Original article :

Safety and Feasibility of Laparoscopic Major Hepatectomy after Portal Vein Embolization

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Abstract

Background & Aims:
The operative safety and feasibility of laparoscopic major hepatectomy in patients after portal vein embolization is unknown, prompting our investigation of its safety and feasibility in patients at our center.

Methods:
Fifteen patients (male=13, female=2, with median age of 58 years), underwent laparoscopic major hepatectomy after portal vein embolization. Ten patients had hepatocellular carcinoma, two had combined hepatocellular carcinoma and cholangiocarcinoma, and 2 colorectal liver metastases, and 1 cholangiocarcinoma.

Results:
All patients were Child-Turcotte-Pugh score, 10 had liver fibrosis, and 10 had viral hepatitis. The median interval between portal vein embolization and laparoscopic major hepatectomy was 21 days. The median operative time was 324 min, estimated blood loss was 100 mL. White (2.5 mm) and blue (3.5 mm) cartridg-

الملخص

الخلفية و الاهداف:
خلصت بعض الدراسات إلى أمان و فعالية عمليات الإستئصال الكبرى لشرائح الكبد بالمنظار الجراحي، ولكن أمان و فعالية مثل هذه العمليات بعد إجراء إصمام الوريد البوابي، لم يتم توثيقها بعد، و تهدف هذه الدراسة إلى تقصي أمان و فعالية عمليات الإستئصال الكبرى لشرائح الكبد بالمنظار الجراحي بعد إجراء إصمام الوريد البوابي.

طريقة البحث:
تم اجراء ١٥ عملية إستئصال كبرى لشرائح الكبد بالمنظار الجراحي بعد إصمام الوريد البوابي في مركز سامسونغ الطبي بالعاصمة سيؤول بكوريا الجنوبية. ١٠ مرضى عانوا من سرطان الكبد، مريضين عانوا من سرطان مزدوج في الخلايا الكبدية والخلايا المرارية بالكبد، مريضين عانوا من نقائل سرطانية ذات منشأ قولوني، و مريض عانى من سرطان القنوات المرارية خارج الكبد.

النتائج:
كل المرضى كانوا مصنفين في المرحلة أ من تصنيف تشايلد لإعتلال وظائف الكبد، ١٠ مرضى عانوا من تليف في الكبد، ١٠ مرضى عانوا من إلتهابات فيروسية في الكبد.
وسيط مدة العملية كان ٣٢٤ دقيقة ، وسيط كمية الدم النازف المقدرة كان ١٠٠ مليليتر.

es were used in one patient each and Tri-Staple tan (2–3 mm) in 11 patients, and two patients required a combination of tan and purple cartridges (3–4 mm). There was one biliary leak and stricture after using a white cartridge, one transient hepatic insufficiency, and three minor complications. One patient died from a stroke on postoperative day 37. The mortality rate was 6.6% (1/15), and the morbidity rate was 33% (5/15).

Conclusion:

Laparoscopic major hepatectomy after portal vein embolization seems relatively safe and feasible. We advise against using a white cartridge and recommend a thicker cartridge for a more secure staple line.

Keywords:

feasibility, laparoscopic major hepatectomy, portal vein embolization, safety.

تم إستخدام خرطوش أبيض (٢.٥ مم) في مريض واحد، و خرطوش أزرق (٣.٥ مم) في مريض آخر، في حين تم إستخدام خرطوش ثلاثي أسمر (٢-٣ مم) في ١١ مريض، و تم إستخدام خرطوشين في مريض واحد (خرطوش أسمر، و خرطوش أرجواني بسمك ٣-٤ مم).

كان هناك تسريب مراري مع تضيق مراري في مريض واحد (خرطوش أبيض) ، بينما عانى مريض آخر من إعتلال حاد و قصور وظيفي حاد و لكن مؤقت وعابر في الكبد ، في حين عانى ثلاثة مرضى من مضاعفات صغرى.

توفي مريض واحد من جلطة دماغية في اليوم السابع و الثلاثين بعد العملية.

معدل الوفيات كان ٦.٦٪ (١/١٥)، و معدل المضاعفات كان ٣٣٪ (٥/١٥).

الإستنتاج:

خلصت الدراسة إلى أن عمليات الإستئصال الكبرى لشرائح الكبد بالمنظار الجراحي بعد إجراء إصمام الوريد البوابي هي فعالة بنفس فعالية الإجراء المفتوح، و كذلك هي آمنة نسبياً بمعدل وفاة و مضاعفات مقبول. و ينصح المؤلفين بعدم إستخدام الخرطوش الأبيض لقطع العنيق القليسوني بعد إصمام الوريد البوابي، وذلك للتسمك الشديد الذي يحدث في العنيق القليسوني بعد إصمام الوريد البوابي مما يحتاج خرطوشا أكثر سماكة.

الكلمات المفتاحية:

الفعالية، الآمان، إصمام الوريد البوابي،إستئصال شرائح الكبد بالمنظار الجراحي

Introduction

Primary liver cancer is the 7th most commonly diagnosed cancer type and second leading cause of death from cancer worldwide [1]. It is also the 4th and 6th most common malignancy in men and women, respectively, in South Korea and the 2nd leading cause of death in both sexes in South Korea, 80% of which are caused by hepatocellular carcinoma (HCC) [2]. Liver transplantation and liver resections are the only therapeutic strategies with curative intent and potential [3]; however, liver transplantation potential is limited by the inherent shortage in the donor pool worldwide[4], which makes liver resection the most commonly performed curative procedure for primary liver cancer [5]. The potential of major hepatectomy is limited by the risk of post-hepatectomy hepatic insufficiency [6], especially given that the most common form of primary liver cancer (HCC) is related with cirrhotic parenchy-

ma [7]. Although this morbidity has multiple risk factors, its single most important predictor is the volume of the future liver remnant (FLR) [8], limiting the resectability pool.

Selective portal vein embolization (PVE) is an effective adjunct to increasing the resectability pool, allowing major liver resection to be safely provided to a subset of patients with an inadequate FLR volume [9, 10]. The merits and advantages of the laparoscopic approach to laparoscopic major hepatectomy (LMH) have been well established [11–13]; however, the safety and feasibility of LMH after PVE is not known. Laparoscopic hepatectomy after PVE presents several unique technical challenges. First, a thicker pedicle with surrounding inflammation renders hilar dissection a challenging approach, with poor visibility due to diffuse and profuse oozing of blood[14]. Second, the security and safety of a pedicle transection with a stapler on top of coils can be potentially compromised. Thus, this study aimed to assess the safety and feasibility of LMH after PVE.

Materials and Methods

Patient information

Between May 2012 and September 2014, 15 patients underwent LMH after PVE at our center. After obtaining informed consent from patients and approval from the institutional review board of Samsung Medical Center (Seoul, Republic of Korea), we conducted a descriptive retrospective review of the patient's medical and surgical records for preoperative and postoperative details. Patient's liver function had been assessed with the Child-Turcotte-Pugh score and indocyanine green retention rate at 15 min. The inclusion criteria were as follows: patients of Korean descent, adult patients (>18 years old), patients with a diagnosis of liver cancer, patients who underwent LMH, and patients who underwent preoperative PVE. The exclusion criteria were as follows: withdrawal of consent and breach of surgeon's operative protocol. In this study, no patients were excluded.

Future liver remnant volumetric assessment

The FLR volume was assessed using contrast-enhanced computed tomography and calculated and expressed as a ratio of FLR to standard liver volume (FLR/SLV) and as a net increase of FLR (pre-PVE FLR minus post-PVE FLR divided by SLV) (Table1). The SLV, which is calculated using patients' height and weight, correlates better to the metabolic demands of patients than the total liver volume, which may be confounded by the liver status such as cirrhosis [15]. Moreover, it is a more ac-

curate comparison between pre-PVE FLR and post-PVE FLR when a constant SLV is used as a denominator rather than using the variable total liver volume, making comparisons less reliable [15, 16].

PVE and operative techniques

For PVE, we used a contralateral approach through the FLR pedicle, with an injection of Gelfoam into the distal half of the second-order branches and proximal deployment of coils. First-order branches as well as segmental portal veins were spared to segment IVa and IVb.

All operations were performed by a single attending surgeon, with 11 years of laparoscopic hepatectomy experience, using the temporary inflow control maneuver of the Glissonian pedicle technique. Briefly, a circumferential approach for extra-capsular and extra-fascial hilar dissection was performed, followed by temporary pedicle clamping using a bulldog clamp to control the inflow and visualize the ischemic demarcation line which was marked by cautery. Intraoperative ultrasonography was used to identify the middle hepatic vein and its tributaries. The parenchymal transection was started using Sonicision (Covidien, Mansfield, MA, USA) and bipolar forceps until two-thirds of the parenchymal dissection was achieved and the bifurcation of the Glissonean pedicle was fully exposed. A sling was wrapped around the right pedicle, the bulldog clamp was removed, and the stapler was applied to transect the pedicle while the sling was pulled in the opposite direction as a protective measure to avoid catastrophic injury to the remnant portal vein and bile duct. Tri-Staple tan cartridge (2–3 mm; Medtronic, Minneapolis, MN, USA) or a purple cartridge (3–4 mm) was used after estimating the thickness of the pedicle (Table 2). These procedures were performed in all patients, except for the first case, where a white cartridge (2.5 mm) [17] was used, and contralateral retraction of the remnant Glisson was not done. The cut surface was treated with local hemostatic agents, and a drain was inserted.

Results

Patient demographics are described in Table 1. The median age was 58
(range, 32–79) years. Of the 15 patients, 13 were men and two were women. The diagnoses were HCC (n=10), colorectal liver metastasis (n=2), combined HCC and cholangiocarcinoma (n=2), and cholangiocarcinoma (n=1). Twelve patients had been diagnosed with early-stage (I/II) disease, with one patient having stage IVa cholangiocarcinoma. The median number of tumor was 1 (range, 1–3), the median tumor size was 5 cm (range, 1.8–8

cm), and the median Child-Turcotte-Pugh score was 6 (range, 5–6). Ten patients had background fibrosis, of which one had cirrhosis. Ten patients had viral hepatitis (7 hepatitis B virus (HBV), two had hepatitis C virus (HCV), one had combined HBV/HCV infection).

The median initial FLR/SLV rate was 24.3% (range, 16.8%–28.8%), and the median post-PVE FLR volume rate was 42.6% (range, 33.7%–46.9%), with a median net increase of 71.3% (range, 38.8%–110.4%) over a median interval of 21 (range, 14–42) days (Table 1).

Eleven patients underwent laparoscopic right hepatectomy, with four undergoing laparoscopic extended right hepatectomy. The median operative time was 324 (range, 246–803) min, and the median estimated blood loss was 100 mL (range, 50–300 mL) (Table 2). All patients had a negative resection margin with a median margin of 1 cm (range, 0.1–5 cm). There were no conversions to open surgery, no intraoperative transfusions, and no operative mortality. One patient had postoperative intra-abdominal bleeding, which responded to transfusion therapy. There was one incidence of biliary leak and stricture that responded successfully to percutaneous transhepatic biliary drainage and endoscopic retrograde biliary drainage. Moreover, upper limb deep vein thrombosis (n=1), transient post-hepatectomy hepatic insufficiency (n=1), which was followed by full recovery, and surgical site infection after a combined colectomy (n=1) occurred. The median length of hospital stay was 9 (range, 5–37) days, and one patient died after a stroke on postoperative day 37 (Table 2).

Table 1. Patient Demographics

Patient	Age/sex	Comorbidity	Diagnosis	Tumor burden		CTP	ICG R15	Nontumoral liver status			SLV ml	FLR Pre-PVE %	FLR Post-PVE %	FLR Net increase %	PVE-Surgery Interval (days)
				no	Size cm			Fibrosis	Cirrhosis	CASH					
1	44/m		CCC-B/C	1	6.3	A5	10%	No	No	NA	1278	21%	44%	110%	28
2	58/f	TB	HCC-B	1	5	A6	17%	Septal	No	NA	996	27%	46%	71%	21
3	76/f	Nill	HCC-B	1	1.8	A6	10%	Septal	No	NA	982	20%	41%	110%	21
4	57m	Nill	CLM	1	6	A5	18%	No	No	No	1191	29%	47%	63%	28
5	50/m		CLM	3	3	A5	7%	No	No	No	1365	27%	44%	63%	14
6	57/m	DVT, PE, IHD, DM, HTN	HCC-B	1	3.8	A6	10%	Septal	No	NA	1376	23%	35%	52%	21
7	32/m	Nill	HCC-B	1	2	A5	10%	Septal	No	NA	1396	27%	39%	41%	14
8	78/m	DM, HTN	HCC-B	1	6.5	A6	9%	No	No	NA	1274	25%	43%	73%	21
9	65/m	DM, TB, HTN, HIV	CCC	1	8	A6	16%	Septal	No	NA	1341	28%	46%	62%	14
10	55/m	HTN, DM	HCC-B/ CCC	1	6	A6	70%	cirrhosis	Micronodular	NA	1211	24%	34%	39%	42
11	56/m	, HTN, TB	combined CCC/ HCC-B	1	3.5	A5	16%	Septal	No`	NA	1093	26%	44%	70%	21
12	68/m	HTN	HCC-NBNC	1	4.5	A5	8%	Septal	No	NA	1154	23%	42%	83%	14
13	79/m	DM, COPD	HCC-NBNC	1	12	A6	13%	No	No	NA	1147	17%	35%	105%	14
14	68/m	TB	HCC-C	1	5	A6	24%	Septal	No	NA	1181	19%	38%	102%	14
15	61/m	Nill	HCC-C	1	3.5	A6	17%	Septal	No	NA	1119	24%	43%	79%	14

B, hepatitis B virus; C, hepatitis C virus; CASH, chemotherapy-associated steatohepatitis; CCC, cholangiocarcinoma; CLM, colorectal liver metastasis; COPD, chronic obstructive pulmonary disease; CTP, Child-Turcotte-Pugh; DM, diabetes mellitus; DVT, deep vein thrombosis; F, female; FLR, future liver remnant; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; HTN, hypertension; ICGR15, indocyanine green retention rate at 15 minutes; IHD, ischemic heart disease; M, male; NA, not applicable; NBNC, no hepatitis B or C virus; PE, pulmonary embolism; PVE, portal vein embolization, SLV, standard liver volume; TB, tuberculosis, NA Not applicable

Table 2. Perioperative variables

Patient	Procedure	Operative time mins	Pringle's (no)	Pringle's duration (mins)	EBL (ml)	Margin (cm)	Stapler color code	Complications			LOS (day)
								Type	Grade (CD)	Management	
1	eRH	803	3	45	< 300	1	White*	Postoperative bleeding	Ii	Conservatively Blood component therapy	37
								Bile leak, grade B	Iiia	PTBD/ ERPD	
2	RH	293	0		< 100	5.5	Tan†				9
3	eRH	324	0		< 100	0.5	Tan	Upper limb DVT	Ii	Anticoagulation	14
4	RH & RC	276	0		< 100	2	Tan	SSI: superficial incision	Ii	IV antibiotic/bedside drainage	25
								Organ space (thoracic empyema)	Iiia	IV antibiotics/ICD	
5	RH	363	1	8	< 100	1	Tan				9
6	RH	253	0		< 100	4	Tan				10
7	RH	266	0		< 100	1	Tan				8
8	RH	246	0		< 50	0.1	Tan				5
9	RH	332	2	30	< 300	2	Tan				8
10	RH	570	3	45	< 300	0.5	Tan	Post-hepatectomy liver insufficiency	Iva	Supportive ICU care	20
11	RH	272	1	15	< 50	5	Tan				10
12	RH	248	2	30	< 100	1.4	Tan				6
13	eRH	421	5	75	< 300	0.5	Tan, purple‡	Brain air embolism	V	Supportive ICU care	35
14	eRH	452	1	20	< 300	1	Tan, purple				7
15	RH	343	0		< 100	1.1	Blue #				7

CD, Clavien-Dindo Classification; DVT, deep vein thrombosis; ERBD, endoscopic retrograde biliary drainage; eRH, extended right hemihepatectomy; ICD, intercostal drainage tube; ICU, intensive care unit; IV, intravenous; PTBD, percutaneous transhepatic biliary drainage; RC, right hemicolectomy; RH, right hemihepatectomy; SSI, surgical site infection

* (2.5 mm) thickness

† (2–3 mm, Tri-Staple) thickness

‡ (3–4 mm, Tri-Staple) thickness

(3.5 mm) thickness

Discussion

In this case series, we investigated the safety and feasibility of LMH for this specific subpopulation of patients in our center. Fifteen patients underwent LMH post PVE, with a morbidity rate of 33%, and a mortality rate of 6.6%.

The laparoscopic approach to major hepatectomy is being increasingly adopted, with many technical challenges having now been overcome, establishing its safety and feasibility [18–20]. However, in patients

who undergo PVE, LMH poses a unique set of technical challenges related to dissection and transection of the ipsilateral Glissonean pedicle because the pedicle is thicker resulting from surrounding inflammation, which causes oozing of blood and poor visibility, and the security and safety of a pedicle transection with a stapler can be potentially compromised [14]. Thus, the safety and feasibility of LMH in this particular subpopulation remains under study. The first patient from the series had postoperative bleeding, bile leak, and stricture, reflecting a staple line failure. It's the author's opinion that the bleeding and biliary leak was probably caused by the inappropriate use of a thin white cartridge for a thick Glissonean pedicle found in patients with PVE, and that biliary stricture was probably due to not implementing the sling technique (pulling away towards the contralateral side during stapling for protection from potential involvement or narrowing of the remnant structure). These complications were taken into consideration for the rest of our patients, in which a thick Tri-Staple tan cartridge was used, and contralateral traction of the sling was applied, and staple line failure was not observed subsequently.

Only one patient experienced surgical site infection, most likely due to a simultaneous colectomy. The liver function recovered well except in a 55-year-old patient who had background cirrhosis with an indocyanine green retention rate of 70% before PVE (it was assumed preoperatively that most of the retention was in the difunctional specimen side due to PVE and multiple trans-arterial chemoembolization sessions were performed). The patient's FLR increased by only 39% despite waiting for 42 days, and after right hepatectomy, the patient had an estimated FLR of 34%, suggesting an inadequate regenerative capacity. Moreover, the Pringle maneuver had to be used three times with a total ischemic time of 45 min because of bleeding tendency resulting from severe cirrhosis during the parenchymal dissection; all these combined risk factors contributed to the patient's transient post-hepatectomy hepatic insufficiency. The upper limb deep vein thrombosis (only other complication) and a single mortality (a stroke from air embolism after a postoperative central line insertion for total parenteral nutrition) were not necessarily related to the laparoscopic approach. PVE is associated with increased liver-specific morbidities including post-hepatectomy hepatic insufficiency, but not overall morbidities, even in open major hepatectomy (which is less challenging than LMH) [21].

Another alternative competing strategy to preoperative PVE is associating liv-

er partition and portal vein ligation for staged hepatectomy (ALPPS) [22]; however, this strategy was traditionally reserved for non-cirrhotic parenchyma [22]. A recent study showed that PVE did not confer an additional increase in morbidity and mortality compared with ALPPS and did not find a statistically significant difference in overall survival between the two strategies. However, in cirrhotic patients, ALPPS was statistically significantly more effective in increasing the resectability pool, as PVE failed to induce sufficient hypertrophy to achieve the minimum required FLR to proceed to resection in 33 patients (67.7% resection rate) compared with the only one patient in the ALPPS group (97.8% resection rate) ($p = 0.001$) [22]. Another promising strategy to increase the FLR preoperatively is by combined hepatic and PVE (HPVE) [23]. A recent systematic review showed that HPVE has an 85.3% resection rate and the FLR volume hypertrophy increased, which ranged from 33% to 63.3% (compared with 71.3% in our series), with a 0% rate of post-hepatectomy hepatic insufficiency, 10.3% morbidity rate, and 5.1% mortality rate post-hepatectomy [23]. However, such a favorable outcome may be caused by the confounding effect of not controlling for non-cirrhotic parenchyma as only 5.9% of the sample had cirrhosis [23] compared with 6.6% cirrhosis rate and 66.7% fibrosis rate in our series. Considering this series of challenging cases, the morbidity, albeit relatively high, could be regarded as acceptable.

Nevertheless, this study has limitations, including small sample size, potential for selection bias due to patient recruitment from only one center, descriptive design, lacks comparisons between any active or passive group, and non-generalizable conclusions and results to different populations. The strengths of this study were as follows: all cases were performed by the same surgeon ensuring strict compliance to the protocol and diverse patient characteristics reflect the Korean patient population with liver cancer. This study should prompt further research to enroll a larger sample in a randomized controlled trial to explore the safety and feasibility of LMH after PVE in a more rigorous manner.

In conclusion, we believe that LMH after PVE may be feasible in highly selected patients, with adequate FLR increase after PVE (> 40%), in the hands of surgeon with more than 5 years of experience in LMH, in a high volume center (> 50 LMH/year), and relatively safe in the short term, and extended follow up is needed to determine its long term safety, keeping in mind that transection of the thick Glissonean pedicle requires a thick cartridge, and implementing the sling technique to protect the rem-

nant pedicle.

Conflict of interest:

Choon H. D. Kwon is a consultant of Covidien, Ethicon, and Novartis. All the other authors have no financial relationships with any pharmaceutical or device company.

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