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Effectiveness of Laparoscopic Repeat Hepatectomy for Recurrent Liver Cancer

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Background: Patients with recurrent hepatocellular carcinoma or metastatic liver cancer from colorectal cancer after surgical resection have traditionally been treated with conventional open surgery. However, recent technical advances have facilitated laparoscopic repeat hepatectomy (LapRH), which has advantages over open laparotomy. We describe the results of LapRH at our institution and retrospectively compare short-term outcomes after LapRH and initial laparoscopic partial liver resection (LapPLR).
Methods: From April 2010 through December 2017, 24 patients (16 men, 8 women; median age, 69 years) underwent LRH for cancer recurrence or metastasis after initial partial hepatectomy at our institution. LapRH involved partial hepatectomy in 21 patients and lateral segmentectomy in 3 patients. Short-term outcomes (operative time, intraoperative blood loss, and postoperative hospital stay) for these 24 patients were compared with those for 117 patients who underwent initial LapPLR during the same period.
Results: There were no significant differences between the LapPLR and LapRH groups in baseline characteristics, including patient age and underlying disease. No LapRH procedure required conversion to open surgery. There were no statistically significant differences between the groups in median operation time (268 min for LapPLR, 294 min for LapRH; $p = 0.55$), blood loss (224.0 mL for LapPLR, 77.5 mL for LapRH; $p = 0.76$), or length of hospital stay (11.0 days for LapPLR, 10.2 days for LapRH; $p = 0.83$).
Conclusions: LapRH for recurrent liver cancer yielded satisfactory outcomes when compared with those of initial hepatectomy. Further studies are needed, however, to confirm the present results.
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Key words: reoperation, hepatectomy, laparoscopy, adhesions

Introduction

Laparoscopic techniques have been widely applied to various fields of surgery, and the number of favorable reports on laparoscopic liver resection (LapLR) is increasing. Many groups have provided evidence of the safety, feasibility, and oncological efficiency of LapLR. Accordingly, use of LapLR has dramatically increased and its adoption has expanded[1–5]. We have conducted more than 200 LapLRs to date and have standardized the procedure.

For patients who previously underwent abdominal surgery-for recurrent hepatocellular carcinoma (HCC) or metastatic liver cancer from colorectal cancer[6–8], for example-conventional open surgery was indicated for liver resection[6–10], whereas LapLR has typically been indicated for small, easily accessible tumors[11]. For LapLR, surgeons need to contend with restricted manipulation, lack of manual sensation, and disorientation arising from the lack of overview[12,13]. Moreover, LapLR has technical difficulties related to liver mobilization because of adherences near the liver, which vary by patient.

Reports of laparoscopic repeat hepatectomy (LapRH) have recently been published, probably because of the development of surgical instruments and the consequent

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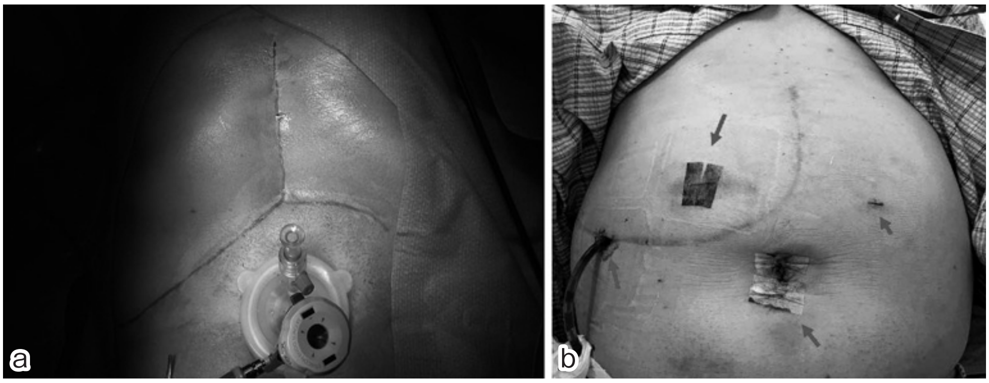

Fig. 1 (a) LapRH after right hepatectomy. A Lap Protector™ was attached to the navel. We used a 12-mm port and 5-mm ports for EZ Access. (b) LapRH after excision of the anterior segment of the liver. We created a 5-mm incision wound that was consistent with previous surgical handiwork.

standardization of laparoscopic procedures[14,15]. In LapRH, however, the technical difficulty of the operation depends on various factors. In contrast, taking advantage of the magnifying effect of laparoscopic surgery, pinpoint surgery in a narrow space has become possible. We have been active proponents of LapRH for recurrent liver cancer and also perform LapRH for patients with a history of upper abdominal surgery or hepatectomy. In this paper we compare the safety, feasibility, and short-term results of our current LapRH approach between a case group in which the first laparoscopic partial liver resection (LapPLR) was recently standardized and a group undergoing LapRH.

Materials and Methods

Patients and Categorization

All laparoscopic hepatectomies performed in this study were covered by Japanese insurance, and written informed consent was obtained from all patients. This study was approved by the ethics committee of Nippon Medical School (No. 28-02-725).

The study sample was selected from among the approximately 200 laparoscopic hepatectomies performed in our department from April 2010 through December 2017; 24 patients had undergone LapRH. All patients underwent first hepatectomy at our hospital, and the procedure included both laparotomy and laparoscopy. Tumor location was distributed throughout all liver segments (segments 1-8).

The LapRH procedure was partial resection of the liver or lateral segmentectomy of the liver. Regarding LapRH indications, the number of tumors was within the Makuuchi criterion[16], and the tumor site was within or adjacent to the same area. Patients were divided into 117 cases undergoing laparoscopic partial liver resection for the first time and 24 cases of LapRH. For both groups, clinical indicators of perioperative course were retrospectively examined from medical records, including operative time, intraoperative blood loss, conversion to laparotomy, morbidity, and postoperative hospital stay.

Upper abdominal surgery was defined as the presence of a distinct scar above the umbilicus, which was derived from an operative procedure involving the subphrenic and subcostal area around the liver.

Surgical Technique

LapRH procedure

The patient is placed in a position with the lower limbs open, except for tumors located in the right dorsal liver. For the first port, we create a 3-cm incision at the navel umbilicus, using an open method in all cases, and use a Lap Protector™ and EZ Access® (Hakko, Nagano, Japan) on the navel. By making a 3-cm incision at the umbilicus, possible adhesions from previous surgery around the umbilicus can be safely exfoliated under direct vision. Therefore, we can place the same first port in all cases, even for patients with a history of upper abdominal laparotomy or operation scars on the umbilicus[17],

We insert a 12-mm port for the camera and two 5-mm ports for the EZ Access (**Fig. 1a**) on the Lap Protector on the navel. After pneumoperitoneum (10 mm Hg, occasionally increased to ≤12 mm Hg) is established through a 12-mm port, a flexible laparoscope is introduced, and the abdominal cavity is observed. In LapRH, the additional port arrangement and the number of ports differ according to the situation, such as the presence of adhesions in the abdominal cavity. After adequate observation of the abdominal cavity, adhesions were detached, as necessary for additional port insertion. In addition to EZ Access at the navel, we typically add 2 or 3 ports to the upper abdomen. The position of the additional ports cannot be standardized because it depends on the type and distribution of adhesions. To ensure adequate aesthetic results, we often insert additional ports alongside previous surgical scars (**Fig. 1b**).

In LapRH, upper abdominal surgery and hepatectomy can result in strong adhesions around the hepatic duodenal ligament, in which case we avoid Pringle maneuver ischemia[18,19] in the secondary operation. We conduct a 3D computed tomography (CT) simulation before surgery, which provides crucial knowledge of the positional relationship between the liver and surrounding organs (**Fig. 2**). Additionally, preoperative simulation enables us to secure the minimum working space necessary for hepatectomy. **Figure 3** shows the actual intraoperative surgical view at the initial insertion of the camera. Intraoperative ultrasonography is routinely used to assess tumor conditions and determine the transection line.

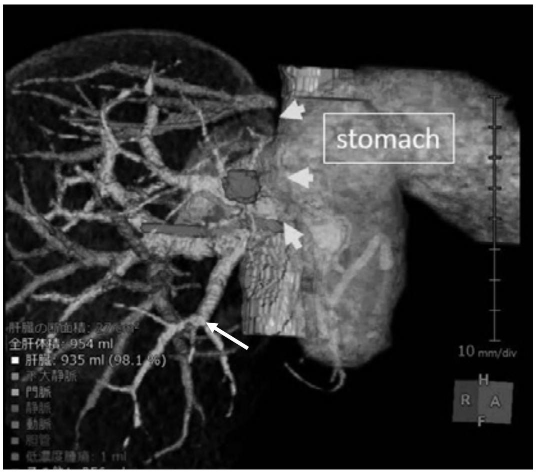

Fig. 2 In a case of recurrence after liver left lobectomy, the relationships between the residual liver and surrounding organs, such as the stomach and duodenum, are shown in a 3D-CT simulation. The image shows the area between the dissected liver section and tumor and the stomach and surrounding organs. The recurrent tumor is near the previously dissected hepatic section.

After evaluating the tumor, we perform hepatectomy. For the main vascular treatment during hepatic resection, we use an ultrasonic coagulation system (LCS) and incision device, for the superficial hepatic parenchyma, and the Cavitron Ultrasonic Surgical Aspirator (Valley lab, Medtronic, Minneapolis, MN, USA), for the deeper hepatic parenchyma. The VIO soft coagulation system is used for hemostasis. After completing liver resection, the specimen is placed in a protective plastic bag and extracted through the incision created by the umbilicus. When tumor location is uncertain or bleeding is uncontrollable, we convert to hand-assisted laparoscopic surgery or conventional open surgery.

Results

LRH was performed in 24 patients (16 men and 8 women; median age, 69 years). The diseases resulting in treatment were 12 cases of HCC, 11 cases of metastatic liver cancer, and 1 case of intrahepatic cholangiocarcinoma. The types of previous hepatectomy and surgical procedures, and extent of adhesions for each patient, are shown in **Table 1**. Most patients underwent 1 abdominal surgery for hepatectomy, However, among the present 24 patients, 2 underwent liver resection and distal gastrectomy, and 1 underwent liver resection and pancreatomy (**Table 1**). Regarding the first operation before LapRH, 24 patients had undergone hepatectomy (19 cases of partial hepatic resection, 1 case of lateral segmentectomy, 1 case of right hepatectomy, 1 case of extended left hepatec-

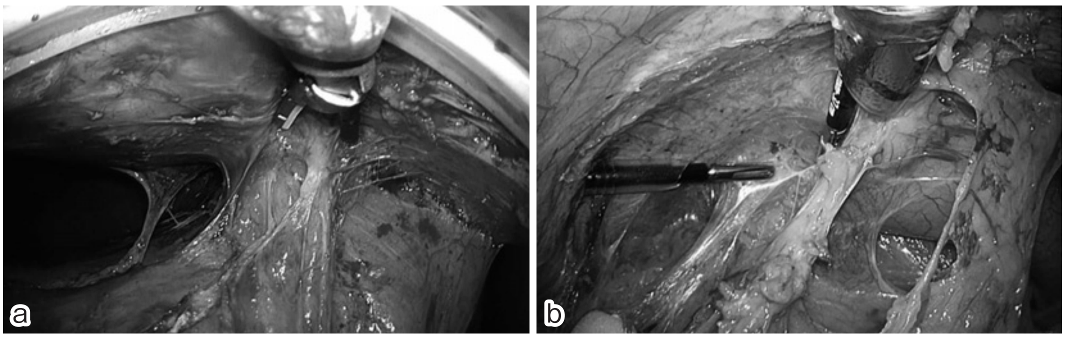

Fig. 3 Intraoperative surgical view. (a) If EZ Access can be attached, observation around the umbilicus by the laparoscope is possible, and adhesion peeling is easy. (b) Adhesive detachment of the peritoneum, intestinal tract, mesentery, and omentum under pneumoperitoneum can be performed with a good visual field and is straightforward.

Table 1

Surgical History	Procedure	Approach	Adhesion
Hepatectomy (n=21)	S8 partial resection	Thoracotomy	Mild
	S5 partial resection	Laparoscopic	Mild
	S5 partial resection	Laparoscopic	Mild
	Extended left lobectomy, Hepatic duct jejunostomy	Laparotomy	Severe
	Posterior segmentectomy	HALS	Severe
	S4 partial resection	Laparoscopic	Mild
	S7, S8 partial resection	Laparoscopic	Severe
	S5 partial resection	Laparoscopic	Severe
	S3 partial resection	Laparoscopic	Mild
	S4, S5, S6, S7 partial resection	Laparoscopic	Severe
	S4 partial resection	Laparoscopic	Mild
	S4, S8 partial resection	Laparotomy	Mild
	S5 partial resection	Laparoscopic	Mild
	Extended right lobectomy	Laparotomy	Severe
	S5 partial resection	Laparotomy	Severe
	Left lobectomy, S8 partial resection	Laparotomy	Severe
	Anterior segmentectomy, S1 partial resection	Laparotomy	Severe
	S8 segmentectomy, MHV combined resection	Laparotomy	Severe
	S5 partial resection	Laparoscopic	Mild
	S8 partial resection	Laparoscopic	Mild
	S2, S3 partial resection	Laparoscopic	Mild
Hepatectomy + Gastrectomy (n=2)	S3, S4, S6 partial resection; Distal gastrectomy	Laparotomy	Severe
	S8 partial resection; Distal gastrectomy	Laparotomy	Severe
Hepatectomy + Pancreatectomy (n=1)	Lateral segmentectomy, Distal pancreatectomy	Laparoscopic	Severe

Operative procedures and approaches before LapRH are tabulated, and adhesions at LapRH are summarized. The degree of adhesion was classified according to Beck et al. (20) (mild = grade 1-2, severe = grade 3-4). S: segment; HALS, hand-assisted laparoscopic surgery

tomy, 1 case of anterior segmentectomy, and 1 case of posterior segmentectomy). These patients did not differ in relation to age, sex, disease, tumor characteristics, or hepatectomy type. Regarding LapRH procedure, 21 patients underwent partial liver resection and 3 underwent lateral segmentectomy. The essence of the laparoscopic surgical approach was a completely laparoscopic operation in 21 cases, single-port in 2 cases, and hand-assisted in 1 case (**Table 2**). There were no cases of conversion to laparotomy because of intraoperative accident, and all LapRH cases were implemented as planned.

We compared surgical time, bleeding volume, and postoperative hospital stay in 117 cases of first LapPLR and 24 cases of LapRH performed during the same period (2010-2017). The male-to-female ratio of the LapPLR patients was 69:48. The underlying diseases for LapPLR were HCC (n = 52) and metastatic liver cancer (n = 65). The LapRH and LapPLR groups did not differ in relation to sex ratio or disease. The short-term outcomes of the 2 groups are shown in **Table 3**. Median operation time was 268 min for LapPLR and 294 min for LapRH (p = 0.55). In addition, median bleeding volume was 224 mL in LapPLR and 77.5 mL in LapRH (p = 0.76). There was no significant difference in mean length of hospital stay after surgery (11 days for LapPLR and 10.2 days for LapRH; p = 0.83). In sum, although there were no significant short-term differences between the groups, LapRH patients tended to do better (**Table 3**). Regarding postoperative comorbidity, only 1 patient with bile leakage in the LapPLR group required surgical drainage as part of postoperative management. Surprisingly, no patient required surgical management for postoperative complications in the LapRH group, indicating the minimally invasive nature of the procedure.

Discussion

Recent studies have shown the safety and usefulness of repeat hepatectomy for recurrent liver cancer and metastatic liver cancer, and demand is increasing. One problem at reoperation is adhesion within the abdominal cavity, and surgical procedures may differ depending on the extent of such adhesion. Patients with a history of upper abdominal surgery and liver resection often have intra-abdominal adhesions. Postoperative adhesions increase

Table 2 Characteristics of the patients with LRH

	Sex	Age	Disease	LRH procedure	No. of tumors	Size of tumor (mm)	Chronic liver disease
1	F	66	Met	Lateral segmentectomy	1	32	−
2	M	73	HCC	S5 partial resection	1	20	+
3	M	67	HCC	S3, S8 partial resection	2	15, 18	+
4	F	78	ICC	S8 partial resection	1	25	−
5	M	69	Met	S4, S8 resection (HALS)	2	15, 18	−
6	M	60	HCC	Lateral segmentectomy	1	27	+
7	M	76	HCC	S3 partial resection	1	18	+
8	F	82	Met	S8 partial resection	1	22	−
9	F	53	Met	S8 partial resection	1	20	−
10	M	76	HCC	S6, S7 partial resection	2	16, 18	+
11	M	73	Met	S3 partial resection (3rd Hx)	1	25	−
12	M	56	Met	Lateral segmentectomy, S1 partial resection (3rd Hx)	2	22, 15	−
13	M	60	HCC	S3 partial resection (TANKO)	1	28	+
14	F	59	Met	S3 partial resection (TANKO)	1	32	−
15	F	53	Met	S5 partial resection	1	30	−
16	F	73	HCC	S4 partial resection	1	25	+
17	M	68	HCC	S8 partial resection	1	20	+
18	M	69	HCC	S8 partial resection	1	22	+
19	M	73	HCC	S2 partial resection	1	18	+
20	M	73	HCC	S3 partial resection	1	22	+
21	M	60	Met	S6 partial resection	1	25	−
22	M	64	Met	S6 partial resection	1	32	−
23	M	83	Met	S2, S3 partial resection	2	18, 20	−
24	F	78	HCC	S2 partial resection	1	22	+

HCC: Hepatocellular carcinoma; ICC: Intrahepatic cholangiocarcinoma; Met: metastasis; HALS: Hand-assisted laparoscopic surgery; TANKO: single-port surgery

Table 3 Perioperative characteristics of the LLR and LapRH groups

	LapPLR	LapRH	p Value
Age	69 (37-84)	69 (53-83)	0.96
Sex (M/F)	69/48	43/28	0.83
Operation time (min)	257 (57-836)	228 (125-751)	0.80
Bleeding (mL)	248 (0-2,885)	70 (0-1,500)	0.76
Postoperative hospital stay (days)	12 (4-48)	8 (6-20)	0.23

operative time of subsequent surgeries, owing to the need for adhesiolysis and the risk of injury to the bowel and surrounding organs[20].

Fibrotic adhesions can hinder visualization, which is often crucial in Laparoscopic liver resection (LLR) procedures. In addition, bleeding may occur during adhesion exfoliation. Therefore, depending on the condition of the abdominal cavity, the possibility of converting from laparoscopy to laparotomy may increase for patients with postoperative adhesions[21]. Surgeons must carefully evaluate how laparoscopic surgery can be adapted for patients with a history of abdominal surgery.

Technical and instrumental improvements have allowed the adoption of laparoscopic procedures for patients with a surgical history. However, the LLR procedure is more complicated. In particular, anatomical hepatectomy and hepatectomy in the subdiaphragmatic region, and cases in which the inferior vena cava has been operated on even once, have to be approached carefully and are often contraindicated for LapRH. Tumors that recur at the lower ventral liver might be suitable for LapRH. In this regard, it is important to determine surgical indications, which we were able to accomplish by preoperative 3D-CT simulation in all 24 cases scheduled for laparoscopic surgery.

In LapRH, we first approach from the umbilicus. The presence or absence of adhesions under the umbilicus is important, and in all the present cases we could open the navel via laparotomy. Using a 3-cm incision of the umbilicus, we can obtain information on the circumference of the umbilicus under direct vision. If there is adhesion, we perform peeling treatment within the range where the EZ Access is attached. Although a previous study reported use of a fast port in a patient whose adhesion was predicted by an optical method[22], our method provides a relatively good field of view and presents little difficulty upon laparoscope insertion, in contrast to abdominal cavity insufflation. Another study reported the use of body surface ultrasonography for preoperative assessment of adhesions in the peritoneal cavity[23,24]. We also use preoperative ultrasonography to identify adhesions around the umbilicus; therefore, care is taken when making the 3-cm incision at the navel. In our procedure, we do not first insert the port but consider it safe in cases of adhesion to perform laparotomy during observation under direct vision and to attach a Lap Protector.

We believe that laparoscopic hepatectomy is possible regardless of the extent of adhesion if we can install the EZ Access and insert a laparoscope under pneumoperitoneum (**Fig. 3a**). Laparoscopic surgery is more useful than conventional laparotomy for adhesion treatment in the abdominal cavity, especially those at the abdominal wall and omental or intestinal adhesions. Some reports have described the usefulness of laparoscopic adhesion-detaching surgery (**Fig. 3b**)[25–27]. We believe that it is better to use gravity, pneumoperitoneum pressure, and the magnifying effect from the organ side instead of proceeding from the abdominal wall of the adhered side, because pneumoperitoneum in the abdominal cavity and the "zoom" effect of the laparoscope make the boundary between the intestinal tract and other organs easier to discern.

For patients with a history of abdominal surgery, we resect the liver parenchyma after conventional abdominal surgery, with detachment of adhesions on the abdominal wall and surrounding hepatic tissues and organs. Particularly in repeat hepatectomies, conventional laparotomy involves unnecessary exfoliation and surgical operations to secure a suitable space for the operative field, further prolonging operating time. However, in LapRH, the time required for adhesion-stripping operations can usually be minimized.

For partial resection of liver segment 8 after posterior segmentectomy of the liver, hepatectomy under hand-assisted treatment instead of pure laparoscopic surgery is recommended, because the liver has been removed from the diaphragm in the previous operation and placed adjacent to the previous hepatic cross-section. This sometimes forms a biloma in the cross-section of the liver, and tumors near the diaphragm or inferior vena cava should be considered contraindicated in future LapRH guidelines. LapRH indications should be carefully reconsidered as the number of cases increases.

Intraoperative ultrasonography is an indispensable tool in LLR because we cannot confirm the tumor directly by laparoscopy. In cases of repeat hepatectomy, intraoperative ultrasonography cannot be used successfully if the liver surface is deformed or if the liver is displaced by adhesion. In addition, there are frequent limitations on movement. Because of liver deformation and mutation, repeat hepatectomy cannot be regarded as a conventional dissection, so it is important to recognize the space within the abdominal cavity.

By simulating the liver tumor with the preoperative volume analyzer Synapse Vincent (Fuji, Tokyo, Japan), it is possible to reach the liver parenchyma and tumor by the shortest route, that is, by securing a space where the device can move with minimal adhesion. Unlike conventional laparotomy, LapRH does not require a wide surgical field. In LapRH, magnification allows for pinpoint surgery in a narrow, limited space. In our experience LapRH secures a working space only for hepatectomy and eliminates other adhesions. These procedures can be planned in advance by simulating the position of the tumor and the relationships between the area of hepatic resection and surrounding organs.

We found that the smaller working space required by LapRH allows for minimal adhesion dissections and a direct tumor approach. For example, in a LapRH after right lobectomy, the previous segment of the liver apex and stomach wall adhered, but because this was identified by preoperative simulation, as shown in **Figure 2**, a strategy to detach the adhesion could be devised. Surgical adaptations also differ in relation to the surrounding adherent organs. LRH may be contraindicated for adhesions affecting the duodenum, jejunum, and colon wall, because these are extremely difficult to overcome.

Conventional repeat hepatectomy requires adhesion treatment of the site and the range to secure the operative field, which is not necessary for hepatectomy because of the large laparotomy. Therefore, as compared with open surgery, LapRH reduces the time spent before hepatectomy. Adhesions around the hepatic duodenal ligament are highly advanced in many LapRH cases, and all cases of ischemia by Pringle maneuver are avoided. There are often adhesions of the upper part of the hepatic duct, duodenum, and pancreas, and supplementing the surgical procedure increases the risk of unexpected complications. Indeed, the amount of bleeding did not increase during surgery without ischemia by the Pringle method. There was no significant difference in the amount of intraoperative bleeding between LapRH and LapPLR performed under ischemia. One factor that has reduced the amount of bleeding during surgery is the development of energy devices. It is equally important not to damage multiple organs and expose them to bleeding during hepatectomy.

We believe that preoperative simulation is useful and important in delineating the relationship between liver surface and surrounding organs for intraoperative LapRH, in addition to the relationship between the regular tumor and intrahepatic vessels. In our experience, meticulous dexterity and preparation resulted in good LapRH outcomes.

Although the difference was not significant, duration of hospital stay was shorter after LapRH surgery than after initial surgery, owing to the minimally invasive nature of LapRH. In addition to fewer postoperative days until discharge, the patients who underwent LapRH had satisfactory bed rest and left the hospital in good spirits.

As LapRH becomes more widespread, most cases of repeat hepatectomy will likely be performed by partial hepatectomy, without requiring anatomical hepatectomy. In LapRH, hepatectomy can be performed with an effective operative field, which cannot be achieved with conventional laparotomy, and takes advantage of adhesions. For example, surgery while the liver is lifted can be done by using adhesion of the peritoneum and liver surface directly under the previous surgical handiwork. This is often convenient for LLR. The liver is unusual among parenchymal organs: because of its weight, a situation in which the liver is lifted by adhesion may be useful.

When the principal locus of the tumor is dorsal to the extrahepatic area and ventral to liver adhered to the abdominal wall, it is possible to excise it very efficiently from the dorsal side without lifting the liver. In conventional LLR it is difficult to sever the tumor unless the liver is lifted with forceps. On the basis of our experience, LapRH is an excellent technique for tumors close to the liver surface on the ventral side. However, it is necessary to carefully examine the situation with respect to the site to which the surgical approach has been applied, the diaphragm, and the area adjacent to the inferior vena cava.

LapRH is better with respect to stress relief and bodily regulation, and it is possible to perform the procedure in the minimum space necessary for hepatectomy, as indicated by our results. The use of LapRH as a treatment for recurrent liver cancer will increase in the future. We also need to increase the number of cases in order to gain experience, formalize the procedure, and further its development.

Unexpectedly, the present results (**Table 3**) show that the LapRH group was not worse than the LapPLR group in operation time and bleeding, probably because of surgical skill, teamwork, or refinements of the instruments. Future studies should enroll a larger number of patients, because only a small number of the present patients underwent LapRH.

Conclusions

Magnification during laparoscopy enables hepatectomy in a more limited space, largely because of technical improvements in laparoscopic hepatectomy and the development of energy devices. LapRH is useful for treating recurrent HCC, because, when compared with laparotomy reversal resection, it yields better results in intraoperative bleeding volume and hospital length of stay after surgery[14,15]. LapRH promises to become the preferred surgical technique for treatment of recurrent liver cancer.

Conflict of Interest: The authors declare that they have no conflict of interest.

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