의학석사 학위논문

복강경 재간절제술의 유용성

Feasibility and benefit of the laparoscopic repeat liver resection

울산대학교대학원

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강 병 주

복강경 재간절제술의 유용성

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이 논문을 의학석사 학위 논문으로 제출함

2022년 1월

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강병주의 의학석사학위 논문을 인준함

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국문요약

서론: 복강경 간 절제술은 간 종양의 근치적 절제를 위한 수술방법으로 받아들여지고 있다. 그러나 복강경 재간절제술은 널리 활용되고 있지 못한데, 이는 수술 절차의 복잡성 및 해부학적 왜곡에 따른 인접 혈관의 손상에 대한 우려와 예기치 않은 개복 수술로의 전환 가능성 때문이다. 이에 본 연구에서는 복강경 재간절제술 후 단기 결과를 초회 복강경 간절제술 및 개복 재간절제술의 단기 결과와 각각 비교 분석하여 복강경 재간절제술의 효용성을 평가하고자 하였다.

연구 대상 및 방법: 2008 년 9 월부터 2018 년 10 월까지 울산대학교병원에서 간 절제술을 받은 658 명의 환자를 대상으로 하였다. 복강경 간 절제술 환자 100 명과 개복 재간절제술 환자 20 명에 대하여 수술 절차, 개복 절제술로의 전환율, 수술시간, 수술 중 출혈량, 수혈량, 수술 후 입원 기간, Clavien-Dindo 분류법에 따른 수술 후 합병증 발생여부 등의 인자 및 사망률을 조사했다. 또한 복강경 재간절제술 환자군과 개복 재간절제술 환자군의 병변 위치 및 크기를 분석했다. 복강경 재간절제술을 실시한 환자 10 명의 결과를 초회 복강경 간절제술을 실시한 환자 90 명 및 개복 재간절제술을 실시한 환자 20 명의 결과와 비교하였다.

결과: 복강경 재간절제술 환자군과 초회 복강경 간절제술 환자군 간에 수술 시간 및 수술 중 출혈량, 수혈량, 수술 후 입원 기간, 수술 후 합병증 발생 여부와 관련하여 유의한 차이를 보이지 않았다. 한편, 개복 재간절제술 환자군과 비교하여 복강경 재간절제술 환자군의 종양 크기가 유의하게 작았고 (2.0±1.119 cm vs. 4.0±2.743cm, p=0.006), 종양의 위치는 유의하게 간의 전외측부, 즉 복강경 간절제술이 용이한 위치에 많았다 (90% vs. 40%, p=0.017). 수술 시간 및 재원기간은 복강경 재간절제술 환자군에서 유의하게 짧았다 (261±48 분 vs. 377±134 분, p=0.014 및 9.5±2.6 일 vs. 20.5±14.5 일, p=0.025).

결론: 복강경 절제술은 간 종양이 재발하여 재간절제술을 실시해야 하는 환자 중에서 선택된 환자에게서 안전하면서도 효과적인 수술이 될 수 있다. 복강경 재간절제술 대상으로 특정할 수 있는 기준은 아직 확립되지 않았다. 현재로서는 충분한 수술 경험이 축적되어 추후 수술 대상의 선택 기준이 확장될 때까지 간의 전외측 영역에 발생한 작

은 종양에 대하여 실시하는 것이 적합할 것이다.

차 례

그림 차례

표 차례

Introduction

The first non-anatomical laparoscopic liver resection (LLR) for a benign liver tumor was performed in 1992, the first anatomical LLR in 1996, and the first LLR for hepatocellular carcinoma in 1995 (1). However, the adoption of LLR has been much slower than other laparoscopic surgical fields. Reasons include the fear of uncontrollable bleeding during parenchymal transection, complex vascular and biliary anatomy, difficulty in exposure of deep posterior retroperitoneal attachments, lack of a dedicated instrument, and concern about oncological outcomes such as adequate margins (2). Nevertheless, LLR has become a widely accepted option of curative resection for liver tumors by continuous progression of surgeons' experience and skills, laparoscopic equipment such as 3 dimensional videoscope, surgical devices and understanding about liver anatomy over the past two decades. LLR has general benefits of minimal invasive surgery including reduced pain, shorter length of hospital stay, earlier postoperative recovery, and cosmesis, as well as some additional liver-specific advantages, such as less bleeding and lower incidence of postoperative ascites or liver failure in cirrhotic patients (3).

Laparoscopic repeat liver resection (LRLR), however, is not wide spreading, because of concerns about the added difficulty in surgical procedure due to adhesion, inadvertent injury to the adjacent vasculature due to distorted anatomy and possible unexpected open conversion. LRLR was discussed at the first European Guidelines Meeting on Laparoscopic Liver Surgery in Southampton in 2017 (4). The experts suggested that LLR for re-do liver surgery is an appropriate option, and an initial LLR may facilitate repeat resections by limiting the amount of adhesions, thereby providing an important advantage. The indications for LRLR have not been clearly described yet.

Several recent studies have reported on the feasibility and safety of LRLR. In a collective review of 271 cases from 16 small reports by 2018 (5), it is reported that LRLR has better

short-term outcomes such as reduced bleeding, less or similar morbidity, and shorter hospital stay compared to the open repeat liver resection (ORLR), and complete adhesiolysis can be avoided in LRLR. However, there are still few studies on LRLR. In this regard, the author conducted this study.

The aims of this study were to assess the feasibility of LRLR by comparing the early operative outcomes to those of the laparoscopic primary liver resection (LPLR) and to assess the benefits of LRLR by comparing to ORLR.

Method

Between September 2008 and October 2018, a total of 658 patients underwent liver resection at Ulsan University Hospital. Among them, 60 patients who underwent concomitant biliary reconstruction were excluded. 498 patients underwent OLR (open primary liver resection (OPLR); n=478, open repeat liver resection (ORLR); n=20), and 100 patients underwent LLR (laparoscopic primary liver resections (LPLR); n=90, laparoscopic repeat liver resection (LRLR); n=10) (Figure 1).

For patients in the LLR group (n=100) and ORLR group (n=20), the following parameters were investigated; diagnosis, operative procedures, open conversion rates, operative time, intraoperative bleeding amount, transfusion rates, length of postoperative hospital stay and postoperative complications according to the Clavien-Dindo classification system(6), and mortality rates. The location and size of the lesion were investigated and compared in LRLR and ORLR groups.

These operative and postoperative parameters of 10 patients in LRLR group were compared to 1) the LPLR group (n = 90) and 2) ORLR group (n = 20).

Chi-square test was used for categorical variables and independent t-tests are used for continuous variables. A p-value of < 0.05 was considered to be statistically significant. Statistical analyses were performed using SPSS statistical software version 25 (SPSS, Chicago, IL, USA).

Results

Among the 100 patients who underwent LLR, 75 patients had malignant disease including hepatocellular carcinoma (HCC) in 48 and colorectal cancer liver metastasis (CRLM) in 15. The diagnosis of these patients were shown in Table 1. Laparoscopic major resection was performed in 27 patients. The details of the operative procedures of these patients were shown in Table 2. Postoperative complication rate in this LLR group was 11%. Table 3 shows the details of the postoperative complication in LLR group patients.

There were 10 patients who underwent LRLR (Table 4). The indications for LRLR were; HCC (n=5), CRLM (n=3), prostatic cancer liver metastasis (n=1) and liver cyst (n=1). Locations of the tumor were segment 2 (n=2), segment 3 (n=6), segment 4a (n=1) and segment 5 (n=1). There were 5 cases of anatomical resection and 5 cases of non-anatomical resection. One patient underwent a 4^{th} liver resection and another one patient a 3^{rd} resection. Table 4 shows the indications and procedures of LRLR. Intraoperative data and short-term outcomes of the patients who underwent LRLR and those who underwent LPLR are shown in Table 5. Open conversion rates were 20% (n = 2) for LRLR and 3.3% (n = 3) for LPLR, but this difference was not statistically significant (p=0.077). The reasons for open conversion were as follows: bleeding (n=3); unable to proceed (n=1); and poor localization (n=1). Between the LRLR and LPLR groups, there were no significant differences in operative time, intraoperative blood loss, transfusion requirement, length of postoperative stay, and postoperative complication rates.

Tumor characteristics, intraoperative data and short-term outcomes of the patients who underwent LRLR and those who underwent ORLR are shown in Table 6. Tumor size of the LRLR group was significantly smaller than that of the ORLR group (2.0±1.119 cm vs. 4.0±2.743cm, p=0.006). Tumors located in the anterolateral segments in the LRLR group were significantly more than the ORLR group (90% vs. 40%, p=0.017) Operative time was

different significantly, favoring laparoscopic approach for repeat liver resection (261±48 min vs. 377±134 min, p=0.014). Length of postoperative stay was significantly shorter for the LRLR group compared to the ORLR group (9.5±26 ds. vs. 20.5±14.5 ds., p=0.025).

There was no in hospital mortality in any of these 120 patients.

Discussion

The number of LLRs performed worldwide has increased steadily after the First International Consensus Conference on Laparoscopic Liver Surgery in 2008 (7). The consensus meeting suggested that the best indications for LLR were patients with solitary lesions, ≤ 5 cm in diameter, located in the peripheral liver segments, and also suggested that laparoscopic left lateral sectionectomy should be considered as the standard of care. The Second International Consensus Conference on Laparoscopic Liver Resections was held in 2014 (8). It was mentioned that minor LLR is confirmed to be a standard practice in surgery but is still in the assessment phase, and major LLR is an innovative procedure in the exploratory, learning phase.

With accumulation of experience and improvement of surgical techniques and instruments, safety of LLR have been improved and indications of LLR has been expanded (5). But LRLR is one of the most challenging laparoscopic procedures and remained slow in dissemination. Adhesiolysis should be performed during LRLR, and is associated with risk of bowel injury and longer operating time. Because of adhesion, bleeding can occur from capsular tears of the liver as a result of traction (9). Adhesion can also disrupt the dissection of hilar area and hepatoduodenal ligament. A deformity of the liver and adhesion make it difficult to identify the tumor and the important structures. These things increase the risks of intraoperative injury to vascular or biliary structures (10).

In this study, there were no significant differences in intraoperative and short-term outcomes between the LRLR and LPLR groups. It means that LRLR is as safe and feasible as LPLR for selected patients. Our result is consistent with other previous studies. Ome et al. (11) mentioned that there were no differences with regard to the operation time, postoperative complications, and mortality between the LRLR and LPLR groups. Shelat et al. (12) reported that the operative time and blood loss were significantly greater in the LRLR group than the LPLR, but the procedure was safer and much feasible.

Laparoscopic procedure facilitates more meticulous adhesiolysis by the pneumoperitoneum and magnified view. LRLR can avoid complete adhesiolysis when adhesion does not affect the operative procedure. So, it could provide less operation time and less damage to other structures compared to the ORLR (5). These advantages could affect our results, that the LRLR group had shorter operation time than the ORLR group. However, the difference in operation time would be also influenced by the selection criteria making the operation easier such as smaller tumor size and anterolateral tumor location. A recent multicenter propensity score-matching study showed that LRLR for colorectal liver metastasis was associated with shorter duration of operation (13).

The difficulty scoring system for LLR proposed by Ban et al. has been used as an indicator of the difficulty of LLR (14). It is scored by the extent of liver resection, tumor location, tumor size, liver function, and tumor proximity to major vessels. The tumors located in anterolateral segments 2, 3, 5, 6, and 4b had low difficulty score than those in posterosuperior segments 1, 7, 8, and 4a. In addition, large size tumor got higher score than smaller tumor (14, 15). We didn't score for our patients, but the tumor size in LRLR group was significantly smaller than that of ORLR group ($p=0.006$). Also, the tumors of LRLR group were mainly located in the anterolateral side ($p=0.017$). It might be said that tumor less than 4.0 cm and located at the anterolateral segments was selected as a good candidate for LRLR in this study.

The open conversion rate in LPLR is 3.3%, that is consistent with other studies (12, 16). The conversion rate in LRLR after previous LLR is 20%. This rate looks higher than other studies, that could be attributed to small sample size ($n=10$). 6 out of 10 patients had LRLR with previous OLR (Table 4). Of those 6 patients, one patient required open conversion (17%). Wakabayashi et al. reported that 11% of the patients who underwent LRLR with the previous OLR required conversion to open surgery in their meta-analysis. It also showed that LRLR after OLR is associated with longer operative time and a much blood loss compared

to LRLR after LLR, but there was no difference between LRLR after OLR and LLR in hospital stay and morbidity (17). Onoe et al. mentioned that there was no difference in operative and short-term outcomes between LRLR after OLR and LLR (18).

Indication criteria for LRLR have not to be clearly defined. Belli et al. reported that the selection criteria for LRLR are well-compensated chronic liver disease without signs of severe portal hypertension; a maximum size of 4 to 5 cm; and tumor located in anterolateral segments (19). Hu et al. performed LRLR for recurrent HCC in specific selection criteria: tumor located in segment 2-6; tumor size <5cm; no major vessel invasion; and Child-Pugh grade A or B (20). A recent published international, multi-institutional, propensity score-based study reported that LRLR could be beneficial in blood loss and morbidity for the HCC patient without the proximity to major vessels. In line with the advancement of surgical techniques and instruments, it is expected that indications for LRLR could be expanded (21).

The limitations of this study include single center retrospective study and small sample size, especially small cases of LRLR. Actually, cases of repeat liver resection are not so many that multi-institutional study is needed to enroll sufficient number of cases. And further studies are needed to address long-term outcomes.

Conclusion

Laparoscopic surgery can be a safe and feasible procedure for repeat liver resection in selected patients with recurred liver tumor. Even though the selection criteria are not firm yet, small tumor located at the anterolateral segments would be suitable until more surgical experience is accumulated to expand the criteria.

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Abstract

Introduction: Laparoscopic liver resection (LLR) has become a widely accepted option of curative resection for liver tumors. Laparoscopic repeat liver resection (LRLR), however, is not widespreading, because of concern about the difficulty in surgical procedure and inadvertent injury to the adjacent vasculature due to distorted anatomy and possible unexpected open conversion. The aims of this study were to assess the feasibility of LRLR by comparing the early operative outcomes to those of the laparoscopic primary liver resection (LPLR) and to assess the benefits of LRLR by comparing to open repeat liver resection (ORLR).

Methods: Between September 2008 and October 2018, a total of 658 patients underwent liver resection at Ulsan University Hospital. For patients in the LLR group (n=100) and ORLR group (n=20), the following parameters were investigated; diagnosis, operative procedures, open conversion rates, operative time, intraoperative bleeding amount, transfusion rates, length of postoperative hospital stay, postoperative complications according to the Clavien-Dindo classification system, and mortality rates. The location and size of the lesion were investigated and compared in LRLR and ORLR groups. Operative and short-term postoperative parameters of 10 patients in LRLR group were compared to 1) the LPLR group (n = 90) and 2) ORLR group (n = 20).

Results: Between the LRLR and LPLR groups, there were no significant differences in operative time, intraoperative blood loss, transfusion requirement, length of postoperative stay, and postoperative complication rates. Tumor size of the LRLR group was much smaller than that of the ORLR group (2.0±1.119 cm vs. 4.0±2.743cm, respectively, p=0.006), and tumors located in the anterolateral segments in the LRLR group were significantly more than the ORLR group (90% vs. 40%, respectively, p=0.017). Length of stay were significantly shorter for the LRLR group compared to the ORLR group (9.5±2.6 days vs. 20.5±14.5 days, p=0.025).

Conclusion: Laparoscopic surgery can be a safe and feasible procedure for repeat liver resection in selected patients with recurred liver tumor. Even though the selection criteria are not firm yet, small tumor located at the anterolateral segments would be suitable until more surgical experience is accumulated to expand the criteria.

Sep. 2008 ~ Oct. 2018

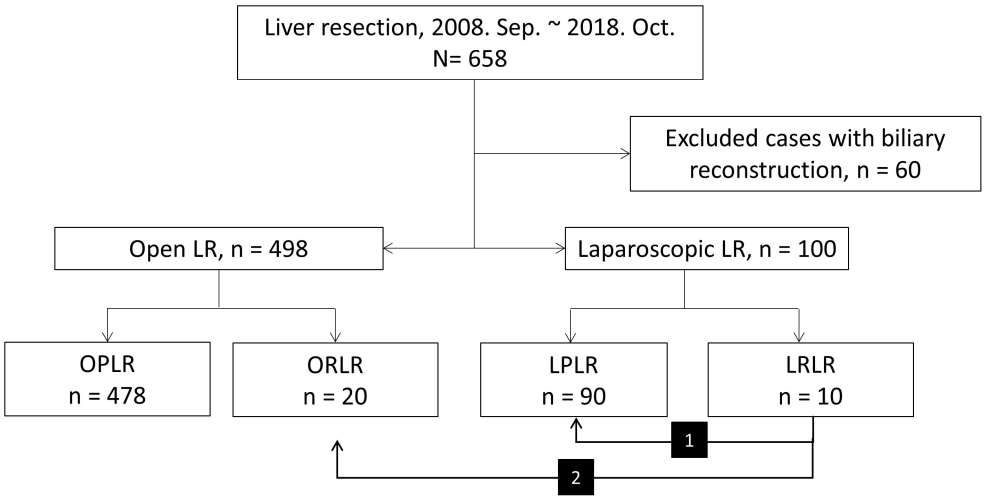

Figure 1. Flow diagram of patient selection. Operative and short-term postoperative parameters of 10 patients in LRLR group were compared to 1) the LPLR group (n=90) and 2) ORLR group (n=20). LLR; laparoscopic liver resection, LPLR; laparoscopic primary liver resection, LR; liver resection, LRLR: laparoscopic repeat liver resection, OLR; open liver resection, OPLR; open primary liver resection, ORLR; open repeat liver resection.

Table 1. Indications of laparoscopic liver resection

Diagnosis		Total (N=100)
Malignant (75)		
	HCC	48
	CCC + mixed tumor	4
	CRLM	15
	Other metastasis	6
	GBC	2
Benign (25)		
	IHD stone	8
	FNH	7
	Others	10

CCC; cholangiocellular carcinoma, CRLM; colorectal cancer liver metastasis, FNH; focal nodular hyperplasia, GBC; gallbladder cancer; HCC; hepatocellular carcinoma, IHD; intrahepatic duct

Table 2. Operative procedures of laparoscopic liver resection

		Total (N=100)
Procedure		
Laparoscopic major*		
	RHH	10
	LHH	12
	RPS	5
Laparoscopic minor		
	Lateral sectionectomy	29
	Segmentectomy/ Wedge resection	44

LHH; left hemihepatectomy, LLS; left lateral segmentectomy, RHH; right hemihepatectomy, RPS; right posterior segmentectomy.
*Laparoscopic major liver resection includes removal of more than 2 Couinaud's segments except LLS.

Table 3. Postoperative complications (≥ Clavien-Dindo grade 2) after laparoscopic liver resection (N=100)

Complication	Grade	n	comments
Wound (dehiscence, bleeding)	3b/2	4	
Ascites	3a	2	Diuretics + paracentesis
Fluid collection with fever	3a	1	PCD
Liver abscess	3a	1	PCD
Post-EMR bleeding	3a	1	Endoscopic control POD#1
Pneumonia	2	1	MRSA
PVT, partial	2	1	Warfarin

EMR; endoscopic mucosal resection of stomach, MRSA; methicillin resistant S aureus, PCD; percutaneous drainage, POD; postoperative day, PVT; portal vein thrombosis,

Table 4. Indications and procedures laparoscopic repeat liver resection

patient	Diagnosis	1st op	2nd op	3rd op	4th op	Reason to OC
1	CRLM	IVb-V [O]	LLS [L]			
2	CRLM	WR S6 [L]	RHH [O]	WR S2&3 [OC]		localization
3	Cyst	fenestration [L]	LLS [L]			
4	HCC	WR S6 [L]	Segtx. 5 [L]			
5	PrCLM	WR S8 [L]	WR S5 [OC]			bleeding
6	CRLM (No.2)				WR S3 [L]	
7	HCC	RHH [O]	WR S3 [L]			
8	HCC	Segtx. 8 [O]	LHH [L]			
9	HCC	Ext. LHH [O]	WR S5 [L]			
10	HCC	Segtx. 8 [O]	LLS [L]			

CRLM; colorectal cancer liver metastasis, ext; extended, HCC; hepatocellular carcinoma, L; laparoscopic, LHH; left hemihepatectomy, LLS; left lateral sectionectomy, O; open, OC; open conversion, PrCLM; prostatic cancer liver metastasis, RHH; right hemihepatectomy, segtx; segmentectomy, WR; wedge resection.

Table 5. Comparison of laparoscopic primary and repeat liver resection

	Primary (n=90)	Repeat (n=10)	p value
Open conversion (n)	3 (3.3%)	2 (20%)	0.077
Op time (minutes)	231 ± 103	261 ± 48	0.131
Estimated blood loss (ml)	525 ± 477	555 ± 486	0.852
Transfusion (n)	13 (14.4%)	2 (20%)	0.643
Length of stay (days)	11.7 ± 8.9	9.5 ± 2.6	0.439
Complication* (n)	6 (6.7%)	1 (10%)	0.533

* Clavien-Dindo classification grade 2 or higher excluding wound complications.

Table 6. Comparison of open and laparoscopic repeat liver resection

	Open (n=20)	Laparoscopic (n=10)	p value
Tumor size (mean, cm)	4.0	2.0	0.006
Anterolateral location	8 (40%)	9 (90%)	0.017
Cirrhosis	12 (60%)	3 (30%)	0.121
Open conversion (n)	n.a.	2 (20%)	
Op time (minutes)	377 ± 134	261 ± 48	0.014
Estimated blood loss (ml)	970 ± 1052	555 ± 486	0.249
Transfusion (n)	3 (15%)	2 (20%)	1.000
Length of stay (days)	20.5± 14.5	9.5±2.6	0.025
Complication* (n)	5 (25%)	1 (10%)	0.633

n.a.; not available.
*Clavien-Dindo classification grade 2 or higher excluding wound complications.