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Short Running Head:

Laparoscopic segmentectomy 2

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Abstract

Background Anatomic liver resection (ALR) has been established to eliminate the tumor-bearing hepatic region with preservation of the remnant liver volume for liver malignancies. Recently, laparoscopic ALR has been widely applied; however, there are few reports on laparoscopic segmentectomy 2. This study aimed to present the standardization of laparoscopic segmentectomy 2 with surgical outcomes.

Methods This study included seven patients who underwent pure laparoscopic segmentectomy 2 by the Glissonean approach from January 2020 to December 2021. Four of them had hepatocellular carcinoma, two had colorectal liver metastasis, and one had hepatic angiomyolipoma, which was preoperatively diagnosed with hepatocellular carcinoma. In all patients, preoperative three-dimensional (3D) simulation images from dynamic CT were reconstructed using a 3D workstation. The layer between the hepatic parenchyma and the Glissonean pedicle of segment 2 (G2) was dissected to encircle the root of G2. After clamping or ligation of the G2, 2.5 mg of indocyanine green was injected intravenously to identify the boundaries between segments 2 and 3 with a negative staining method under near-infrared light. Parenchymal transection was performed from the caudal side to the cranial side according to the demarcation on the liver surface, and the left hepatic vein was exposed on the cut surface if possible.

Results The mean operative time for all patients was 281 min. The mean blood loss was 37 mL, and no transfusion was necessary. Estimated liver resection volumes significantly correlated with actual liver resection volumes (r = 0.61, p = 0.035). After the operation, one patient presented with asymptomatic deep venous and pulmonary thrombosis, which was treated with anticoagulant therapy. The mean length of hospital stay was 8.9 days.

Conclusions Laparoscopic segmentectomy 2 by the Glissonean approach is a feasible and safe procedure with the preservation of the nontumor-bearing segment 3 for liver tumors in segment 2.

Keywords:

anatomic liver resection, Glissonean approach, hepatectomy, indocyanine green, liver resection, segmentectomy

Introduction

Laparoscopic liver surgery has been widely performed worldwide for patients with liver cancers. Anatomic liver resection (ALR) after portal staining or inflow clamping of the target territory was established to remove the tumor-bearing hepatic region with the preservation of the remnant liver function and volume for liver cancers (1). Meanwhile, it was technically demanding to perform parenchymal transection using laparoscopic ALR (LALR) according to segments or sections. Recently, LALR has been applied because the anatomical features of the Glissonean pedicles and hepatic veins have been understood, and the Glissonean approach has been adopted (2,3). Some studies reported that LALR can provide comparable oncological outcomes to open ALR for hepatocellular carcinoma (4). In addition, the use of indocyanine green (ICG) fluorescence imaging allows for the visualization of the demarcation line and intersegmental/sectional planes in LALR (5–9). However, performing LALR is more difficult for tumors in cranio-dorsal segments compared to those in ventral and caudal segments due to the visual field and movement limitations specific to laparoscopic surgery.

For tumors in segment 2 (S2), laparoscopic left lateral sectionectomy has been applied because it is technically easier than laparoscopic segmentectomy 2; however, the preservation of parenchyma of segment 3 (S3), which is a nontumor-bearing hepatic region, is disregarded. In particular, patients with hepatocellular carcinoma often had underlying chronic hepatitis or liver cirrhosis; therefore, the preservation of the more residual parenchyma is important to avoid post-hepatectomy liver failure. The difficulty score of laparoscopic segmentectomy 2 is calculated between 5 to 8 points, which is considered a procedure with intermediate or high-level difficulty based on the scoring system for laparoscopic liver resection by Ban et al. (10). A few studies showed the feasibility of laparoscopic segmentectomy 2. This study aimed to demonstrate the standardization of laparoscopic segmentectomy 2 with the procedures and surgical outcomes.

Materials and Methods

Patients

This study was approved by the institutional review board of Kobe University Hospital, and informed consent was obtained from all patients. This study included seven patients who underwent laparoscopic segmentectomy 2 by the Glissonean approach at the Kobe University Hospital, Kobe, Japan, from January 2020 to December 2021. Four patients had hepatocellular carcinoma, two had colorectal liver metastasis, and one had hepatic angiomyolipoma, which was preoperatively diagnosed with hepatocellular carcinoma.

In all patients, preoperative three-dimensional (3D) simulation images from dynamic computed tomography were reconstructed using a 3D workstation (SYNAPSE VINCENT; Fujifilm Medical, Tokyo, Japan) to evaluate anatomical variations of the Glissonean pedicles and hepatic veins (Fig. 1). Moreover, virtual hepatectomy on the simulation images was performed, and a cutting point of the Glissonean pedicle of segment 2 (G2) was determined to predict the direction of the transection plane and estimated resecting liver volume.

Surgical procedures of laparoscopic segmentectomy 2

All surgical procedures were performed using the five-port system. After the round ligament was dissected and ligated by an endoloop, its stump was raised up to the ventral abdominal wall to lift the liver edge. The hepatoduodenal ligament was encircled by cotton tape for the Pringle maneuver. Intraoperative ultrasonography was performed to locate the G2 at the dorsal side of the liver and tumor. The Glissonean approach was applied to encircle the G2 (Fig. 2). In many cases, liver parenchyma at the pons between left lateral and left medial sections was transected to expose the G2 (Fig. 2C). The layer between the Glissonean sheath of G2 and liver parenchyma was dissected without destroying as much parenchyma as possible to encircle the root of G2 by a silk thread (Fig. 2B, D). After confirming the demarcation by clamping the root of

G2, the root of G2 was ligated by the thread and clipped with a polymeric clip. After clipping of the G2, 2.5 mg of ICG (Diagnogreen; Daiichi Sankyo, Tokyo, Japan) was injected intravenously to identify the demarcation line clearly between S2 and S3 with a negative staining method under the ICG fluorescence imaging system (VISERA ELITE II; Olympus, Tokyo, Japan) (Fig. 3). Parenchymal transection was initiated along the demarcation on the liver surface using ultrasonic shears (HARMONIC HD 1000i Shears; Ethicon Endo-Surgery, Cincinnati, USA). The clamp crushing method with the ultrasonic shears was applied for the intrahepatic parenchymal transection under intermittent clamping for 15 or 20 min, which was released for 5 min using the Pringle maneuver. A suction device with a monopolar electrode connected to a soft-coagulation system was used to stop the oozing or bleeding on the transection plane. At the dorsal part of the left lateral lobe, parenchymal transection was performed gradually from the root side of the G2 to the peripheral side from between the patient's legs. At the ventral part of the left lateral lobe, parenchymal transection was performed from the left side of the patient's position to make the transection plane smooth. After returning to the position between the legs, the root of the G2 was cut. The main trunk of the left hepatic vein (LHV) was exposed following parenchymal transection to the cranial part. The hepatic veins from segment 2 (V2) were clipped and cut (Fig. 4A), and transection was finished (Fig. 4B).

The patients' preoperative data, operative videos, operative time, blood loss, the weight of the specimens, postoperative morbidity, and length of postoperative hospital stay were recorded. In addition, the surgical outcomes were compared with the patients who underwent laparoscopic left lateral sectionectomy for tumors in segment 2 as a historical control. Before the introduction of laparoscopic segmentectomy 2, all patients with tumors in segment 2 usually undergo laparoscopic left lateral sectionectomy.

Statistical analysis

All statistical analyses were performed using JMP software version 10 (SAS Institute, Cary, NC, USA). Continuous variables were expressed as mean ± standard deviation and were compared using Student's t-test between laparoscopic segmentectomy 2 and laparoscopic left lateral sectionectomy groups. Between-group differences in categorical variables were evaluated using Fisher exact tests. $P < 0.05$ was considered to be significant.

Results

The preoperative data and surgical outcomes of the patients are summarized in Table 1. There were five men and two women, with a mean age of 63.9 years. The mean tumor size is 4.0 cm. All patients had Child-Pugh A, but two patients (Case no.2 and 7) had cirrhotic livers. The difficulty score for laparoscopic liver resection is 6 for all (10). The mean operative time for all patients was 281 min. The mean blood loss was 37 mL, and no transfusion was necessary. The estimated liver resection volumes significantly correlated with actual liver resection volumes (r = 0.61, p = 0.035) (Fig. 5). After the operation, there was one patient with asymptomatic deep venous and pulmonary thrombosis who was treated with anticoagulant therapy. The mean length of hospital stay was 8.9 days. The surgical margin was negative in all patients. Intraoperative procedures of these patients are shown in Supplementary Video 1 (Case no. 3) and 2 (Case no. 6). In comparison between the patients who underwent laparoscopic segmentectomy 2 and laparoscopic left lateral sectionectomy, no significant differences between groups were identified in the preoperative patients' data and operative outcomes except for the difficulty scores (Table 2).

Discussion

Anatomic liver resection was defined as the complete removal of liver parenchyma confined within the responsible portal territory (11). Minimally invasive ALR is gaining popularity due to the progress in understanding the anatomical features of the Glissonean pedicles and hepatic veins (2). This study shows that the LALR of segment

2 by the Glissonean approach is a feasible and safe procedure with satisfactory surgical outcomes and reasonable accuracy of ALR. Several case reports also showed the feasibility of laparoscopic segmentectomy 2 (12–14); however, no studies have demonstrated the standardization of laparoscopic segmentectomy 2. Herein, we discuss the standardization of the procedures of laparoscopic segmentectomy 2 by the Glissonean approach.

In laparoscopic segmentectomy 2, the Glissonean approach of the G2, the identification of the demarcation line between S2 and S3, and the exposure of the LHV on the raw surface are key factors to performing precise ALR. First, the Glissonean approach is required to visualize accurate demarcation of the S2. It also facilitates favorable outcomes in blood loss and postoperative complications within a short operative time (3). Encircling of the G2 is technically demanding due to the secluded location of the root. Liver parenchyma at the pons between the left lateral and left medial sections often covers the root of the G2. Intraoperative ultrasonography is useful for detecting the location of the root. Five of the seven patients had the pons that had to be transected to expose the dorsal side of the root (Fig. 2C). Therefore, an intrahepatic Glissonean approach can be applied more than the extrahepatic Glissonean approach. Second, the ventral demarcation line is located on the more cranial side of the left lateral lobe than expected, and the dorsal one is located at the center of the dorsal surface, but it is often intricate. We use ICG fluorescence imaging to determine transection lines on the liver surface for LALR because it provides excellent visualization of demarcation lines even if patients have cirrhotic livers. Thus, it facilitates less possibility of remaining in the ischemic hepatic region in the remnant liver. Finally, the exposure of the main trunk of the LHV on the transection plane is important to adjust the plane to the intersegmental plane between S2 and S3. Theoretically, there are fewer Glissonean pedicles across the intersegmental plane; therefore, it is considered to be a suitable plane for transection. We consider that exposing hepatic veins from the root to the periphery has a technical advantage in preventing split injury of V2s (15). The preservation of the LHV by cutting V2 branches is also reasonable in preventing congestion of the blood perfusion in S3. However, attention should be paid to anatomical variation of hepatic veins because the LHV does not always run on the intersegmental plane between S2 and S3. Kobayashi et al. have reported that an umbilical fissure vein (UFV) was seen in 91.2%, and it was a tributary of the LHV (72%), middle hepatic vein (MHV) (17.2%), or the confluence of the LHV and the MHV (10.8%) in a total of 102 healthy living donor candidates (16). In the present study, only one patient (Case no. 6) had a thick UFV draining into the MHV and a thin LHV (Fig. 1B). In this case, the LHV, which was a main drainage vein of S2, did not run on the intersegmental plane. As the plane was located between the LHV and the UFV, the LHV was cut.

The surgical outcomes of laparoscopic segmentectomy 2 are satisfactory. The surgical outcomes are comparable to those in the patients who underwent laparoscopic left lateral sectionectomy, although the left lateral sectionectomy group was a historical control. Laparoscopic segmentectomy 2 should be mastered as well as laparoscopic left lateral sectionectomy because cirrhotic patients with worse liver reserve need this procedure. In addition, preservation of remnant liver reserve would make the next intervention easy when recurrence is seen. However, there are some relative contraindications. The tumor in contact with or close to the proximal left hepatic vein should be removed by left lateral sectionectomy. The macrovascular invasion should also be contraindicated.

We consider that evaluating the accuracy of ALR is important because an objective quantitative evaluation method is limited (17). In this study, the 3D volume analyzer was used to evaluate the accuracy of laparoscopic segmentectomy 2. There was a correlation between the estimated resecting liver volume and the actual resected liver weight, although it was not strong. Cutting thin Glissonean branches which were not detected by preoperative imaging may have affected the result. We need to recognize that there are a few branches around the main trunk of the G2. Moreover, experiences with difficult liver segments under the standardization could improve the accuracy of ALR.

Preoperative 3D simulation images are used not only to estimate resecting volume but also to understand 3D vascular anatomy because it is intuitively understandable and sharable for operators and assistants. 3D simulation is quite essential for performing liver resections, especially above segmentectomy. The resecting liver volume and the future remnant liver should be understood to preserve enough liver reserve that is associated with prognosis. In addition, understanding 3D vascular structures facilitates accurate anatomical resection. However, we need to understand that 3D simulation images are not perfect enough to delineate all branches of Glissonean pedicles and hepatic veins. Optimal dose and timing of administration of contrast agent should be determined, and 3D workstations are expected to be improved in the future.

There are several limitations to the present study. It was a retrospective study with a small sample size and short-term outcome. Therefore, further studies with a larger number of patients are required to confirm that laparoscopic segmentectomy 2 contributes to better short- and long-term outcomes.

In conclusion, laparoscopic segmentectomy 2 by the Glissonean approach is a feasible and safe procedure with the preservation of nontumor-bearing segment 3. At specialized facilities, it can be an optional procedure for liver tumors in segment 2 instead of left lateral sectionectomy.

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Disclosures

Takeshi Urade, Masahiro Kido, Kaori Kuramitsu, Shohei Komatsu, Hidetoshi Gon, Kenji Fukushima, Shinichi So, Takuya Mizumoto, Yoshihide Nanno, Daisuke Tsugawa, Tadahiro Goto, Sadaki Asari, Hiroaki Yanagimoto, Hirochika Toyama, Tetsuo Ajiki, and Takumi Fukumoto have no conflicts of interest or financial ties to disclose.

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Figure Legends

Figure 1. Preoperative three-dimensional simulation images from dynamic computed tomography

A. Umbilical fissure vein (white arrowhead) as tributary to the left hepatic vein. B. Umbilical fissure vein (white arrowhead) as tributary to the middle hepatic vein.

Figure 2. Glissonean approach for the Glissonean pedicle of segment 2 (G2)

A. Extrahepatic Glissonean approach without parenchymal dissection. B. Encircling G2. C. Intrahepatic Glissonean approach after transection of the pons. D. Encircling G2.

Figure 3. Indocyanine green fluorescence imaging by the negative staining method

A. Demarcation on the dorsal part of the left lateral lobe. B. Demarcation on the ventral part of the left lateral lobe.

Figure 4. Exposure of the left hepatic vein (LHV)

A. After the exposure of the root of the LHV, some hepatic vein branches of segment 2 (V2) were cut. B. The LHV (blue arrows) and the stump of the Glissonean pedicle of segment 2 (Green arrow) were exposed on the transection plane.

Figure 5. The correlation between the estimated resecting liver volume and actual resected liver weight

Table 1. The preoperative data and surgical outcomes of the patients

Case no.	Sex/ Age	BMI (kg/m^2)	Final diagnosis	Tumor size (cm)	ICGR15 (%)	Difficulty score†	Operative time (min)	Blood loss (ml)	Morbidity	Hospital stay (days)
1	M/69	24.0	HCC	3.3	12.2	6	247	20	-	7
2	M/62	27.8	HCC	4.5	8.3	6	302	100	-	9
3	F/47	20.0	AML	3.0	4.6	6	229	min	-	7
4	M/62	21.6	CRLM	5.8	3.5	6	321	min	-	8
5	M/60	18.3	CRLM	5.5	4.4	6	286	50	-	8
6	F/77	32.8	HCC	3.7	17.4	6	309	30	DVT, PE	15
7	M/70	22.7	HCC	2.3	7.6	6	270	60	-	8

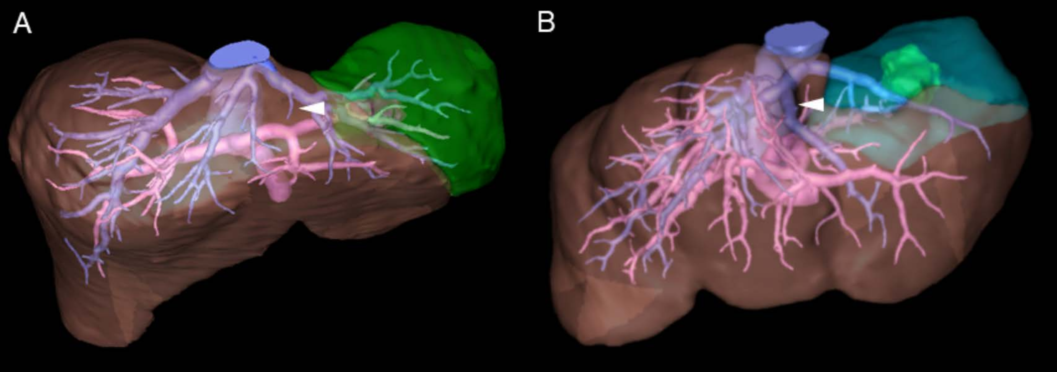
AML, angiomyolipoma; *BMI,* body mass index, *CRLM,* colorectal liver metastasis; DVT, deep vein thrombosis; *F,* female; *HCC,* hepatocellular carcinoma; *ICGR15,* indocyanine green retention rate at 15 min; *M,* male; min, minimum; *PE,* pulmonary embolism

† Difficulty score was calculated according to the difficulty scoring system for laparoscopic liver resection by Ban et al. (10).

Table 2. Comparison of preoperative data and surgical outcomes between patients who underwent laparoscopic segmentectomy 2 and laparoscopic lateral sectionectomy for tumors in segment 2

Variables	Laparoscopic segmentectomy 2 (n=7)	Laparoscopic left lateral sectionectomy (n=6)	P-value
Age years (range)	63.9 ± 9.5 (47-77)	69.7 ± 4.2 (64-74)	0.20
Sex male: female	5: 2	4: 2	1.0
BMI kg/m^2 (range)	23.9 ± 5.0 (18.3-32.82)	24.0 ± 6.0 (18.12-32.37)	0.98
Solitary tumor: Multiple tumors	7: 0	4: 2	0.19
Maximum tumor size cm (range)	4.01 ± 1.30 (2.3-5.8)	3.41 ± 1.43 (1.9-5.5)	0.45
Proximity to major vessels n (%)	0 (0%)	1 (17%)	0.46
Macrovascular invasion n (%)	0 (0%)	1 (17%)	0.46
ICGR15 % (range)	8.29 ± 5.0 (3.5-17.4)	12.0 ± 7.1 (5.6-25.2)	0.30
Child-Pugh A n (%)	7 (100%)	6 (100%)	
Cirrhosis n (%)	2 (29%)	0 (0%)	0.45
Repeat hepatectomy n (%)	0 (0%)	2 (33%)	0.19
Difficulty score (range)	6 ± 0 (6)	4.8 ± 0.8 (4-6)	0.0017
Operative time min (range)	280.6 ± 33.7 (229-321)	327.1 ± 55.9 (247-407)	0.09
Blood loss ml (range)	37.1 ± 35.9 (0-100)	11.7 ± 19.4 (0-50)	0.15
Morbidity (Clavien-Dindo Classification≧GradeⅢ) n (%)	0 (0%)	0 (0%)	
Hospital stay days (range)	8.9 ± 2.8 (7-15)	8.3 ± 1.0 (7-10)	0.67
Pathological findings HCC: CRLM: IHCC: others	4: 2: 0: 1	4: 1: 1: 0	
Surgical margin negative n (%)	7 (100%)	6 (100%)	

BMI, body mass index, *CRLM,* colorectal liver metastasis; *HCC,* hepatocellular carcinoma; *ICGR15,* indocyanine green retention rate at 15 min; *IHCC,* intrahepatic cholangiocarcinoma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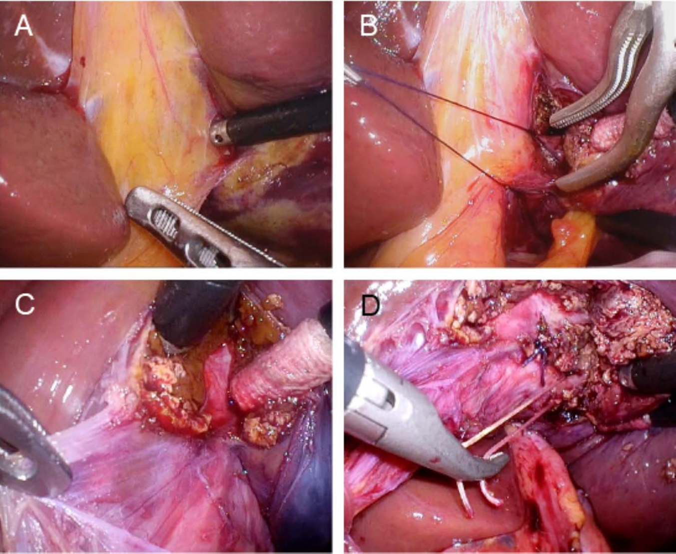
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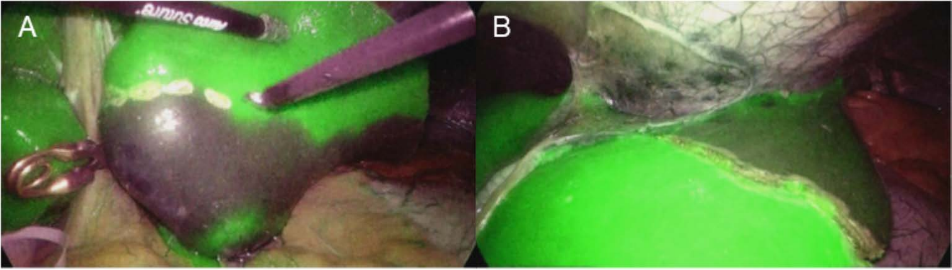
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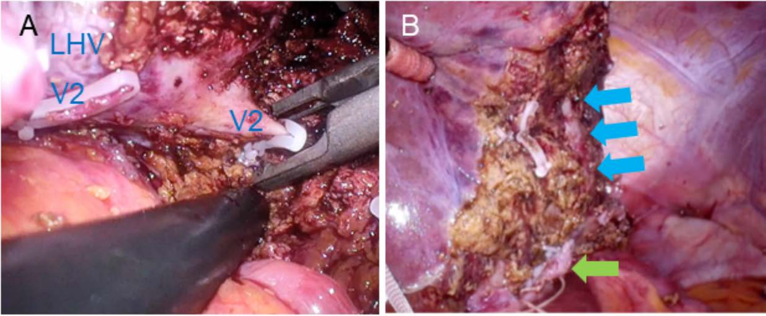
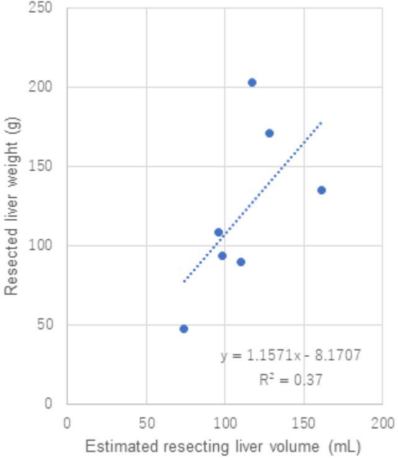

A
LHV
V2
V2
B



250
200
150
100
50
0
Resected liver weight (g)
0
50
100
150
200
Estimated resecting liver volume (mL)
y = 1.1571x - 8.1707
R² = 0.37