP database lacks data on procedure-specific complications, including liver failure and encephalopathy. This greatly limited our ability to determine the impact of obesity on liver-specific complications. Further, the VASQIP does not record preoperative conditions such as previous ablation treatment, cancer stage, and histological findings, which may potentially affect outcomes. Other limitations common to VASQIP- and American College of Surgeons National Surgical Quality Improvement Program–based studies are the lacking data on patient selection, preoperative management, and surgical volume, which may also affect variations in postoperative outcomes.

One of the many factors that are currently not captured by surgical quality improvement databases but could affect outcomes of liver resection is the presence of liver steatosis. Steatosis is not always quantifiable preoperatively unless a liver parenchyma biopsy is performed. Although its incidence is higher in obese patients (25%), steatosis does not universally occur in patients with a high BMI.35,43,44

Kooby et al44 have demonstrated that steatosis is associated with greater perioperative complications after liver resection. Of note, in the same study, no correlation could be demonstrated between BMI itself and complication rate.

CONCLUSIONS

Our study examined the influence of various degrees of obesity on short-term outcomes following liver resection in a population of veterans. Our analysis shows that a high degree of obesity (BMI ≥ 40.0) is an independent risk factor for higher transfusion rates and increased mortality. This information should be taken into consideration when discussing therapeutic alternatives (eg, ablative procedures) in patients with extreme obesity and liver malignant neoplasms.

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Additional Contributions: The VA Surgical Quality Data Use Group acted as scientific advisors and provided critical review of the data use and analysis presented in this article.

REFERENCES


INVITED CRITIQUE

Are Surgeons Rising to the Challenge of Managing Morbidly Obese Patients Undergoing Hepatic Resection?

The article by Saunders et al1 attempts to address an issue that is frequently confronted in all areas of surgery: what role, if any, does obesity play in surgical outcomes? As surgeons, we know that operations are more challenging, complications more frequent, and diagnosis of postoperative complications more difficult in obese patients and especially in morbidly obese patients. Does obesity make the job of the surgeon more difficult, or does it really impact outcomes? Saunders and colleagues attempt to answer the question for hepatic resections. In their review of 403 liver resections in the VASQIP, 297 patients were overweight or obese (BMI ≥25.0). The only decrement in survival identified was in the extremely obese group (BMI ≥40.0; n=11), and the reason for a decrease in survival was from postoperative cardiac arrest. I would categorize this article as a further analysis of the question rather than an answer. It should be noted that the database used is not designed to specifically address hepatic surgery; therefore, no information is available in the database regarding the underlying hepatic disease or quality of the remnant hepatic lobe or segment, and the ability to obtain details on a set of patients is limited. The major conclusion by Saunders and colleagues that extreme obesity is an independent risk factor for mortality secondary to cardiac arrest is countered by the fact that there were no myocardial infarctions in this group of 11 patients. Can we conclude that the cardiac arrests were a result of noncardiac events such as multiple organ failure from postoperative complications, hemorrhage, and other factors routinely thought of as surgical in nature? The question surgeons really want answered is, how can we optimally manage obese patients with surgical problems of the liver? That question is left open for future studies.

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