Clinical Surgery

Robot-assisted laparoscopic liver resection for hepatocellular carcinoma: short-term outcome


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KEYWORDS:
Hepatocellular carcinoma; Liver neoplasm; Laparoscopic liver resection; Partial hepatectomy; Robotic surgery

Abstract

BACKGROUND: This study aimed at analyzing the perioperative and early survival outcomes of robotic liver resection of hepatocellular carcinoma (HCC).

METHODS: The study population included a consecutive series of patients with HCC who underwent robotic liver resection at a single center.

RESULTS: During the study period, 41 consecutive patients with HCC underwent 42 robotic liver resections. Five resections (11.9%) were carried out for recurrent HCC, and 23.8% (n = 10) were hemihepatectomy procedures. The mean operating time and blood loss was 229.4 minutes and 412.6 mL, respectively. The R0 resection rate was 93%. The hospital mortality and morbidity rates were 0% and 7.1%, respectively. The mean hospital stay was 6.2 days. The 2-year overall and disease-free survival rates were 94% and 74%, respectively.

In the subgroup analysis of minor liver resection, when compared with the conventional laparoscopic approach, the robotic group had similar blood loss (mean, 373.4 mL vs 347.7 mL), morbidity rate (3% vs 9%), mortality rate (0% vs 0%), and R0 resection rate (90.9% vs 90.9%). However, the robotic group had a significantly longer operative time (202.7 mins vs 133.4 mins).

CONCLUSIONS: This study demonstrated the feasibility and safety of robotic surgery for HCC, with favorable short-term outcome. However, the long-term oncologic results remain uncertain.

Hepatocellular carcinoma (HCC) accounts for 80% to 90% of primary liver cancer cases. HCC is a major health problem worldwide, with an estimated incidence ranging between 500,000 and 1,000,000 new cases annually. It is the fifth most common cancer in the world and the third most common cause of cancer-related death.1,2 Potentially curative treatments for HCC include liver resection, liver transplantation, and local ablative therapy. Among these, liver resection is regarded as a standard treatment that offers a chance of cure for patients with preserved liver function. In the past decade, different modalities of minimally invasive curative treatment for HCC were actively investigated.3,4

The development of minimally invasive surgery over the past 2 decades has had a great impact on surgical practice. Laparoscopic liver resection has also become possible with the availability of new instruments that allow a relatively bloodless liver transection. The potential advantages of laparoscopic liver resection include minimally invasive surgery, early recovery, shorter hospital stays, and better

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cosmetic outcome. The postoperative course after laparo-
scop ic liver resection may also improve in patients with
liver cirrhosis because the abdominal wall is preserved,
kine tics of the diaphragm are improved, collateral venous
drainage is better, and there is less postoperative ascites.
Conventional laparoscopic liver resection has been shown
to be safe and feasible in experienced hands.5–7 However,
the restrictive movement of laparoscopic instruments, lim-
ited by a fixed pivot point with only 4° of freedom and a
2-dimensional view, limits its utility in hepatobiliary sur-
gery with its complex repertoire of operations. Currently,
the laparoscopic approach is used mainly for minor hepatic
resections over anterop eripheral segments.8

Robotic surgery has evolved as a minimally invasive
 technique aimed at improving clinical outcomes. Robotic
surgery has the potential to alleviate the inherent limitations
of conventional laparoscopic surgery such as 2-dimensional
imaging, limited instrument movement, and intrinsic
human tremor. Available data about robotic liver surgery,
 especially survival and oncologic outcomes, in the litera-
ture are very limited.9–14

The aim of the present study was to study the periop-
erative outcomes and short-term survival outcomes of
robot-assisted laparoscopic liver resection of HCC.

Methods

A prospective evaluation of robot-assisted laparoscopic
liver resection was initiated in our department in May 2009.
At the end of 2010, we also started performing major
hepatectomy using robot-assisted laparoscopic surgery,
including right and left hemihepatectomies. The study
population was a consecutive series of patients with HCC
who underwent robot-assisted laparoscopic liver resection
in a tertiary referral center from May 2009 to March 2012.
During this period, a total of 73 robot-assisted laparoscopic
liver resections for benign liver tumors, primary hepatoli-
thasis, colorectal liver metastases, and HCC were per-
formed. This comprises 60.8% of all the liver resections in
our unit during that time. Among these 73 robot-assisted
laparoscopic liver resections, 42 (59.7%) procedures were
performed for HCC.

All patients underwent chest radiography, ultrasonogra-
phy of the abdomen, and contrast computed tomography
(CT) of the abdomen. Magnetic resonance imaging (MRI)
or lipiodol-CT was performed in selected patients. Labora-
tory blood tests, including determinations of hepatitis B
surface antigen, antibodies to hepatitis C, serum alpha-
fetoprotein (AFP), serum albumin, serum total bilirubin,
appartate aminotransferase, alanine aminotransferase, and
prothrombin time were obtained, and the Pugh modification
of Child’s criteria was determined. Further investigations
were performed only when there was clinical suspicion of
extrahepatic metastases. Radiologic studies were reviewed
in a multidisciplinary case management meeting held
weekly. The selection criteria were as follows: tumor
5 cm or less in diameter, no major vascular invasion,
noncirrhotic liver or Child-Pugh class A cirrhosis, and
American Society of Anesthesiologists score of 3 or less.
Solitary exophytic tumors larger than 5 cm that were
accessible by the laparoscopic approach were also consid-
ered. Patients were informed about the surgical procedure,
and consent was obtained before surgery. All procedures
were performed by consultant surgeons with expertise in
hepatobiliary and laparoscopic surgery. During the early
postoperative period, all patients received care in the
intensive care unit. Liver function was monitored. For
those patients with impaired consciousness, the serum
ammonia level was checked to rule out hepatic encephal-
opathy. During outpatient follow-up, all patients had serial
AFP assays, and ultrasonography or CT of the abdomen
was performed every 3 to 6 months.

Operative procedure

Our operative technique for robot-assisted laparoscopic
liver resection has been described previously in the litera-
ture.12–14 The patient is placed in a supine position with
legs apart and then in a 20° reverse Trendelenburg position.
Five ports are generally used. They are positioned along a
semicircular arc facing the epigastrium. The da Vinci S
Surgical System (Intuitive Surgical Inc, Sunnyvale, CA)
was used for all robot-assisted procedures in this study.
A 12-mm camera port, 12-mm operative port, and 3 working
8-mm robotic ports were used (Fig. 1). The abdominal cav-
ity and liver are assessed visually with a 30° telescope and
laparoscopic ultrasonography. The procedure then has 3
stages: (1) portal dissection and vascular control; (2) hep-
tic mobilization; and (3) parenchymal transection. The ro-
botic surgical system’s patient cart is placed at the
patient’s head for the docking phase. The first surgeon
is seated at the robotic console, while an assistant surgeon
is positioned on the right side of the patient.

Statistical method

Prospectively collected data, including intraoperative
parameters, postoperative complications, hospital mortality,
and disease progress, were analyzed retrospectively. Con-
tinuous variables were expressed as mean ± standard
deviation (SD) or mean and range. Continuous variables
were compared using the Student’s t test. Categorical vari-
ables were compared using the chi-square test or the Fisher
exact test. P less than .05 was considered statistically sig-
nificant. Survival outcome was calculated by the Kaplan-
Meier method.

Operative time was calculated as the time between skin
incision and the last port skin closure. Staging laparoscopy
and robotic docking were incorporated into the operative
time as well. Morbidity and mortality were defined as
occurring within 1 month of surgery. Postoperative liver
failure was defined as a prothrombin time less than 50%
International normalized ratio (INR) > 1.7) and a serum bilirubin level higher than 50 μmol/L (>3.0 mg/dL) on postoperative day 5.15

Results

From May 2009 to March 2012, a total of 41 patients with HCC underwent 42 robot-assisted laparoscopic liver resections in our surgical unit. These 42 resections were carried out on 31 male and 10 female patients, with a mean age of 61.4 years. Five resections were carried out for recurrent HCC. One of these 5 patients underwent robot-assisted laparoscopic segment 4 resection for recurrent HCC after robot-assisted laparoscopic left lateral sectionectomy for HCC 19 months before. Demographic data and preoperative status of the 41 patients are shown in Table 1.

Intraoperative results

Surgical procedures and details are shown in Table 2. The mean operative time was 229.4 minutes. The median blood loss during surgery was 412.6 mL. Only 3 patients (7.1%) needed postoperative blood transfusions. Conversion to open laparotomy and conversion to a hand-assisted approach occurred in 4.8% (n = 2) and 2.4% (n = 1) of cases, respectively. All resulted from injury to hepatic venous branches, which resulted in moderate bleeding, and the patients underwent immediate conversion with hemostasis and liver resection.

Postoperative results

Pathologic examination results are shown in Table 3. Among the 43 liver resections, 40 (93%) resections were R0 and 3 (7%) were R1. Postoperative outcomes are shown in Table 4. The mean hospital stay was 6.2 days. There was no in-hospital death after operation. Three patients (7.1%) had postoperative complications. Two patients had postoperative bile leakage from the minor bile ducts at the transection plane. One of these cases was further complicated by intra-abdominal abscess. Both patients were treated successfully with percutaneous drainage. One patient had urinary bladder injury during specimen retrieval through a Pfannenstiel incision. It was detected during operation and was primarily repaired. None of the patients experienced respiratory complications, liver failure, or encephalopathy.

Survival and recurrence

After a median follow-up of 14 months, 5 (13.5%) of the 37 patients with nonrecurrent HCC experienced disease recurrence, and only 1 (20%) of the 5 patients with robot-assisted laparoscopic liver resection for recurrent HCC had another recurrence. All 6 recurrences were isolated intrahepatic recurrences. The 2-year overall and disease-free survival was 94%, and 74%, respectively (Figs 2, 3).

Subgroup analysis: robot-assisted laparoscopic minor liver resection (<3 Couinaud segments) vs conventional laparoscopic minor liver resection

In the subgroup analysis, which excluded patients who had undergone major hepatectomies, patients with HCC who underwent robot-assisted laparoscopic liver resection (n = 33) were compared with patients with HCC who underwent conventional laparoscopic liver resection (n = 33) performed from October 1998 to March 2012. There was no significant difference between the 2 groups regarding blood loss (373.4 mL [range, 10 to 3,500 mL] vs 347.7 mL [range, 5 to 2,000 mL; P = .86] and complication rate (3% vs 9%; P = .61). Both groups had the same mortality rate (0% vs 0%), and R0 resection rate (90.9% vs
90.9%). However, the robotic group had a significantly longer operative time (202.7 ± 69.8 minutes vs 133.4 ± 42.7 minutes; *P* < .001).

**Comments**

The introduction of minimally invasive techniques has dramatically transformed surgery in the past 2 decades. Patient benefits from laparoscopic liver resection include less operative blood loss, less postoperative pain and requirement for narcotics, and a shorter length of hospital stay, with postoperative morbidity and mortality comparable to that of open liver resection. Laparoscopic liver resection of HCC is a relatively new option. Difficult learning curves, adequate resection margins, tumor seeding, metastasis of the wounds, and the long-term outcome are the major concerns in laparoscopic surgery for HCC. It has not gained wide acceptance and remains a subject of controversy among liver surgeons. With more and more studies, the controversy is less and less. A number of nonrandomized comparative studies suggested that the laparoscopic approach was similar to the open approach for selected patients with HCC for perioperative outcome and survival outcome.16–22

**Table 1** Characteristics of the 41 patients with HCC

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ratio (M:F)</td>
<td>31:10</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>61.4 ± 10.9 (SD)</td>
</tr>
<tr>
<td>Liver status</td>
<td></td>
</tr>
<tr>
<td>Liver cirrhosis (n)</td>
<td>34</td>
</tr>
<tr>
<td>Noncirrhotic liver (n)</td>
<td>7</td>
</tr>
<tr>
<td>Hepatitis status</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B carrier (n)</td>
<td>36</td>
</tr>
<tr>
<td>Hepatitis C carrier (n)</td>
<td>3</td>
</tr>
<tr>
<td>Recurrent HCC</td>
<td>1</td>
</tr>
<tr>
<td>Median AFP level (ng/mL)</td>
<td>21.3 (range, 1.4–112,290)</td>
</tr>
</tbody>
</table>

Preoperative laboratory results

[mean ± SD]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.6 ± 1.8</td>
</tr>
<tr>
<td>Platelet count (10^9/L)</td>
<td>174.9 ± 76.4</td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>11.8 ± 1.0</td>
</tr>
<tr>
<td>Bilirubin (μmol/L)</td>
<td>11.3 ± 7.1</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>38.1 ± 4.6</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>83.5 ± 27.5</td>
</tr>
<tr>
<td>15-minute retention rates of ICG (%)</td>
<td>9 ± 3.8</td>
</tr>
</tbody>
</table>

*AFP = alpha-fetoprotein; HCC = hepatocellular carcinoma; ICG = Indocyanine green; SD = standard deviation.*

**Table 2** Surgical procedure and intraoperative detail of the 41 patients with 42 robotic liver resections

<table>
<thead>
<tr>
<th>Episode of operation (n)</th>
<th>42</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of liver resections</td>
<td>43</td>
</tr>
<tr>
<td>Type of liver resection (n)</td>
<td></td>
</tr>
<tr>
<td>Wedge resection</td>
<td>10</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>7</td>
</tr>
<tr>
<td>Bisegmentectomy</td>
<td>4</td>
</tr>
<tr>
<td>Left lateral sectionectomy</td>
<td>12</td>
</tr>
<tr>
<td>Right hepatectomy</td>
<td>7</td>
</tr>
<tr>
<td>Left hepatectomy</td>
<td>3</td>
</tr>
<tr>
<td>Concomitant procedures (n)</td>
<td></td>
</tr>
<tr>
<td>RFA</td>
<td>2</td>
</tr>
<tr>
<td>Wedge resection of stomach</td>
<td>1</td>
</tr>
<tr>
<td>Left adrenalectomy</td>
<td>1</td>
</tr>
<tr>
<td>Mean operating time (min)</td>
<td>229.4 ± 82.8 (SD)</td>
</tr>
<tr>
<td>Median blood loss (mL)</td>
<td>412.6 (range, 10–3,500)</td>
</tr>
<tr>
<td>Vascular clamping used (n)</td>
<td>22</td>
</tr>
<tr>
<td>Mean duration of vascular clamping (min)</td>
<td>40 ± 17.8 (SD)</td>
</tr>
<tr>
<td>Conversion to open approach (n)</td>
<td>2</td>
</tr>
<tr>
<td>Conversion to hand-assisted approach (n)</td>
<td>1</td>
</tr>
</tbody>
</table>

*RFA = radiofrequency ablation; SD = standard deviation.*

**Table 3** Tumor characteristics and histopathologic characteristics of the 43 liver specimens after 42 robotic liver resections

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of liver specimens</td>
<td>43</td>
</tr>
<tr>
<td>Mean tumor size (cm)</td>
<td>3.4 ± 1.9 (SD)</td>
</tr>
<tr>
<td>Number of tumor nodules (n)</td>
<td>47</td>
</tr>
<tr>
<td>HCC (n)</td>
<td>42</td>
</tr>
<tr>
<td>Combined</td>
<td>1</td>
</tr>
<tr>
<td>hepatocellular-cholangiocarcinoma (n)</td>
<td>5</td>
</tr>
<tr>
<td>Well-differentiated carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Moderately differentiated carcinoma</td>
<td>38</td>
</tr>
<tr>
<td>Poorly differentiated carcinoma</td>
<td>4</td>
</tr>
<tr>
<td>Main tumor with satellite nodules in specimen</td>
<td>4</td>
</tr>
<tr>
<td>R0 resection</td>
<td>40</td>
</tr>
<tr>
<td>R1 resection</td>
<td>3</td>
</tr>
</tbody>
</table>

**Table 4** Postoperative outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with complications</td>
<td>3 (7.1%)</td>
</tr>
<tr>
<td>Complications (n)</td>
<td></td>
</tr>
<tr>
<td>Liver failure</td>
<td>0</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0</td>
</tr>
<tr>
<td>Bile leakage</td>
<td>2</td>
</tr>
<tr>
<td>Intra-abdominal abscess</td>
<td>1</td>
</tr>
<tr>
<td>Urinary bladder injury</td>
<td>1</td>
</tr>
<tr>
<td>Mortality (n)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Mean postoperative hospital stay (d)</td>
<td>6.2 ± 3.6 (SD)</td>
</tr>
</tbody>
</table>

SD = standard deviation.
ergonomics. These limitations translate into a long learning curve, requiring a lot of time and effort to develop and maintain such advanced laparoscopic skills. These shortcomings of laparoscopic surgery were the impetus behind the development of robotic surgery. This is the latest technologic advance in minimally invasive surgery. Its future implementation will depend on the advantages that it can provide over conventional laparoscopy or open surgery. However, the number of reported cases in the literature is still limited. Reports of oncologic outcomes are even more scarce. The largest cohort was reported by Giulianotti et al from Chicago and comprised a cohort series of 70 robot-assisted laparoscopic liver resections. Indications for resection were malignant tumors in 42 (60%) patients and benign tumors in 28 (40%) patients. Major liver resections were performed in 27 (38.5%) patients. There were 4 (5.7%) conversions to open surgery. The median operating time for a major and minor resection was 313 minutes (range, 220 to 480 minutes) and 198 minutes (range, 90 to 459 minutes), respectively. The median blood loss was 150 mL (range, 20 to 1,800 mL) for minor resection and 300 mL (range, 100 to 2,000 mL) for major resection. The mortality rate was 0%, and the overall rate of complications was 21%.

We initiated a program of robot-assisted laparoscopic liver resection for HCC based on our proficiency in the management of patients with cirrhosis and more than 10 years of experience in laparoscopic liver surgery. Our group has previously reported the clinical outcomes of a cohort series of 42 patients with HCC who underwent conventional laparoscopic resection (n = 33) and robot-assisted laparoscopic liver resection (n = 9), including 9 patients with HCC in the current study. Later, we also reported the feasibility of a small heterogeneous series of 55 robotic hepatobiliary-pancreatic operations, including 13 patients with HCC in the current study. We have also described the technique and perioperative outcome of robot-assisted laparoscopic hemihepatectomy (n = 10), including 2 patients with HCC in the current study. In our preliminary experience, robot-assisted laparoscopic liver surgery could broaden the scope of minimally invasive liver surgery by overcoming some of the limitations of conventional laparoscopy, including the difficulty of plicating bleeding hepatic parenchyma laparoscopically, performing complex hilar dissections, performing liver resections requiring biliary-enteric reconstructions, and by minimizing the learning curve for these complex procedures. In our experience, with the help of a robotic system, major anatomic hepatobiliary-pancreatic operations became feasible, because extraparenchymal dissection of the portal pedicles and hepatic veins is possible before transection. This earlier control of the feeding vessels facilitates transection and minimizes blood loss. After these preliminary results and the familiarity of our techniques, the number of robot-assisted laparoscopic liver resections dramatically increased in our unit. In the current study, we aimed at analyzing the perioperative outcomes and short-term survival outcomes for a larger homogeneous group of patients with HCC. Follow-up was not long enough for long-term survival calculation in this study. However, this work covered the largest number of robot-assisted laparoscopic resections for HCC (n = 42) reported to date. The number of patients with HCC who underwent robot-assisted laparoscopic resections in the current study was much larger than our previous report, and the short-term survival data after robotic surgery for HCC was available. In our study, 23.8% of resections were hemihepatectomies. Our cohort series had no mortality and a very low complication rate (7.1%). In addition to the benefit of minimally invasive surgery, an adequate oncologic resection is important for a curative procedure for malignant disease. In our series, a high rate of R0 resection (93%) was reported. Only 7% of cases had R1 resection. At the time of censor, only 1 of the 6 patients who had recurrences had intrahepatic tumor recurrence, which was at the resection site. No port site recurrence occurred.
This study demonstrated the feasibility and safety of robot-assisted laparoscopic liver resection of HCC without increasing tumor dissemination. However, the long-term oncologic results of this approach and its presumed benefits remain uncertain. The short-term favorable findings of robot-assisted laparoscopic liver resection for HCC need further investigation.

References