Comparison of Short-term Outcomes in Laparoscopic vs Open Hepatectomy

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**IMPORTANCE** Despite the increasing role of laparoscopy in partial hepatic resection, its short-term benefit compared with traditional open surgery remains unclear.

**OBJECTIVE** To compare short-term (30-day) outcomes between laparoscopic (LH) and open (OH) partial hepatectomies.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective matched case-control study from April 1, 2004, to March 31, 2013, in a tertiary hepatobiliary referral center. Patients who underwent partial hepatic resection (OH or LH) for benign or malignant disease were matched first by extent of resection, then by pathological diagnosis, and finally by age and sex to the extent possible.

**EXPOSURE** Partial hepatectomy for liver disease.

**MAIN OUTCOMES AND MEASURES** Thirty-day morbidity and mortality rates.

**RESULTS** After the matching process, we included 104 patients (52 undergoing LH and 52 undergoing OH) in the study. Patients were evenly matched with respect to age, sex, extent of resection, and diagnosis. Cirrhosis was present in 17 patients (33%) in each group. We found no difference in positive margin status (1 patient [2%] for LH vs 2 patients [4%] for OH; \(P > .99\)). Although the estimated blood loss differed significantly between groups (237 mL for LH vs 387 mL for OH; \(P = .049\)), we found no difference in the rate of perioperative blood transfusion (1 patient [2%] for LH vs 5 [10%] for OH; \(P = .20\)). Operative time (219 minutes for LH vs 198 minutes for OH; \(P = .16\)), hospital length of stay (5 days for LH vs 6 days for OH; \(P = .13\)), and readmission rate (4 patients [8%] for LH vs 5 [10%] for OH; \(P = .70\)) were similar in both groups. The rates of major complications (4 patients [8%] for LH vs 4 patients [8%] for OH; \(P = 1.0\)), overall 30-day morbidity (22 patients [42%] for LH vs 19 [37%] for OH; \(P = .70\)), and 30-day mortality (1 patient [2%] for LH vs 2 [4%] for OH; \(P > .99\)) were not significantly different.

**CONCLUSIONS AND RELEVANCE** Patients who undergo LH have similar short-term outcomes when compared with those who undergo OH. Laparoscopic hepatectomy was associated with lower intraoperative blood loss, although the clinical significance of this finding is uncertain given the lack of difference in perioperative transfusion or morbidity rates. In addition, we found no difference in margin status between the 2 groups. Future studies are needed to define which patients derive benefit from LH and to determine oncologic equivalence to OH.
Laparoscopic liver resection was first performed in the 1990s, with the first nonanatomical hepatectomy performed in 1992 and the first formal anatomical resection in 1996. Improvements in technology and surgeon skill with laparoscopy have led to its increased use for the treatment of benign and malignant liver masses, primarily at specialized centers. Although the use of laparoscopy has gradually gained favor, whether the short-term benefits generally observed with laparoscopy apply to patients undergoing partial hepatic resection remains unclear. Selection bias related to patient and pathological factors has made it difficult to conduct a randomized study comparing laparoscopic hepatectomy (LH) and open hepatectomy (OH). Prior retrospective studies have used the case-match approach to help reduce bias; however, the specific criteria used for matching may or may not reduce the effect of selection bias, depending on which criteria are used. One major criticism of prior retrospective studies is that they have not adequately addressed the effect of tumor size, location, and severity of cirrhosis on the observed outcome. By matching based on the extent/location of hepatectomy and pathological diagnosis, this study attempts to address these concerns and better delineate the true difference in short-term outcome between laparoscopic and open partial hepatectomy.

Methods

This study was approved by the institutional review board of Kaiser Permanente. We performed a retrospective review of all patients undergoing partial hepatic resection by a single surgeon (L.A.D.) at a single institution from April 1, 2004, to March 31, 2013. Laparoscopic hepatectomy was based on intention to treat. Patients were matched from a group of 436 undergoing OH and 79 undergoing LH. Patients younger than 18 years were excluded. In addition, patients undergoing reoperation, cyst fenestration, or simultaneous extrahepatic resection were excluded from the study. Finally, patients with incomplete medical records with regard to the matching criteria were excluded from the study. After these exclusions, 231 patients in the OH group and 64 in the LH group remained. We used an intention-to-treat analysis and included LH cases converted to OH within the LH group. Generally speaking, LH was offered selectively to those patients with 1 or 2 masses, masses away from major vessels/portal structures, and masses located mostly in segments 2 to 3, 4b, 5, or 6. Size and central location were not necessarily contraindications to LH. These selection criteria did not change during the study period.

An investigator who was blinded to the outcome of each case (B.L.) performed the case matching. Patients were matched first based on extent of hepatectomy (subsegmental wedge resection, single anatomical segment, 2 anatomical segments, or major hepatectomy) and location based on Couinaud segments. A major hepatectomy was defined as 3 or more Couinaud liver segments. If patients with resections of the same segments could not be identified, patients were matched to those who had resections of neighboring segments. Patients were then matched based on preoperative diagnosis, including hepatocellular carcinoma, metastatic colorectal cancer, or other. Finally, to the extent possible, patients were matched based on sex and age.

The primary outcomes were 30-day morbidity and mortality. Morbidities were graded in severity from I to IV according to the Clavien-Dindo classification. Grade I complications included any deviation from the normal postoperative course. Grade II complications required pharmacological treatment, including total parenteral nutrition and blood transfusions. Grade III complications required surgical, endoscopic, or radiological intervention. Grade IV complications were life threatening and required intensive care unit monitoring. A minor complication was defined as Clavien-Dindo grade I or II, whereas a major complication was defined as Clavien-Dindo grade III or IV. A pulmonary complication was defined as pleural effusion, pulmonary edema, pneumonia, reintubation, or acute respiratory distress syndrome. A cardiac complication was defined as arrhythmia, decompensated congestive heart failure, or myocardial infarction. Perioperative transfusion was defined as any transfusion within 30 days of surgery.

Operative Procedure

All operations were performed under general anesthesia in the supine position. A central catheter was placed for intraoperative central venous pressure monitoring. Goal central venous pressure was maintained at less than 5 cm of water during hepatic parenchymal transection.

Open hepatic resections were performed through standard incisions. The hepatic pedicle was isolated and hepatic vascular inflow occlusion was used as needed. Intraoperative ultrasonography was used for surgical planning. Formal anatomical hepatectomy was usually performed using an intrahepatic glissonian technique. Dissection of liver parenchyma was performed with an ultrasonic dissector (Cavitron Ultrasonic Surgical Aspirator; Valleylab) or a laparoscopic vessel sealer and divider (LigaSure; Covidien PLC). Vessels were ligated and divided with electrocautery, clips, or a linear stapling device. Hemostasis was obtained with use of electrocautery, coagulation (Argon Beam Coagulator; ConMed Corporation), and tamponade (thrombin-soaked Gelfoam; Pfizer).

Laparoscopic liver resections were performed with an insufflation pressure of 12 to 15 mm Hg using a combination of four or five 5- and 12-mm ports. Otherwise we found no difference in intraoperative surgical planning, surgical technique, vessel management, or hemostatic control. The hepatic pedicle was rarely encircled for vascular inflow occlusion, however. Formal major hepatectomies were similarly performed using the intrahepatic glissonian approach. One of the port site incisions was extended at the conclusion of the case to function as an extraction site. The incision was generally no larger than the size of the tumor itself (usually 5-8 cm). Hand ports were infrequently used.

Statistical Analysis

Continuous variables were compared using a 2-tailed, unpaired, 2-sample equal variance (homoscedastic) t test. Categorical variables were compared using either the $\chi^2$ test or the...
Fisher exact test (Excel, GraphPad software; Microsoft Corporation). Statistical significance was defined as $P < .05$.

Results

After the matching process, 104 patients (52 in the LH group and 52 in the OH group) were included. Twelve patients in the LH group did not have suitable OH matches, 10 owing to the extent of resection and/or tumor location and 2 owing to the pathological diagnosis. Table 1 summarizes patient demographics and tumor and operative variables. The patients were well matched for age, sex, presence of cirrhosis, preoperative Model for End-Stage Liver Disease score, and location of resection. However, we found a statistically significant difference in mean body mass index (calculated as weight in kilograms divided by height in meters squared) between the 2 groups (29.5 [range, 17.2-58.7] for LH vs 26.3 [range, 18.8-38.3] for OH; $P = .01$).

With respect to extent of the resection, similar numbers of patients had subsegmental (50% for LH vs 31% for OH; $P = .32$), segmental (21% for LH vs 29% for OH; $P = .49$), bisegmental (15% for LH vs 27% for OH; $P = .20$), and major hepatic (13% for LH vs 13% for OH; $P > .99$) resections. The most common indication for resection was hepatocellular carcinoma, accounting for 54% of each group. Colorectal metastasis represented 10% of the LH group and 23% of the OH group ($P = .10$). All other benign indications (hepatolithiasis, hepatic adenoma, biliary cystadenoma, cyst, focal nodular hyperplasia, and hemangioma) represented 25% of the LH group and 15% of the OH group ($P = .30$). All other resections for malignant disease (including metastatic adenocarcinoma, gallbladder adenocarcinoma, and cholangiocarcinoma) represented 12% of the LH group and 8% of the OH group ($P = .74$). The mean largest dimension of the resected segment was similar in both groups (10.6 [range, 3.8-21.2] cm in the LH group vs 11.0 [range, 2.8-20.8] cm in the OH group). The mean largest dimension of

<table>
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<th>Characteristic</th>
<th>Patient Group*</th>
<th>$P$ Value</th>
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<tr>
<td><strong>Age, mean (range), y</strong></td>
<td>LH 60.0 (24-82)</td>
<td>OH 57.5 (24-80)</td>
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<td><strong>Sex, No. male/female</strong></td>
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<td>31/21</td>
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<tr>
<td><strong>BMI, mean (range)</strong></td>
<td>29.5 (17.2-58.7)</td>
<td>26.3 (18.8-38.3)</td>
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<tr>
<td>Median preoperative MELD score</td>
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**Indications for resection**

- Hepatocellular carcinoma: 28 (54) LH vs 28 (54) OH, >.99
- Colorectal metastasis: 5 (10) LH vs 12 (23) OH, .10
- Other malignant disease: 6 (12) LH vs 4 (8) OH, .74
- Other benign disease: 13 (25) LH vs 8 (15) OH, .30

**Extent and location of resection**

- Subsegmental wedge: 26 (50) LH vs 16 (31) OH, .32
- Location: Segment 1 0 1 (2), >.99
- Left lateral, segment 2 or 3: 6 (12) LH vs 3 (6), .50
- Left medial, segment 4: 3 (6) LH vs 1 (2), .60
- Right posterior, segment 6 or 7: 6 (12) LH vs 5 (10), >.99
- Right anterior, segment 5 or 8: 11 (21) LH vs 6 (12), .30
- Segmental: 11 (21) LH vs 15 (29), .49
- Location: Left lateral, segment 2 or 3: 2 (4) LH vs 1 (2), >.99
- Left medial, segment 4: 4 (8) LH vs 8 (15), .40
- Right posterior, segment 6 or 7: 2 (4) LH vs 1 (2), >.99
- Right anterior, segment 5 or 8: 3 (6) LH vs 5 (10), .70
- Bisegmental: 8 (15) LH vs 14 (27), .20
- Segments 2 to 3: 7 (13) LH vs 4 (8), .50
- Segments 4 to 5: 1 (2) LH vs 2 (4), >.99
- Segments 3 to 4: 0 3 (6), .20
- Segments 5 to 6: 0 3 (6), .20
- Segments 6 to 7: 0 2 (4), .50
- Major hepatic resection: 7 (13) LH vs 7 (13), >.99
- Left hepatectomy: 6 (12) LH vs 6 (12), >.99
- Right hepatectomy: 1 (2) LH vs 1 (2), >.99

**Table 1. Patient Demographics and Tumor and Operative Variables**

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); LH, laparoscopic hepatectomy; MELD, Model for End-Stage Liver Disease; OH, open hepatectomy. *Unless otherwise indicated, data are expressed as number (percentage) of patients.
the mass was also similar in both groups (4.4 [range, 1.0-10.5] cm in the LH group vs 4.3 [range, 1.1-19.8] cm in the OH group). Within both groups, most of the patients had a solitary mass (49 patients [94%] in the LH group and 47 [90%] in the OH group; \( P = .70 \)) and some had 2 masses (3 patients [6%] in the LH group and 2 [4%] in the OH group; \( P = .70 \)).

Table 2 summarizes the short-term outcomes. The LH group included 7 patients (13%) who underwent conversion to OH. Positive margin status was similar between groups (1 patient [2%] for LH vs 2 [4%] for OH; \( P > .99 \)). Mean operative time was 219 (range, 84-449) minutes in the LH group, which was comparable to 198 (range, 107-347) minutes in the OH group (\( P = .16 \)). Mean estimated blood loss was less in patients undergoing LH (237 [range, 10-1200] mL) than those undergoing OH (387 [range, 25-3000] mL) (\( P = .049 \)). However, we found no significant difference in the rate of perioperative blood transfusion (2% vs 10%; \( P = .20 \)).

Overall morbidity (42% for LH vs 37% for OH; \( P = .70 \)) and severity of complications were not different between groups. Specifically, the rate of minor morbidity (Clavien-Dindo grades I-II) was similar (35% for LH vs 29% for OH; \( P = .67 \)), as was the rate of major morbidity (Clavien-Dindo grades III-IV) (8% in each group; \( P > .99 \)). Pulmonary complications were the most frequent complication; however, we noted little difference between the LH and OH groups (21% for LH vs 17% for OH; \( P = .80 \)). In addition, no difference was observed in cardiac complications (6% in each group) or in bile leakage (0 for LH vs 4% for OH; \( P = .49 \)). Although not statistically significant, we found a trend toward more surgical site infection in the LH group (10%) than the LH group (2%) (\( P = .21 \)). Mean length of hospital stay was 5 (range, 1-17) days with LH and 6 (range, 3-23) days with OH (\( P = .13 \)). Readmission rate was comparable (8% for LH vs 10% for OH; \( P = .70 \)). Overall 30-day mortality was also similar (2% for LH vs 4% for OH; \( P > .99 \)).

When we excluded the patients with LH who underwent conversion to OH along with their matched OH counterparts, we found little change with regard to results. The 2 groups remained comparable in terms of mean operating time (\( P = .14 \)), perioperative blood transfusion (\( P = .20 \)), readmission rate (\( P > .99 \)), mortality (\( P > .99 \)), morbidity (\( P > .99 \)), Clavien-Dindo grades I to II (\( P = .80 \)), Clavien-Dindo grades III to IV (\( P > .99 \)), pulmonary complications (\( P > .99 \)), cardiac complications (\( P > .99 \)), bile leakage (\( P > .99 \)), and wound infection (\( P = .20 \)). Mean estimated blood loss was still significantly different, with LH patients showing less blood loss than OH patients (\( P = .02 \)). When we excluded the patients who underwent a converted procedure and their counterparts, we found a significant difference in mean length of hospital stay, with LH patients staying fewer days (mean stay, 4 days) postoperatively compared with OH patients (mean stay, 6 days; \( P = .02 \)).

Discussion

For many abdominal operative procedures, laparoscopy has become the standard of care. Since the 1990s, as surgeons have become more facile with laparoscopic techniques, they have expanded its use into far more complex operations. One of the initial barriers to performing laparoscopic partial hepatic resection was concern about the safety of laparoscopic hemo-
stic technique. As the use of laparoscopic surgery has expanded, the availability of new laparoscopic energy devices that parallel open instrumentation has helped to address these concerns. Specifically, in LH procedures, better visualization of vessels, high intra-abdominal pressure caused by pneumoperitoneum, and low central venous pressure may contribute to improved intraoperative hemostasis. All of these factors likely explain the decreased blood loss seen with the LH group in our study and other studies.5,6 However, despite the decreased blood loss, no significant difference in need for perioperative blood transfusion occurred in our study or in other studies.3 This distinction is important because blood transfusion has been linked to recurrence of hepatocellular carci-
noma after hepatectomy and increased infectious complications.

The largest meta-analysis to date on the subject of LH vs OH reported a 59.9% lower risk of postoperative complications after LH. However, the decrease in complications was not universally observed among the included studies. Only 8 of those 26 studies even reported a liver-specific complication (bile leakage), and no significant difference was noted. In addition, a subsequent matched-pair comparison from Memorial Sloan Kettering Cancer Center reported a 3-fold higher rate of short-term complications in the OH group. However, on further review, the only specific complication that showed a significant difference was the incidence of postoperative fever.

Inconsistent reporting of surgical morbidity has been observed in the surgical literature, and an inherent publication bias promotes articles that demonstrate a significant benefit of one technique over another. In recent years, national quality measures have led to more uniform adherence to perioperative best practices regardless of operative technique. These measures have, in turn, had a positive effect on reducing perioperative complications. This significant confounding variable may help account for the differences seen in LH vs OH observed in prior studies.

Given the current lack of a randomized clinical trial comparing LH with OH, investigators must strive to eliminate the selection bias inherent to nonrandomized studies. The most significant factor affecting patient recovery after hepatic resection is the physiologic insult to the liver itself, which is generally independent of the method of resection. This physiologic insult has yet to be fully defined in the literature, but it is most likely related to the extent and location of liver resection, preoperative liver quality, and intraoperative blood loss. Therefore, the most important factors we matched for were extent and location of resection. Although another study that specifically looked at short-term complications, including nonsteroidal anti-inflammatory drugs, intravenous acetaminophen, and elastometric pain pump devices that deliver local anesthetic along the incision site itself, may contribute to improved pain control. Additional strategies that have improved postoperative outcomes and shortened the length of stay include early start of oral nutrition and avoidance of drainage tubes when possible. Although length of stay is an important benchmark, confounding factors may limit its effectiveness when directly comparing laparoscopic and open partial hepatic resection.

Although the present study demonstrates that among equally matched patients, the short-term benefits of a laparoscopic approach are modest, we are aware of some study limitations, primarily a significant risk for selection bias. Although we believe that the extent and location of resection and preoperative liver quality are the most important determinants of short-term outcomes, other confounding variables may account for our findings. Because we did not match for preoperative comorbidities, the LH group may have had a less complex disease process, which may have biased the outcomes observed. On the other hand, overmatching has the risk of eliminating clinically significant exposures that could result in differences. Several other studies excluded cases that were converted to OH; however, our goal was to determine whether the intention to treat with LH is associated with improved short-term outcomes.

Not every patient undergoing LH could be included in the analysis, owing to the inability to find a suitable patient undergoing OH to match. Therefore, a subset of patients may indeed have more significant benefit from LH. Although the overall sample size is larger than most studies to date, it may lack sufficient power to detect smaller differences in short-term outcomes. For example, although we found a clinically significant trend toward decreased wound infection with LH, this trend did not reach statistical significance. However, other complications are more specific to the partial hepatectomy itself rather than the operative technique. Finally, long-term complications, such as incisional hernia and adhesive bowel obstructions, may contribute to improved pain control. Additional strategies that deliver local anesthetic along the incision and itself may have more significant benefit from LH. Although the overall sample size is larger than most studies to date, it may lack sufficient power to detect smaller differences in short-term outcomes. For example, although we found a clinically significant trend toward decreased wound infection with LH, this trend did not reach statistical significance. However, other complications are more specific to the partial hepatectomy itself rather than the operative technique. Finally, long-term complications, such as incisional hernia and adhesive bowel obstructions, may contribute to improved pain control. Additional strategies that deliver local anesthetic along the incision and itself have further decreased the morbidity associated with open surgery. Early transition to oral pain medications, in addition to the use of nonnarcotic medications, including nonsteroidal anti-inflammatory drugs, intravenous acetaminophen, and elastometric pain pump devices that deliver local anesthetic along the incision site itself may contribute to improved pain control. Additional strategies that have improved postoperative outcomes and shortened the length of stay include early start of oral nutrition and avoidance of drainage tubes when possible. Although length of stay is an important benchmark, confounding factors may limit its effectiveness when directly comparing laparoscopic and open partial hepatic resection.

Conclusions

Patients who undergo LH have similar short-term outcomes when compared with those who undergo OH. Although LH is associated with decreased blood loss compared with OH, the need for blood transfusion is not significantly different. Margin status does not appear to be compromised by LH. Future studies are needed to define which patients derive benefit from LH and to determine oncologic equivalence to OH.
Laparoscopic vs Open Hepatectomies

ARTICLE INFORMATION

Accepted for Publication: April 11, 2014.
Published Online: July 30, 2014.

Author Contributions: Dr Franken had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Franken, DiFronzo.
Acquisition, analysis, or interpretation of data: Franken, Lau, Putchakayala.
Drafting of the manuscript: Franken, Putchakayala, DiFronzo.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Franken, Putchakayala.
Study supervision: DiFronzo.

Conflict of Interest Disclosures: None reported.

Previous Presentation: This paper was presented at the 85th Annual Meeting of the Pacific Coast Surgical Association; February 17, 2014; Dana Point, California.

REFERENCES