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Laparoscopic and Open Splenectomy and Hepatectomy

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ABSTRACT

Background and Objectives: Patients undergoing synchronous open splenectomy and hepatectomy (OSH) for concurrent hepatocellular carcinoma (HCC) and hypersplenism usually have major surgical trauma caused by the long abdominal incision. Surgical procedures that contribute to rapid recovery with the least possible impairment are desired by both surgeons and patients. The objective of this study was to explore outcomes in patients treated with simultaneous laparoscopic or open splenectomy and hepatectomy for hepatocellular carcinoma (HCC) with hypersplenism.

Methods: We retrospectively evaluated the treatment outcomes in 23 patients with cirrhosis, HCC, and hypersplenism, who underwent simultaneous laparoscopic splenectomy and hepatectomy (LSH; $n = 12$) or open splenectomy and hepatectomy (OSH; $n = 11$) from January 2012 through December 2015. Their perioperative variables were compared.

Results: LSH was successful in all patients. There were nonsignificant similarities between the 2 groups in duration of operation, estimated blood loss, and volume of blood transfused ($P > .05$ each). Compared with OSH, LSH had a significantly shorter postoperative visual analog scale pain score ($P < .001$); shorter time to first oral intake ($P < .001$), passage of flatus ($P < .05$) and off-bed activity ($P < .001$); shorter postoperative duration of hospitalization ($P < .001$); fewer days of postoperative temperature >38.0°C ($P < .01$); fewer postoperative complications ($P < .05$); and better liver and renal function on postoperative days 7 ($P < .05$ each).

Conclusions: Simultaneous LSH is safe for selected patients with HCC and hypersplenism associated with liver cirrhosis.

Key Words: Hepatectomy, Hepatocellular carcinoma, Hypersplenism, Laparoscopy, Splenectomy.

INTRODUCTION

In China, hepatocellular carcinoma (HCC) is the fifth most common malignant cancer and the third leading cause of cancer-related mortality.[1] About 90% of patients with HCC also have various levels level of liver cirrhosis, mainly caused by chronic liver disease after hepatitis B and C, especially in patients associated with hypersplenism caused by cirrhotic portal hypertension.[2] Patients with concurrent cirrhosis and portal hypertension often have liver malfunction and coagulation disorders. Over the past few decades, liver resection was regarded as a contraindication for patients with both HCC and portal hypertension,[3–5] and some patients with Child-Pugh Class A cirrhosis even developed postoperative decompensation in liver function.[5]

Perioperative liver dysfunction and difficult bleeding control are the major problems associated with hepatectomy in patients who have HCC with portal hypertension.[3–5] Splenectomy has proved to be a feasible strategy to overcome these problems.[6,7] In 2000, Shimada et al[7] reported that hepatectomy after laparoscopic splenectomy is a solution for patients with cirrhotic hypersplenism with HCC. Synchronous open splenectomy and hepatectomy (OSH) is also a safe treatment strategy that may solve hypersplenism and prolong disease-free survival, without an increased perioperative risk for patients with cirrhotic hypersplenism and HCC.[8,9] Minimally invasive surgical procedures that contribute to rapid recovery are desired by doctors. In the present study, we investigated whether simultaneous laparoscopic splenectomy and hepatectomy

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(LSH) is a feasible and safe surgical treatment for cirrhotic hypersplenism with HCC.

MATERIALS AND METHODS

Patients

From January 2012 through December 2015, 23 patients were identified in our department as having HCC and secondary hypersplenism due to liver cirrhosis. Of those, 11 underwent conventional OSH (OSH group). Simultaneous LSH was introduced in our department in January 2015, and 12 patients have undergone the procedure (LSH group). The clinical characteristics of these patients were analyzed. Inclusion criteria were age 18–75 years, cirrhosis of any etiology, Child–Pugh class A or B liver function, platelet count $<5.0 \times 10^4/mm^3$, tumor size less than 5 cm, and tumor location in the peripheral right lobe or left lobe.

The present study was not a clinical randomized trial. It was approved by the Ethics Committee of the Clinical Medical College of Yangzhou University. Before the operation, all patients were notified that, compared with typical OSH, minimally invasive LSH is in the experimental stage. Each patient selected his or her preferred type of surgical procedure, and signed an informed consent.

Clinical data were collected as follows: patient sex, age, etiology of cirrhosis, Child–Pugh class, Acute Physiology and Chronic Health Evaluation (APACHE) II score, tumor size, length of the spleen, duration of operation, blood loss, and blood transfusion. Other data were estimated as follows: postoperative visual analog scale (VAS) pain score; times to first oral intake, passage of flatus, and off-bed activity; postoperative duration of hospitalization; number of days of postoperative temperature >38.0°C; perioperative complications; and white blood cell (WBC) count and absence of fever on postoperative days 1 and 7. Blood analyses were as follows: white blood cell (WBC) count, platelet count, and level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and creatinine (CRE), determined before and 1 and 7 d after surgery.

Surgical Procedures

LSH

A 5-port (**Figure 1**) or 5+1-port (**Figure 2**) method was used for LSH. A 10-mm trocar (A) was inserted through an umbilical incision for the laparoscope. Trocar B was located in the right midclavicular line halfway between the costal margin and the umbilicus. Trocar C was located in the right midclavicular line immediately below the costal margin. Trocar D was located in the left midclavicular line halfway between the costal margin and the umbilicus. Trocar E was located in the left anterior axillary line below the border of the spleen. Trocar F was located in the right anterior axillary line just below the costal margin. Trocars B–E were used for laparoscopic splenectomy and for laparoscopic left partial hepatectomy. Trocars B–D and F were used for laparoscopic right partial hepatectomy.

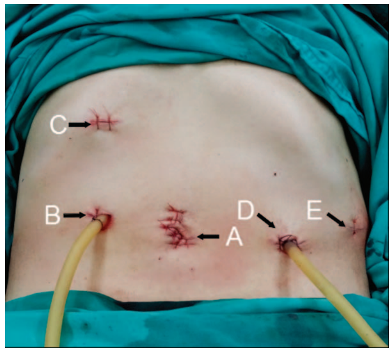

Figure 1. Five ports of the LSH.

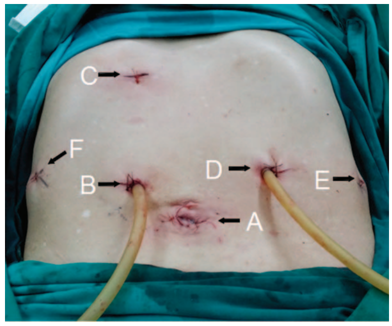

Figure 2. Five+one ports of the LSH.

During the LSH procedure, laparoscopic hepatectomy was performed after laparoscopic splenectomy. The procedure for laparoscopic splenectomy has been described.[10] Laparoscopic partial hepatectomy was performed as follows. First, the device for the modified Pringle maneuver, prepared as described elsewhere,[11] could be used to block the inflow of blood into the entire liver if necessary. If the tumor was located in the right lobe, trocar E was commonly used for the device. If the tumor appeared in the left lobe, trocar F was prepared for the device, when needed. With increasing experience with laparoscopy, trocar F was omitted in the laparoscopic left hemihepatectomy or laparoscopic hepatic left lateral lobectomy.

If the laparoscopic approach was a wedge hepatectomy, ultrasonography was used to assess the relationship between the tumor and the major vascular structures and the boundaries of the tumor. A 1-cm hepatic resection line beyond the margin of the tumor was scored by electrocautery.

The entire spleen was removed through trocar D with an electromechanical morcellator (TSCS, Hangzhou, China)[10]; spleen samples had a cylindrical appearance (**Figure 3**). The tumor specimen was loaded into a specimen bag and removed though the enlarged umbilical incision, usually <5 cm, which was extended to a proper length along the linea alba, according to the size of the tumor. At the end of the operation, 2 surgical drainage tubes were placed at the epiploic foramen and under the left diaphragm.

OSH Procedures

For tumors in the left liver, a midline laparotomy was selected. For those in the right liver, a large inverse L-shaped incision was selected. The procedure for OSH was similar to that described above for LSH.

Statistical Analysis

Data are presented as the mean ± SD, median (range), or percentage. Student's *t* test was used to compare parametric data, the Mann-Whitney U test was used to compare nonparametric data, and Fisher's exact test was used to compare percentages. $P < .05$ indicated statistical significance. SPSS version 16.0 software (SPSS, Chicago, Illinois, USA) was used for statistical analysis.

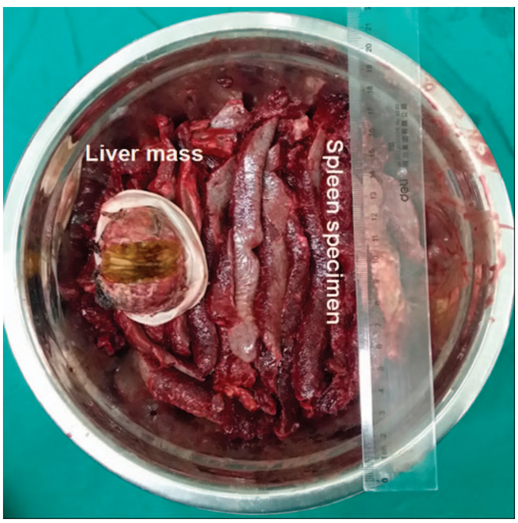

Figure 3. Liver specimen and cylindrical spleen tissue.

RESULTS

Eleven patients who had cirrhotic hypersplenism with HCC underwent OSH, and 12 underwent LSH. The OSH and LSH groups were similar in sex, age, etiology of cirrhosis, APACHE II score, Child-Pugh class, tumor size, length of the spleen, preoperative WBC and platelet counts, and preoperative AST, ALT, BUN, and CRE levels (**Table 1**).

Operation

Duration of the operation and the volume of intraoperative estimated blood loss and blood transfused were similar in the 2 groups ($P > .05$ each; **Table 2**).

Postoperative Recovery

Compared with the OSH group, the LSH group exhibited a lower visual analog (VAS) pain score on the first day after surgery, and shorter times to first oral intake, flatus, off-bed activity, and hospital stay (all $P < .05$; **Table 2**).

Complications

All 11 patients in the OSH group and 7 of 12 in the LSH group had postoperative complications ($P < .05$). The 11 complications in the OSH group were as follows: 2 patients with incision complications, 2 with pneumonia, 1 with an emergency operation for bleeding, 1 with pancreatic fistula, and 5 with asymptomatic portal vein thrombosis. Of the 7 patients who had complications in the LSH group, 1 had pneumonia, 1 had an incision complication, and 5 had asymptomatic portal vein thrombosis. All complications were successfully managed. No emergency laparotomy for bleeding was performed after LSH (**Table 2**).

Body Temperature and WBC Counts

There was no fever in either group before surgery. Compared with the OSH group, the LSH group had fewer days of postoperative temperature >38.0°C ($P < .01$; **Table 3**). Postoperative fever was absent in only 2 patients in the LSH group and in none in the OSH group, and there was nonsignificant similarity between the groups ($P > .05$). Although the WBC counts of the groups were similar at admission ($P > .05$), mean WBC counts on postoperative days 1 ($P < .01$) and 7 ($P < .01$) were significantly lower after LSH than after OSH. Compared with the OSH group, the percentage of patients with normal WBC counts on postoperative day 7 was significantly higher in the LSH group ($P < .05$).

Table 1.
Baseline Demographic and Clinical Characteristics of the OSH and LSH Groups

Variable	OSH (n = 11)	LSD (n = 12)	*P*
Sex, male/female, n	6/5	8/4	.680
Age, mean ± SD, years	57.1 ± 8.9	59.7 ± 6.4	.448
Etiology, n			
HBV cirrhosis	6	8	.680
HCV cirrhosis	2	2	1.000
Schistosome cirrhosis	1	0	.478
Alcoholic cirrhosis	0	1	1.000
Autoimmunity liver cirrhosis	0	1	1.000
Idiopathic cirrhosis	2	0	.217
APACHEII, mean ± SD	3.7 ± 2.0	4.8 ± 2.2	.251
Child-Pugh classification, A/B, n	7/4	5/7	.414
Tumor size, mean ± SD, cm	3.30 ± 0.62	3.12 ± 0.56	.464
Length of spleen, mean ± SD, mm	178.5 ± 20.6	179.7 ± 31.4	.921
WBC, mean ± SD, $10^{9/L}$	2.63 ± 0.69	2.87 ± 0.58	.380
PLT, mean ± SD, 10^9/L	43.9 ± 4.0	38.6 ± 10.5	.129
AST, mean ± SD, U/L	32.2 ± 17.3	30.5 ± 6.9	.759
ALT, mean ± SD, U/L	21 (17–34)	21.5 (13–39)	.757
BUN, mean ± SD, mM	5.05 ± 1.49	5.77 ± 1.75	.305
CRE, median (range), μM	72 (54–90)	78.5 (59–83)	.216

Data are mean ± SD, median (range) values, or number of patients, as indicated. HBV, hepatitis B virus; HCV, hepatitis C virus; PLT, platelet

Postoperative Liver and Renal Function

There were similarities between the groups of preoperative AST and ALT levels. Although the AST level was similar on postoperative day 1 ($P > .05$), median AST on postoperative day 7 ($P < .001$) was significantly lower in the LSH group than in the OSH group (**Table 4**). Moreover, although the ALT level on postoperative day 1 was not significantly different in the 2 groups, median ALT was significantly lower in the LSH group than in the OSH group on postoperative day 7 ($P < .05$).

There were also similarities between the groups in preoperative BUN and CRE levels (**Table 1**). Compared with the OSH group, the LSH group had significantly lower mean BUN levels on postoperative days 1 ($P < .001$) and 7 ($P = .001$) (**Table 4**). Similarly, the LSH group has lower mean CRE levels on postoperative days 1 ($P < .001$) and 7 ($P = .001$).

The median observation period was 9 months (range, 5–14) for the LSH group and 33 months (range, 16–52) for the OSH group. Two patients had HCC recurrence and no patients died in the LSH group, whereas in the OSH group, 4 patients had HCC recurrence and 2 patients died of cancer-related causes and liver failure.

DISCUSSION

Worldwide, HCC is one of the most common malignant tumors. Hepatectomy is regarded as an effective treatment for HCC. However, it is often accompanied with hypersplenism caused by cirrhotic portal hypertension,[2] resulting in low WBC and platelet counts. Because of poor liver function and coagulation disorders, hepatectomy has been controversial in patients with both HCC and portal hypertension.[3–5] Studies have shown that the advantages of splenectomy are that it may improve coagulation and liver function,[12–14] nutritional metabolism,[13] and Child-Pugh scores for patients with cirrhotic hypersplenism.[7] Hence, 2 types of 2-stage operations have been introduced for clinical management. One is open splenectomy followed by hepatec-

Table 2.
Intraoperative and Postoperative Characteristics of the OSH and LSH Groups

Variable	OSH (n = 11)	LSD (n = 12)	*P*
Duration of operation, mean ± SD, min	197.7 ± 28.8	202.1 ± 34.0	.745
Estimated blood loss, mean ± SD, mL	266.4 ± 91.7	229.2 ± 64.1	.269
Blood transfused, median (range), mL	0 (0–400)	0 (0–0)	.740
VAS pain score on the first day, mean ± SD	6.2 ± 0.6	3.4 ± 0.9	<.001
Time to first oral intake, mean ± SD, d	2.9 ± 0.5	1.9 ± 0.5	<.001
Time to first flatus, mean ± SD, d	3.7 ± 1.0	2.7 ± 0.9	.014
Time to off-bed activity, mean ± SD, d	4.4 ± 0.7	2.5 ± 0.7	<.001
Duration of hospitalization, mean ± SD, d	15.1 ± 2.3	8.6 ± 1.3	<.001
Perioperative complications, n	11	7	.037
Incision complications	2	1	.590
Incisional hernia	0	0	1.000
Superficial SSI	2	1	.590
Deep SSI	0	0	1.000
Pneumonia	2	1	.590
Organ space SSI	0	0	1.000
Emergency operation for bleeding	1	0	.478
Pancreatic fistula	1	0	.478
Asymptomatic portal vein thrombosis	5	5	1.000

Data are the mean ± SD or number of patients. SSI, surgical site infection.

Table 3.
Postoperative Fever and WBC Counts of the OSH and LSH Groups

Variable	OSH (n = 11)	LSD (n = 12)	*P*
Postoperative fever, mean ± SD, d	4.5 ± 1.4	2.1 ± 1.9	.002
No fever, n	0	2	.478
WBC day 1, mean ± SD, 10^9/L	19.7 ± 5.8	13.3 ± 3.2	.003
WBC day 7, mean ± SD, 10^9/L	14.6 ± 4.0	9.5 ± 3.0	.002
Normal WBC, d 1, n	0	1	1.000
Normal WBC, d 7, n	1	7	.027

Data are mean ± SD or number of patients. Postoperative fever, the number of days of postoperative body temperature >38.0°C; d 1, postoperative day 1; d 7, postoperative day 7.

tomy, and the other is laparoscopic splenectomy followed by open hepatectomy.[7] However, these 2-stage operations may result in more complications[6,15] and delay timely surgical treatment for HCC that may grow or metastasize during the waiting time for the second operation.

A previous study and a meta-analysis all reported that, compared with open hepatectomy group, laparoscopic hepatectomy group is associated with fewer complications, more rapid recovery, and lower morbidity.[16,17] A meta-analysis suggested that simultaneous OSH does not increase postoperative complications or perioperative mortality and can solve hypersplenism, improve the functions of coagulation and immunity, and decrease the incidence of postoperative bleeding.[18] Some studies re-

Table 4.
Postoperative Liver and Renal Functions of the OSH and LSH Groups

Variable	OSH (n = 11)	LSD (n = 12)	*P*
AST day 1, mean ± SD, U/L	164.9 ± 46.6	158.7 ± 46.5	.751
AST day 7, median (range), U/L	57 (47–94)	32.5 (17–45)	<.001
ALT day 1, median (range), U/L	154 (107–177)	97.5 (42–192)	.175
ALT day 7, mean ± SD, U/L	65 (51–89)	39 (21–94)	.048
BUN day 1, mean ± SD, mmol/L	11.3 ± 2.4	5.6 ± 1.8	<.001
BUN day 7, mean ± SD, mmol/L	10.5 ± 3.5	6.1 ± 1.6	.001
CRE day 1, mean ± SD, umol/L	138.7 ± 20.9	92.7 ± 17.6	<.001
CRE day 7, mean ± SD, umol/L	99.7 ± 24.0	70.7 ± 14.1	.001

Data are mean ± SD or median (range) values. d 1, postoperative day 1; d 7, postoperative day 7.

ported that, compared with open hepatectomy alone, simultaneous OSH is associated with improved 5-year tumor-free survival in patients who have HCC with hypersplenism.[8,9]

With the rapid development of minimally invasive laparoscopic techniques, LSH was devised and successfully performed by surgeons with excellent laparoscopic skills.[19–21] In 2009, hand-assisted LSH was first described to be safe in a case report.[19] In 2013, another case report described uneventful simultaneous LSH without hand assistance.[20] In comparison to OSH, Miyoshi et al[21] demonstrated that LSH is safe and useful in the treatment of HCC with hypersplenism within limited criteria. However, the advantages of LSH compared with OSH have not yet been clarified. We think the surgeon and surgical assistants should possess skillful laparoscopy techniques and have abundant experience with laparoscopic splenectomy and laparoscopic hepatectomy. Before performing the new operation, we had performed ~200 laparoscopy splenectomies and ~80 laparoscopic hepatectomies.

In this study, patients who underwent conventional OSH complained of pain associated with the large incision, usually 30–45 cm, that was held open by retractors. In contrast, the total length of all incisions with LSH was ~10 cm without muscle injury caused by the retractors, and postoperative abdominal pain was rare. Furthermore, minimally invasive LSH had more rapid recovery and lesser postoperative complication rates, owing to the small incisions required. The alleviated abdominal pain due to LSH may be associated with other benefits. For example, the absence of pain may improve appetite and shorten postoperative time to oral intake. Reduced pain may also shorten the time to first off-bed activity and flatus. In addition, a small incision with reduced pain may decrease patients' psychological trauma and increase their confidence in overcoming their concerns.

Compared with OSH, LSH also significantly shortened the number of days after surgery that patients had a body temperature >38.0°C. Although preadmission WBC count was similar in the 2 groups, compared with OSH, LSH had significantly lower WBC count on postoperative day 7 ($P < .01$). These findings were consistent with each other, because high WBC count is associated with high body temperature.

Compared with the OSH group, the LSH group had significantly lower ALT and AST concentrations on postoperative day 7. We also found that BUN and CRE concentrations on postoperative days 1 and 7 were lower in the LSH group, providing further evidence of the benefits of LSH. These findings also demonstrated a difference between 2 groups of the recovery of the liver and kidneys due to surgical trauma.

We are in the initial developmental stages of LSH, and patients with HCC who elect to undergo the procedure should meet the following indications: tumor size <5 cm, tumor location in the peripheral right or left lobe of the liver, and Child-Pugh Class A or B.

CONCLUSIONS

With appropriate indications, synchronous LSH is a safe, feasible, and effective surgical procedure with satisfactory recovery, and it allows for optimal minimally invasive treatment for patients with cirrhotic hypersplenism and HCC. This study was limited by its small sample size;

therefore, prospective studies with a larger cohort, including randomized comparisons with open surgery, should be performed.

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