Background: The introduction of laparoscopic liver resection has been challenging because new and safe surgical techniques have had to be developed, and skepticism remains about the use of laparoscopy for malignant neoplasms. We present herein a large-volume single-center experience with laparoscopic liver resection.

Design: Retrospective study.

Setting: Rikshospitalet University Hospital.

Patients: One hundred thirty-nine patients who underwent 177 laparoscopic liver resections in 149 procedures from August 18, 1998, through October 14, 2008. One hundred thirteen patients had malignant lesions, of whom 96 had colorectal metastases.

Intervention: Laparoscopic liver resection for malignant and benign lesions.

Main Outcome Measures: Perioperative and oncologic outcomes and survival.

Results: Five procedures (3.4%) were converted to laparotomy and 1 (0.7%) to laparoscopic radiofrequency ablation. The remaining 143 procedures were completed laparoscopically, during which 177 liver resections were undertaken, including 131 nonanatomic and 46 anatomic resections. The median operative time and blood loss were 164 (50-488) minutes and 350 (/<50-4000) mL, respectively. There were 10 intraoperative (6.7%) and 18 postoperative (12.6%) complications. One patient (0.7%) died. The median postoperative stay and opioid requirement were 3 (1-42) and 1 (0-11) days, respectively. Tumor-free resection margins determined by histopathologic evaluation were achieved in 140 of 149 malignant specimens (94.0%). The 5-year actuarial survival for patients undergoing procedures for colorectal metastases was 46%.

Conclusions: In experienced hands, laparoscopic liver resection is a favorable alternative to open resection. Perioperative morbidity and mortality and long-term survival after laparoscopic resection of colorectal metastases appear to be comparable to those after open resections.


FOR MANY ABDOMINAL PROCEDURES, LAPAROSCOPY HAS WELL-DOCUMENTED BENEFITS FOR THE PATIENTS COMPARED WITH LAPAROTOMY.1 Many hepatobiliary centers perform laparoscopic liver resection, and the feasibility and safety of this procedure have been documented in several reports.2-9 However, most centers still offer only open liver resection owing to problems related to education and the long learning curve typical for laparoscopic resection. Furthermore, long-term oncologic outcome after laparoscopic resection has been poorly documented.10-13 Adequate evaluation of the long-term oncologic outcome could facilitate the introduction of the technique at more centers worldwide.

We present herein our large-volume single-center experience of laparoscopic liver resection, with a focus on the perioperative results and oncologic outcome as documented by resection margin status and survival.

See Invited Critique at end of article

Rikshospitalet University Hospital is a referral center for hepatobiliary procedures. From August 18, 1998, through October 14, 2008, laparoscopic liver resection with the intention of radical treatment was attempted in 139 patients. In total, 149 laparoscopic procedures were performed in these patients. Ten procedures were referred for a second laparoscopic resection owing to tumor recurrence (7...
colorectal metastases, 1 metastasis from pancreatic glucagonoma, 1 biliary cystadenoma, and 1 case of suspected melanoma recurrence). The total numbers of open and laparoscopic liver resections performed in the period evaluated are indicated in Figure 1.

One hundred thirteen patients underwent operations for malignant and 27 for benign lesions (Table 1). The patient characteristics are described in Table 2. Most of the patients undergoing operations for malignant lesions had had previous abdominal surgery, in contrast to the patients with benign lesions.

Initially, patients considered for nonanatomic (local) resection or for left lateral sectionectomy were selected to undergo laparoscopy. Since July 2006, we have accepted patients considered for any type of liver resection, including right and left hemihepatectomy. During the first 8 years of the study period, all procedures were performed or guided by one surgeon (B.E.). Therefore, the availability of the senior laparoscopic surgeon was a prerequisite for the laparoscopic approach at that stage. This led to a loss of potential laparoscopic candidates during that period and prompted us to increase capacity by teaching other surgeons the procedures. Surgeons of the same team gradually participated in and learned the procedure. Currently, 3 surgeons (B.E., B.I.R., and A.R.R.) independently perform laparoscopic liver resections except for hemihepatectomies, which are performed by only one surgeon (B.E.). The Brisbane terminology was applied to classify liver resections.14

Standard preoperative investigations included liver imaging (computed tomography and magnetic resonance imaging and contrast ultrasonography), chest imaging (computed tomography or plain radiography), and clinical biochemistry. The patients received perioperative subcutaneous low-molecular-weight heparin. Intravenous anesthesia was used. At the beginning of surgery, bupivacaine hydrochloride was injected at the trocar port sites. Postoperative analgesia consisted of a nonsteroidal anti-inflammatory drug and intravenous acetaminophen. Opioid analgesics (commonly ketobemidone) were given if additional analgesia was required. The patients were allowed to eat and drink the same day.

Tumor size was measured after fixation in formaldehyde during the histopathologic analyses of the resected specimens. The distance from the tumor to the resection margin, that is, the free resection margin, was measured macroscopically and microscopically after fixation. All resection margins were assessed microscopically by the pathologist with regard to tumor tissue.

For patients discharged to local hospitals, information about the postoperative course was retrieved and incorporated in the analyses of postoperative morbidity and hospital stay. Perioperative chemotherapy was applied in accordance with international guidelines adapted by the Norwegian Gastrointestinal Cancer Group. Neoadjuvant or adjuvant chemotherapy was not applied routinely. Palliative chemotherapy was offered to patients with inoperable disease during follow-up at the discretion of the oncologists. Clinical data were collected from patient journals and registered in a database (Excel; Microsoft, Redmond, Washington).

Perioperative mortality was defined as death within 30 days or before hospital discharge. The dead/alive patient status was controlled by data from the Norwegian National Population Register. The median follow-up for patients with colorectal metastases was 19 (range, 1-90) months. Survival was evaluated starting from the date of the first laparoscopic liver resection (including patients who had previously undergone open liver resection).

### SURGICAL TECHNIQUES

Pneumoperitoneum was established by open technique, and infra-abdominal carbon dioxide gas pressure was set at 8 to 10 mm Hg. A 30° laproscope (Olympus Medical Systems Corp, Tokyo, Japan) and 5- and 12-mm trocars (Tyco/Covidien, Nor-
Cases of 2 concomitant resections

Table 3. Type of Laparoscopic Liver Resections

<table>
<thead>
<tr>
<th>Type of Resection</th>
<th>No. of Resections</th>
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<tr>
<td>Benign Lesions</td>
<td>Malignant Lesions</td>
</tr>
<tr>
<td>Anatomic resections</td>
<td>8</td>
</tr>
<tr>
<td>Left lateral sectionectomy</td>
<td>8</td>
</tr>
<tr>
<td>Right hemiepatectomy</td>
<td>0</td>
</tr>
<tr>
<td>Left hemiepatectomy</td>
<td>0</td>
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<tr>
<td>Nonanatomic resections</td>
<td>20</td>
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</table>

Five of the 149 procedures (3.4%) were converted to open surgery and 1 (0.7%) to laparoscopic tumor ablation (Figure 2). A total of 177 liver resections were performed laparoscopically during these 143 procedures (Figure 2). The resected tumors were located in all liver segments except for segment 1. Altogether 131 nonanatomic and 46 anatomic laparoscopic resections were performed (Table 3). The intraoperative findings are described in Table 4. Procedures performed for malignant lesions were associated with a moderately increased operative time and blood loss compared with procedures for benign lesions. Anatomic and nonanatomic resections are compared in Table 5. A moderately increased operative time for anatomic resections was the only observed statistical difference in intraoperative outcomes.

The conversions to laparotomy were because of intraabdominal adhesions (2 cases) and hemorrhage (3 cases); in 1 case, laparoscopic radiofrequency ablation was performed instead of resection. Repeated resections after open liver resection were associated with a significantly higher rate of conversion to laparotomy: 3 of 13 procedures (23.1%) vs 2 of 136 procedures (1.5%) (P = .005). None of the repeated laparoscopic resections performed after primary laparoscopic liver resections were converted to laparotomy.

Intraoperative complications occurred in 10 of 149 procedures (6.7%), including 7 perforations of adherent or adjacent organs (the small bowel [3 cases], diaphragm and pericardium [1 case], transverse colon [1 case], right bile duct [1 case], and gallbladder [1 case]). These perforations were handled laparoscopically by suturing except for 1 case of bowel perforation (minilaparotomy suturing) and 1 case of gallbladder perforation (concurrent cholecystectomy). Among the 143 procedures that did not undergo conversion, the blood loss exceeded 1000 mL in 24 cases.
and 500 mL in 47 (32.9%). In 1 case of a 4000-mL blood loss, surgery was initiated in the absence of a senior surgeon, but the bleeding was stopped a short time after his arrival and laparotomy was not required.

Six patients received ablation of concomitant nonresectable tumors (4 cryoablations and 2 radiofrequency ablations) combined with laparoscopic liver resection.

**POSTOPERATIVE RESULTS**

The postoperative results are presented in Table 4. One hundred twenty-one of 143 patients (84.6%) were discharged to their private home, whereas 25 patients were transferred to a local hospital. There were no statistically significant differences in the postoperative outcome comparing procedures performed for benign or malignant lesions or between anatomic and nonanatomic resections (Tables 4 and 5).

Postoperative complications occurred in 18 of 143 procedures (12.6%), including pneumonia (2 cases), atelectasis (1 case), liver abscess (2 cases, of which 1 was managed by antibiotics and 1 by percutaneous drainage), abdominal wall abscess (1 case managed by percutaneous drainage), intra-abdominal seroma (1 case managed by percutaneous drainage), pleural fluid (1 case), wound infection (1 case), urinary infection (3 cases), and eventration through the umbilical incision (1 case resutured), bleeding at the trocar site or the umbilical incision site (2 cases controlled by suture), and biliary leakages (3 cases, of which 1 was managed by percutaneous drainage/antibiotics, 1 by laparoscopic drainage/antibiotics, and 1 by reoperation). The last patient with biliary leakage underwent reoperation 3 times (1 laparoscopy and 2 laparotomies) and later developed biliary peritonitis. The patient remained in the hospital for 42 days.

In 1 patient with severe comorbidity (American Society of Anesthesiology grade 4), the procedure was converted to laparotomy because of bleeding from the hilar blood vessels. Severe bleeding from the hepatic veins occurred during the open procedure. The patient underwent reoperation the following day for constriction of the caval vein by a suture, and reconstruction of the caval and hepatic veins was performed. The patient later died of multiorgan failure.

**ONCOLOGIC OUTCOME**

Of the 115 procedures completed laparoscopically for malignant lesions, 100 were R0 resections; 9, R1 resections; and 6, R2 resections. All R2 resections were planned, in that patients presented for the first of a 2-stage surgical treatment. Four of them underwent portal vein em-

<table>
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<th>Table 4. Surgical Outcomes</th>
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<tr>
<td><strong>Benign Lesions</strong></td>
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<td>------------------------</td>
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<tr>
<td><strong>No. of laparoscopically attempted procedures</strong></td>
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<tr>
<td><strong>Complications, No. (%) attempted</strong></td>
</tr>
<tr>
<td><strong>Conversion to laparotomy, No. (%) attempted</strong></td>
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<tr>
<td><strong>Operative time, median (range), min</strong></td>
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<tr>
<td><strong>Blood loss, median (range), mL</strong></td>
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<td><strong>Blood transfusions, No. (%) completed</strong></td>
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<table>
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<tr>
<th>Table 5. Anatomic vs Nonanatomic Liver Resections</th>
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<tr>
<td><strong>Anatomic Resections</strong></td>
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<tr>
<td>------------------------</td>
</tr>
<tr>
<td><strong>No. of laparoscopically attempted procedures</strong></td>
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*Procedures during which both anatomic and nonanatomic resections were performed are excluded.*
Bleeding and biliary leakage are related to the surgeon’s experience and surgical skills. However, the availability of advanced and sophisticated surgical equipment has reduced this problem. Tumor location and size are also associated with the risk of complications. One should always use gravity to facilitate mobilization. This point is especially essential when approaching segments 7 and 8, which present a special technical challenge. The low rate of postoperative infections seen with the laparoscopic approach may be an important contribution in averting postresectional liver failure.

We demonstrated comparable surgical outcomes of liver resection for benign and malignant liver lesions. This was an interesting observation despite the fact that the latter group of patients had worse physical status and a higher rate of previous laparotomy and hepatectomy.

Despite the early introduction of laparoscopic liver surgery in 1992, the technique has not gained general acceptance. Most hepatobiliary centers perform only open liver surgery. In centers performing laparoscopic liver resection, open procedures still dominate. The reasons for this seem to be 2-fold. First, technical aspects of liver resection are still a matter of debate, even if the major challenges have been resolved and accepted. Second, it is time-consuming and difficult to master laparoscopic liver resection. Many surgeons skilled in traditional techniques learned simple laparoscopic procedures quickly and without major difficulty (e.g., cholecystectomy and appendectomy) but found it challenging to learn more technically advanced procedures. Because of the specialization within the units performing liver surgery, simple cases for laparoscopic training are not easily available. This is a main reason for the lack of basic laparoscopic skills among the senior generation of consultant surgeons in specialized hepatobiliary centers and restrains fast development of laparoscopic liver surgery in general as well as in individual centers.

Another reason for the limited use of laparoscopic liver resection is based on the presumption that laparoscopic procedures might be less radical than an open resection. Our pilot comparative study has shown the same rate of negative surgical margins after laparoscopic and open liver resections. Furthermore, in the present series, the 5-year actuarial survival was 46% after laparoscopic liver resection for colorectal metastases. This corresponds to the best reported outcomes after open liver resection and is better than outcomes from our own operated experience with open surgery. Concerns about the classic rule of the 1-cm margin for cancer resections were previously raised with regard to open liver resection. Our median surgical margin was 6 mm, but still we achieved 94% margin-free resections and favorable long-term survival. Careful laparoscopic manipulations averting microruptures of the specimen during sur-

The present report demonstrates that laparoscopic liver resection can be performed safely by an experienced surgical team. We had a low incidence of intraoperative (6.7%) and postoperative (12.6%) morbidities. Similarly, the 30-day mortality was comparable to that of the open series (0.7%). The conversion rate to laparotomy was low (3.4%), although the most frequent indication for surgery was metastases after previous open resection of primary colorectal cancer. Repeated resection after open liver resection was associated with an increased conversion rate compared with repeated resections performed after laparoscopic liver resection.

Bleeding was the most serious intraoperative complication, and we emphasize the importance of keeping the central vein pressure below 5 cm H2O to decrease bleeding during the live tissue transection. Despite the low intraoperative blood loss, our series was associated with a relatively moderate rate of blood transfusions (18.2%). This is in part explained by the conservative and cautious attitude of the anesthesiology team, although there has been a strong tendency toward a restriction of blood transfusion in recent years. We did not register any case of gas embolism, which represented a major cause for anxiety during the early phase of laparoscopic liver surgery. This is possibly explained by strict maintenance of low intra-abdominal pressure during the procedure (8-10 mm Hg).

The median size of the largest tumor resected during each procedure was 3.0 (range, 0.5-13.5) cm. The resection margin showed no identifiable tumor tissue by histopathologic analyses in 140 of 149 specimens (94.0%) resected during the 115 procedures. Positive resection margins were found in 8 patients with colorectal metastases (4 who underwent primary resection and 4 who had a repeated resection) and 1 patient with melanoma. The free resection margin was 10 mm or more in 43 of 148 specimens (29.1%). The median free surgical margin was 6 (range, 0-40) mm.

The estimated 5-year actuarial survival was 46% for patients with colorectal metastases (Figure 3). The median length of survival was 65 (47 to ∞) months.

**Figure 3.** Survival estimates for patients undergoing operation for colorectal lesions (Kaplan-Meier curve). Dashed lines represent the 95% confidence interval.
surgery may reduce the risk of tumor recurrence. Intraoperative ultrasonography is mandatory for tumor identification and margin control. It should be used at the beginning of the procedure to confirm and precisely locate the tumors, to exclude undetected tumors, and to map the vascular and biliary anatomy. During the procedure, it should be used to control the resection.

The concept of segment-oriented anatomic liver resection has made an important contribution to the recent development of liver surgery. Anatomic resections have been demonstrated to be associated with better hemostasis and control of bile leakage compared with nonanatomic resections. However, new surgical technologies of ultrasonography and coagulation-based parenchyma transection have diminished these benefits of anatomic resection. A moderately increased operative time for anatomic resections was the only difference found when comparing anatomic and nonanatomic techniques.

Another argument has been that anatomic resections could potentially provide better oncologic outcomes, but this hypothesis has been demonstrated to be doubtful at least with regard to metastatic malignant neoplasms of the liver. The parenchyma-sparing concept will increase the possibilities of a second resection and the preservation of sufficient liver reserve after that resection. Laparoscopic techniques also facilitate successive parenchyma-sparing resections because of minimal adhesion formation, and the procedure is better tolerated by the patients. We believe it is necessary to perform a parenchyma-sparing liver resection whenever possible.

Hemihepatectomies represent special concerns and are associated with substantially increased technical demands. Consequently, they result in more time-consuming procedures. Initially, we performed minor resections only but, after having accumulated experience, we started to admit all groups of patients considered in accordance with the classic rules of open liver resections. Despite the intraoperative technical challenges of major resections, the laparoscopic approach still provides an improved postoperative course to the patients, as also shown by Gayet and colleagues.

Competence in advanced laparoscopic surgery and liver surgery are prerequisites. Surgical transection equipment is required for success in laparoscopic liver surgery. Hemihepatectomies should be performed only after considerable experience has been acquired with minor resections.

The training of surgeons is a major issue for general acceptance of this technique. Health care managers should be encouraged to promote training in this advanced technique. The time has come to prove the observed benefits of laparoscopic approach by randomized prospective trials.

CONCLUSIONS

Laparoscopic liver resection is a favorable alternative to open resection for benign and malignant liver lesions. It is associated with low morbidity and mortality. Long-term survival after laparoscopic resection of colorectal metastases is comparable to that after open resections.

Experience in liver surgery and laparoscopic techniques is required for success in laparoscopic liver surgery. Hemihepatectomies should be performed only after considerable experience has been acquired with minor resections.

The training of surgeons is a major issue for general acceptance of this technique. Health care managers should be encouraged to promote training in this advanced technique. The time has come to prove the observed benefits of laparoscopic approach by randomized prospective trials.

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Author Contributions: Drs Kazaryan, Pavlik Marangos, and Edwin had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Kazaryan and Edwin. Acquisition of data: Kazaryan and Pavlik Marangos. Analysis and interpretation of data: Kazaryan, Pavlik Marangos, Rosseland, Røsok, Mala, Villanger, Mathisen, Giercksky, and Edwin. Drafting of the manuscript: Kazaryan. Critical revision of the manuscript for important intellectual content: Kazaryan, Pavlik Marangos, Rosseland, Røsok, Mala, Villanger, Mathisen, Giercksky, and Edwin. Statistical expertise: Kazaryan and Pavlik Marangos. Administrative, technical, and material support: Kazaryan, Pavlik Marangos, Rosseland, Røsok, Mala, Villanger, Mathisen, Giercksky, and Edwin. Study supervision: Edwin.

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Additional Contributions: Lien M. Diep, MSc, assisted in the statistical analysis.

REFERENCES

Small Incision, Big Surgeon

Laparoscopic Liver Resection for Tumors Without a Doubt

During a 10-year period, this group has accumulated and studied carefully data on 139 patients who underwent laparoscopic hepatectomies, a large series according to laparoscopic standards. Most (81.3%) underwent operation for malignant neoplasms, chiefly colorectal metastases, with satisfactory operative outcome and reasonable complication rates. The myth of increased venous gas emboli from laparoscopy is shattered. The median hospital stay of 3 days is an improvement over standard open traditional hepatectomies. The 5-year survival of 46% is admirable and compares favorably with...