Safety and efficacy of laparoscopic repeat liver resection and re-operation for liver tumor

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Laparoscopic liver resection (LLR) has been reported as a safe, minimally invasive, and effective surgery for the management of liver tumor. However, the efficacy and safety of laparoscopic repeat liver resection (LRLR) for recurrent liver tumor are unclear. Here, we analyzed the surgical results of LRLR. From June 2010 to May 2019, we performed 575 LLR surgeries in our department, and 454 of them underwent pure LLR for the single tumor. We classified the patients who received pure LLR for the single tumor into three groups: LRLR (n = 80), laparoscopic re-operation after previous abdominal surgery (LReOp; n = 136), and laparoscopic primary liver resection (LPLR; n = 238). We compared patient characteristics and surgical results between patients undergoing LRLR, LReOp and LPLR.

We found no significant differences between LRLR and LPLR in the conversion rate to laparotomy (p = 0.8033), intraoperative bleeding (63.0 vs. 152.4 ml; p = 0.0911), or postoperative bile leakage rate (2.50 vs. 3.78%; p = 0.7367). We also found no significant difference in the surgical results between LReOp and LPLR. However, the number of patients undergoing the Pringle maneuver was lower in the LRLR group than the LPLR group (61.3 vs. 81.5%; p = 0.0004). This finding was more pronounced after open liver resection than laparoscopic liver resection (38.9 vs. 67.7%; p = 0.0270). The operative time was significantly longer in patients with proximity to previous cut surface than patients with no proximity to previous cut surface (307.4 vs. 235.7 min; p = 0.0201). LRLR can safely be performed with useful surgical results compared to LPLR.
Surgical procedure. During surgery, patients were supine for liver resection of a tumor in the left lobe or in the semi left lateral decubitus position for a tumor in the right lobe. The first trocar was inserted at the umbilicus by an open method. To reduce intraoperative bleeding, we tried to prepare for the Pringle maneuver in every case by encircling the hepatoduodenal ligament. However, when strong adhesion was present around the hepatoduodenal ligament, we could not use the Pringle maneuver. In cases of anatomical liver resection, we used the Glissonian pedicle approach and transected the pedicle using a surgical stapling device. Parenchymal transection was performed using an ultrasonic surgical aspirator, laparoscopic coagulation shears, and bipolar clamp coagulation system.

Results
The patient characteristics and surgical results for the three surgical groups are given in Table 1. In the comparison between the LRLR and LPLR groups, we found no differences in gender, Child-Pugh classification, or liver damage. The rate of metastatic liver cancer was significantly higher in the LRLR group than LPLR group (22.5 vs. 4.20%; \( p < 0.0001 \)). The rate of Hr1 and Hr2 liver resection was significantly higher in the LPLR group (\( p = 0.0224 \)), and the difficulty score for LLR was significantly higher in the LPLR group than LRLR group (3.8 vs. 5.0; \( p = 0.0001 \)). In the comparison of LRLR and LPLR, the rate of Pringle maneuver preparation was significantly lower in the LRLR group (61.3 vs. 81.5%; \( p = 0.0004 \)). We found no differences in the other surgical results, including postoperative morbidity. We also found no significant difference in the surgical results between LReOp and LPLR.

In the LRLR group, 62 patients underwent LLR (post-laparoscopic group), and 18 patients underwent open liver resection (post-open group) in their last surgery. The patient characteristics and surgical results of these two groups are given in Table 2. We found no differences in the patients’ characteristics except gender. Comparing the post-laparoscopic and post-open groups, the rate of Pringle maneuver preparation was significantly lower in the post-open group (67.7 vs. 38.9%; \( p = 0.0270 \)). We found no differences in the other surgical results, including operative time (279.3 vs. 296.4 min; \( p = 0.6294 \)), blood loss (64.4 vs. 58.2 ml; \( p = 0.8700 \)), conversion rate, morbidity, and postoperative hospital stay.

We also evaluated the proximity of the first liver resection and second liver resection in the LRLR group. When the first and second liver resections were in the same segment or adjacent segments (lateral-medial–anterior–posterior), we classified these cases as “proximity to previous cut surface”. Other cases we classified as “no proximity to previous cut surface”. The patient characteristics and surgical results of these groups are given in Table 3. In regards to patient characteristics, the Child-Pugh classification and liver damage were worse in the no proximity to previous cut surface group (\( p = 0.0448 \) and \( p = 0.0328 \), respectively). The rate of HCC was

| Table 1. Patient characteristics and surgical results of laparoscopic liver resection. HCC hepatocellular carcinoma, CCC cholangiocellular carcinoma, Mets metastasis, HALS hand-assisted laparoscopic surgery, n.s. not significant. *L: low, I: intermediate, H: high. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | LRLR (n = 80)   | LReOp (n = 136) | LPLR (n = 238)  | LRLR vs. LPLR   |
| Age, years       | Mean ± SD       | Mean ± SD       | Mean ± SD       | Mean ± SD       |
| Gender M/F       | 56/24           | 77/59           | 152/86          | 0.3442          |
| Child-Pugh A/B/C | 78/2/0          | 133/3/0         | 225/13/0        | 0.3718          |
| Liver damage A/B/C | 58/21/1        | 108/28/0        | 184/53/1        | 0.3554          |
| Diagnosis HCC/CCC/Mets/Other | 58/1/18/3 | 42/5/76/11 | 178/6/10/42 | < 0.0001 |
| Extent of liver resection Hr0/Hr5/Hr1/Hr2 | 63/3/6/4 | 85/7/22/22 | 155/1/17/25 | 0.0224          |
| Difficulty score L (1–3)/I (4–6)/H (7–11)* | 41/33/6 | 40/53/43 | 71/98/69 | < 0.0001 |
| Tumor size, mm   | Mean ± SD       | Mean ± SD       | Mean ± SD       | Mean ± SD       |
| Operative time, min | Mean ± SD       | Mean ± SD       | Mean ± SD       | Mean ± SD       |
| Blood loss, ml   | Mean ± SD       | Mean ± SD       | Mean ± SD       | Mean ± SD       |
| Pringle Possible/Impossible | 49/31 | 110/26 | 194/44 | 0.0004          |
| Conversion to Assisted/HALS/Open | 0/2/0 | 1/1/0 | 0/4/2 | 0.8033          |
| Surgical margin (+)/Suspicious/(-) | 0/2/78 | 0/1/13 | 0/3/23 | 0.6029          |
| Postoperative morbidity Hemorrhage | 0 | 1 | 0 | n.s |
| Bilary fistula | 2 | 2 | 9 | 0.7367 |
| Hospital stay, days | Mean ± SD       | Mean ± SD       | Mean ± SD       | Mean ± SD       |
| Postoperative Laboratory Data (POD1) |
| AST, IU/l | Mean ± SD | 413.7 ± 463.3 | 423.0 ± 320.3 | 462.6 ± 468.3 | 0.4184 |
| ALT, IU/l | Mean ± SD | 266.2 ± 308.0 | 297.3 ± 232.5 | 370.0 ± 347.4 | 0.1057 |
| T-Bil, mg/dl | Mean ± SD | 1.04 ± 0.55 | 0.91 ± 0.46 | 0.93 ± 0.48 | 0.0835 |
| WBC, /μl | Mean ± SD | 9019 ± 2948 | 9609.6 ± 2976 | 9776.0 ± 3069 | 0.0547 |
| CRP, mg/dl | Mean ± SD | 1.75 ± 1.59 | 2.16 ± 1.60 | 1.85 ± 2.12 | 0.6407 |

Table 1. Patient characteristics and surgical results of laparoscopic liver resection. HCC hepatocellular carcinoma, CCC cholangiocellular carcinoma, Mets metastasis, HALS hand-assisted laparoscopic surgery, n.s. not significant. *L: low, I: intermediate, H: high.
higher in the no proximity to previous cut surface group; on the other hand, the rate of metastatic liver cancer was higher in the proximity to previous cut surface group. The operative time was significantly longer in the proximity to previous cut surface group (307.4 vs. 235.7 min; \( p = 0.0201 \)). The rate of Pringle maneuver preparation was significantly higher in the proximity to previous cut surface group (69.8 vs. 44.4%; \( p = 0.0277 \)). We found no differences in the other patient characteristics and surgical results, including tumor size, blood loss, conversion rate, morbidity, or postoperative hospital stay.

To adjust for liver resection background, we divided the LRLR and LPLR groups into low difficulty score (1–3), intermittent difficulty score (4–6), and high difficulty score (7–11) groups and compared the patients’ characteristics and surgical results (Table 4). In the low difficulty score group, patient age was significantly older with LRLR than LPLR (73.8 vs. 69.0 years; \( p = 0.0168 \)). In the low and intermediate group, tumor size was significantly smaller in LRLR than in LPLR. In each group, the rate of metastatic liver cancer was significantly higher in the LRLR group (low: 21.9 vs. 7.0%, \( p = 0.0136 \); intermediate: 15.2 vs. 3.0%, \( p = 0.0074 \); high: 66.7 vs. 2.9%, \( p = 0.0007 \)). We found no significant differences in the rate of Pringle maneuver preparation (low: 51.2 vs. 59.1%, \( p = 0.4356 \); intermediate: 69.7 vs. 85.7%, \( p = 0.0656 \); high: 83.3 vs. 98.6%, \( p = 0.1546 \)). In the high difficulty score group, the hospital stay was significantly shorter for the LRLR group (11.3 vs. 22.4 days; \( p = 0.0064 \)). Among the laboratory data (post-operative day 1), total bilirubin after LRLR was significantly higher in the low difficulty score group (1.03 vs. 0.84 g/dl; \( p = 0.034 \)). We found no differences in the other patient characteristics or surgical results.

We compared the patient characteristics and surgical results between the LRLR and LPLR groups only in HCC patients (Table 5). In the comparison between the LRLR and LPLR groups, we found no differences in gender, Child-Pugh classification, or liver damage. The age was significantly older in the LRLR group than in the LPLR group (72.8 vs. 70.1; \( p = 0.029 \)). The tumor size was significantly smaller in LRLR group than in LPLR group (15.2 mm vs. 28.9 mm; \( p < 0.0001 \)). The operative time was significantly shorter in the LRLR group than in the LPLR group (267 min vs 323 min; \( p = 0.0065 \)). We found no differences in the other surgical results, including postoperative morbidity.

**Discussion**

Repeat liver resection is widely performed for primary liver cancer and metastatic liver cancer\(^{14-19}\). In this study, the tumor size was significantly smaller in the LRLR group than in LPLR group. This difference may be caused by early detection of the recurrent tumors because of the routine surveillance after primary liver resection.

In this study, the rate of Pringle maneuver was significantly lower in LRLR group and this finding was more pronounced after open liver resection than laparoscopic liver resection. This difference was also found between the LRLR and LPLR groups only in HCC patients. Although whether we perform the Pringle maneuver or not...
is decided by surgeons, the lower rate may be caused by the difficulty of encircling the hepatoduodenal ligament because of the intra-abdominal adhesion.

Although LRLR was not commonly performed, several studies have been reported regarding the safety and issues\textsuperscript{20–28}. Noda et al.\textsuperscript{20} compared 20 patients undergoing minimally invasive repeat liver resection and 48 undergoing ORLR. Minimally invasive repeat liver resection included 6 hybrid LLR patients and 14 pure LLR patients. The hybrid LLR patients underwent liver resection through a mini-laparotomy incision. The postoperative hospital stay, blood loss, and postoperative complication rate were significantly lower in the minimally invasive repeat liver resection group. They showed the safety of minimally invasive repeat liver resection, but included hybrid laparoscopic resection. In our study, we investigated the safety and efficacy of LRLR for the patients receiving pure LLR.

The use of difficulty scoring was proposed by Ban et al.\textsuperscript{13}. The system has become widely used as an indicator of the difficulty of LLR\textsuperscript{29}. We found a significant difference in the difficulty score between LRLR and LPLR. Therefore, we divided the LRLR and LPLR groups according to difficulty. In the low difficulty score group, the operative time was longer with LRLR. In all difficulty score groups, we found no significant difference in blood loss. The extended operative time may be caused by postoperative adhesions and liver malformation.

In repeat liver resection, many cases are technically difficult because of postoperative adhesions and liver malformation, even if they are scored as low difficulty. Kinoshita et al.\textsuperscript{30} analyzed 60 LRLR patients for HCC, 31 of whom underwent laparoscopic previous liver resection and 29 open previous liver resection. They reported that the predictive factors for difficult LRLR for HCC were an open approach during previous liver resection, a history of two or more previous liver resections, a history of previous major liver resection, tumor near the resected site of the previous liver resection, and intermediate or high difficulty score. In the present study, we also found that proximity to previous cut surface predicted LRLR difficulty, as the proximity to previous cut surface group had a longer operative time. The previous study analyzed LRLR only in HCC patients, whereas we investigated not only HCC, but also metastatic liver cancer and other liver tumors.

This study has some limitations. This is a retrospective, single center study. In addition, there may be some surgeon’s selection bias within the decision of operative strategy. Therefore, to show the effectiveness and safety of LRLR, more studies are needed, including multi-institutional studies and long-term observations. However, to the best of our knowledge, this study describes the largest number of LRLR surgeries at a single institution. Therefore, we showed the safety and effectiveness of LRLR.

### Table 3: Patient characteristics and surgical results of laparoscopic repeat liver resection classified by proximity to previous cut surface of the last hepatectomy. HCC hepatocellular carcinoma, CCC cholangiocellular carcinoma, Mets metastasis, HALS hand-assisted laparoscopic surgery, n.s. not significant. *L*: low, I: intermediate, H: high.

| Proximity to previous Cut Surface | No Proximity to previous Cut Surface |
|----------------------------------|-------------------------------------|
| (n = 53)                         | (n = 27)                             |
| **Age, years**                   |                                     |
| Mean ± SD                        |                                     |
| 73.1 ± 8.8                       | 71.1 ± 8.7                           |
| **Gender**                       |                                     |
| M/F                              |                                     |
| 38/15                            | 18/9                                |
| **Child-Pugh**                   |                                     |
| A/B/C                            |                                     |
| 53/0/0                           | 25/2/0                              |
| **Liver damage**                 |                                     |
| A/B/C                            |                                     |
| 43/10/0                          | 15/11/1                             |
| **Diagnosis**                    |                                     |
| HCC/CCC/Mets/Other               |                                     |
| 34/0/16/3                        | 24/1/2/0                            |
| **Extent of liver resection**    |                                     |
| Hr0/Hr1/Hr2                      |                                     |
| 44/1/4/4                         | 22/2/2/0                            |
| **Difficulty score**             |                                     |
| L (1–3)/I (4–6)/H (7–11)\textsuperscript{a} |                                     |
| 24/23/6                          | 17/10/0                             |
| **Tumor size, mm**               |                                     |
| Mean ± SD                        |                                     |
| 17.0 ± 5.62                      | 18.4 ± 14.1                         |
| **Operative time, min**          |                                     |
| Mean ± SD                        |                                     |
| 307.4 ± 148.8                    | 235.7 ± 67.9                        |
| **Blood loss, ml**               |                                     |
| Mean ± SD                        |                                     |
| 216.5 ± 1058.9                   | 38.1 ± 121.1                        |
| **Pringle**                      |                                     |
| Possible/Impossible              |                                     |
| 37/16                            | 12/15                               |
| **Conversion to**                |                                     |
| Assisted/HALS/Open               |                                     |
| 0/2/0                            | 0/0/0                               |
| **Surgical margin**              |                                     |
| (+)/Suspicious/(-)               |                                     |
| 0/1/52                           | 0/1/26                              |
| **Postoperative morbidity**      |                                     |
| Hemorrhage                       |                                     |
| 0                                | 0                                   |
| Biliary fistula                  |                                     |
| 1                                | 1                                   |
| **Hospital stay, days**          |                                     |
| Mean ± SD                        |                                     |
| 10.5 ± 14.5                      | 18.5 ± 45.3                         |
| **Postoperative Laboratory Data (POD1)** |                         |
| AST, IU/l                        |                                     |
| Mean ± SD                        |                                     |
| 461.8 ± 547.0                    | 319.1 ± 199.5                       |
| ALT, IU/l                        |                                     |
| Mean ± SD                        |                                     |
| 299.3 ± 363.3                    | 202.9 ± 134.1                      |
| T-Bil, mg/dl                     |                                     |
| Mean ± SD                        |                                     |
| 1.02 ± 0.58                      | 1.09 ± 0.49                        |
| WBC, /μl                         |                                     |
| Mean ± SD                        |                                     |
| 9068 ± 2858                      | 8922 ± 3170                        |
| CRP, mg/dl                       |                                     |
| Mean ± SD                        |                                     |
| 2.01 ± 1.69                      | 1.23 ± 1.24                        |

\textsuperscript{a}L: low, I: intermediate, H: high.
### Table 4. Patient characteristics and surgical results of laparoscopic repeat liver resection classified by difficulty score. HCC hepatocellular carcinoma, CCC cholangiocellular carcinoma, Mets metastasis, HALS hand-assisted laparoscopic surgery, n.s. not significant.

| LRLR | LPLR | P |
|------|------|---|
| Low  | Intermediate | High |
| n = 41 | n = 33 | n = 6 |
| 73.8 ± 8.93 | 70.5 ± 8.45 | 73.3 ± 8.61 |
| Gender | M/F | 25/14 | 26/7 |
| Child-Pugh | A/B/C | 41/0/0 | 31/2/0 |
| Liver damage | A/B/C | 27/14/0 | 35/7/1 |
| Diagnosis | HCC/CCC/Mets/Other | 29/1/9/2 | 27/0/5/1 |
| Extent of liver resection | Hr0/HrS/Hr1/Hr2 | 41/0/0/0 | 26/2/4/1 |
| Tumor size, mm | Mean ± SD | 14.9 ± 6.11 | 18.9 ± 10.1 |
| Operative time, min | Mean ± SD | 235.7 ± 9.4 | 308.6 ± 14.0 |
| Blood loss, ml | Mean ± SD | 41.1 ± 121.0 | 81.8 ± 163.3 |
| Pringle Possible/Impossible | 21/20 | 23/10 |
| Conversion to Assisted/HALS/Open | 0/0/0 | 0/0/0 |
| Surgical margin (+)/Suspicious/(−) | 0/0/0 | 0/0/0 |
| Postoperative morbidity | Hemorrhage | 0 | 0 |
| Hospital stay, days | Mean ± SD | 9.2 ± 7.5 |

### Table 5. Patient characteristics and surgical results of laparoscopic liver resection in HCC patients. HCC hepatocellular carcinoma, CCC cholangiocellular carcinoma, Mets metastasis, HALS hand-assisted laparoscopic surgery, n.s. not significant. *L: low, I: intermediate, H: high.

| LRLR | LPLR | P |
|------|------|---|
| Low  | Intermediate | High |
| n = 58 | n = 178 |
| 72.8 ± 7.8 | 70.1 ± 8.8 |
| 42/16 | 116/62 |
| 56/2/0 | 166/12/0 |
| 39/18/1 | 130/6/3 |
| 50/2/0 | 117/10/30 |
| Difficult score | L (1–3)/I (4–6)/H (7–11)* | 29/272 |
| 50/75/35 |
| Tumor size, mm | Mean ± SD | 15.2 ± 5.52 |
| Operative time, min | Mean ± SD | 266.9 ± 123.1 |
| Blood loss, ml | Mean ± SD | 67.7 ± 153.4 |
| Pringle Possible/Impossible | 33/25 | 158/20 |
| Conversion to Assisted/HALS/Open | 0/0/0 | 0/3/2 |
| Surgical margin (+)/Suspicious/(−) | 0/2/6 | 0/2/176 |
| Hospital stay, days | Mean ± SD | 12.9 ± 31.2 |

**Postoperative Laboratory Data (POD1)**

| AST, IU/l | Mean ± SD | 427.8 ± 523.6 |
| ALT, IU/l | Mean ± SD | 262.0 ± 343.9 |
| T-Bil, mg/dl | Mean ± SD | 8769.9 ± 2908 |
| WBC, /μl | Mean ± SD | 1.14 ± 1.35 |
| CRP, mg/dl | Mean ± SD | 1.43 ± 1.35 |

**Postoperative Laboratory Data (POD1)**

| AST, IU/l | Mean ± SD | 427.8 ± 523.6 |
| ALT, IU/l | Mean ± SD | 262.0 ± 343.9 |
| T-Bil, mg/dl | Mean ± SD | 8769.9 ± 2908 |
| WBC, /μl | Mean ± SD | 1.14 ± 1.35 |
| CRP, mg/dl | Mean ± SD | 1.43 ± 1.35 |
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Author contributions
K.T., T.S., Y.O., Y.K, G.S. wrote the main manuscript text. K.K., K.M., Y.K., T.M., A.T., T.H. and K.M. did statistical analysis and prepared tables. All authors reviewed the manuscript.

Competing interests
The authors declare no competing interests.

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