Feasibility and safety of laparoscopic portal vein ligation prior to major hepatectomy for hepatocellular carcinoma

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Abstract

Background: Patients with hepatocellular carcinoma (HCC) demonstrated to have an inadequate future liver remnant (FLR) on preoperative volumetric assessment are potential candidates for laparoscopic portal vein ligation (LPVL). Previous studies have reported that for patients with hepatic malignancies, laparoscopic portal vein ligation (LPVL) is efficient in increasing FLR, which, however, has not been solely reported in HCC. The purpose of this study was to evaluate the safety, feasibility and efficiency of LPVL prior to major hepatectomy for patients with HCC.

Methods: Clinical information of HCC patients who had undergone laparoscopic portal vein ligation (LPVL) at our center was retrospectively reviewed and documented. Demographic, radiographic, clinical and volumetric details (both before and after LPVL) were retrieved to evaluate the feasibility and safety of LPVL prior to major hepatectomy for HCC.

Results: Between April 2020 and December 2021, there were a total of 10 HCC patients undergoing LPVL as a preparation for subsequent major hepatectomy at our center. The mean age of these 10 patients was 61.30 ± 8.83 years old. Of these 10 patients, 9 were male and only 1 was female. 9 patients underwent laparoscopic ligation of the right portal vein and one the left portal vein. All the patients' left or right portal veins were ligated by clips. After LPVL, the mean volume increased from 433.16 ± 103.64 ml to 550.62 ± 123.19 ml ($P < 0.001$). All the 10 patients had adequate hypertrophy of FLR and subsequent major hepatectomy was performed as scheduled. No LPVL-associated complications were recorded.

Conclusion: LPVL is both feasible and could be safely performed. For carefully selected patients, LPVL could be considered as a safe and feasible alternative to portal vein embolization (PVE) given the rather low complication rate and high efficiency of LPVL.

Background

Hepatocellular carcinoma (HCC) is the sixth most common malignant tumor and causes the third most cancer-related deaths [1]. Annually, nearly half of all the HCC patients are diagnosed in China [1, 2]. Curative resection of HCC through hepatectomy or liver transplantation remains the only one method with the potential to cure HCC.

For patients who are scheduled to undergo major hepatectomy but prevented by an inadequate future liver remnant (FLR), portal vein occlusion by embolization or ligation is widely being performed around the world [3–6]. For most patients, the decision to perform portal vein occlusion whether by PVE or LPVL is usually made after the preoperative volumetric assessment is accomplished. However, for a subset of patients are chosen as candidates for procedures occluding the portal vein during staging laparoscopy when accident bilobar involvement is encountered. Additionally, patients with colorectal cancer and synchronous liver metastasis who are qualified for laparoscopic resection of primary tumor are potential candidates for portal vein occlusion.

Laparoscopic portal vein ligation (LPVL), portal vein embolization (PVE), and associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) have been designed and performed in clinical practice to increase FLR. By far, it remains controversial which one is the most appropriate. Isfordink CJ et al reported that PVE should be the preferred choice given its efficiency and minimal invasiveness[7]. Similar results were also reported by Pandanaboyana S et al [8]. However, for patients with extensive portal thrombus and important portal hypertension, PVE should not be recommended[9]. Also in this review, it was pointed out that PVE might promote tumor growth within the embolized liver [9]. LPVL also has some shortcomings, such as LPVL being prevented by abdominal adhesions caused by previous surgeries, procedure-related complications and inadequate liver function reserve[9]. Additionally, for some patients receiving LPVL, subsequent PVE may be needed to further increase FLR. The ability of PVL to ligate the portal vein as well as its potential to avoid subsequent procedures is its another advantage [5].

However, feasibility, safety and efficiency of LPVL in increasing FLR of patients with HCC have not been fully investigated. Considering the aforementioned advantages and disadvantages of LPVL, we performed the present study to assess the safety and feasibility of LPVL among HCC patients eligible for curative hepatectomy but prevented by insufficient FLR.

Methods

Medical records of all the HCC patients who had undergone LPVL between April 2020 and December 2021 at Department of Hepatobiliary and Pancreatic Surgery, Shenzhen Peoples Hospital were reviewed. Information of demographics, diagnosis, range of hepatic involvement on CT scanning, and preoperative or postoperative volumetric assessment was retrospectively collected. LPVL was accomplished as previously described.

As demonstrated in Fig. 1, patients were supine onto the operating table with trocars properly positioned. The Hasson technique was adopted to gain access to the peritoneal cavity and the pneumoperitoneum was maintained between 12 and 13 mmHg. After successful diagnostic laparoscopy, the decision to perform portal vein ligation was made for each patient by combining results of pre-operative radiological examinations and intra-operative findings. An intra-operative ultrasonography examination of the liver was routinely performed in each patient. The harmonic scalpel was used to dissect the portal triad. Initially, we dissected and elevated the bile duct to expose the portal vein trunk. Then bifurcation of the portal vein was identified by a further dissection in the cranial direction. The right or left portal vein was the dissected and encircled using a vessel loop. After being thoroughly dissected, the right or left portal vein was occluded either using clips. In addition to details of LPVL, information of additional procedures performed along with LPVL, mortality, complications and post-operative recovery was retrieved from the medical records.

Extend of hepatic involvement by HCC was evaluated by performing a CT scan and 3-dimensional reconstruction as well as the subsequent volumetric calculation before LPVL. For most patients, a CT scan and 3-dimensional reconstruction as well as the subsequent volumetric calculation was performed

two to three weeks after LPVL. However, for a small number of patients, four to five weeks had passed before the CT scan was performed. Degree of liver hypertrophy (DOLH) was evaluated by performing 3-dimensional reconstruction as well as subsequent volumetric calculation both before and after LPVL. Standard liver volume (SLV) was calculated according to the formula described by T. Kokudo et al, $SLV(ml) = 706 \times \text{body surface area}(m^2) + 2.4$.

Results

Between April 2020 and December 2021, a total of 10 patients with HCC underwent LPVL at Department of Hepatobiliary and Pancreatic Surgery, Shenzhen Peoples Hospital. Demographics and clinicopathological details of these 10 patients were summarized in Table 1. All the patients included in this study were with resectable HCC but prevented by inadequate future liver remnant. The third patient was chosen as the representative, and his preoperative 3-D reconstruction images were demonstrated in Fig. 2 while contrast-enhanced CT before and after LPVL were presented in Fig. 3.

Table 1
Demographics and clinical details of the ten patients included in the study.

Patient#	Age	Sex	Diagnosis	Extend of hepatic involvement	Other hepatic procedure
1	53	M	HCC	VII, VIII	LC
2	50	F	HCC	V, VI	LC
3	58	M	HCC	VIII	LC
4	64	M	HCC	II, III, IV	LC, Microwave ablation
5	67	M	HCC	VII, VIII	LC
6	63	M	HCC	VIII	LC
7	47	M	HCC	VII, VIII	LC
8	71	M	HCC	VI, VII, VIII	LC
9	71	M	HCC	V	LC
10	69	M	HCC	VII, VIII	LC

For nine patients, the right portal vein was ligated while ligature of the left portal vein was performed for one HCC patient. Absorbable vascular clips were used to ligate the left or right portal vein. Apart from LPVL, nine patients underwent cholecystectomy while the remaining one underwent ligation of the left portal vein plus cholecystectomy and microwave ablation of satellite lesion located in segment VIII. Neither mortality nor LPVL-associated complications were recorded. Length of hospital stay after LPVL was between 10 and 28 days (18.66 ± 5.99 days). The expense for LPVL was between 31016 and 65281 yuan (45617.75 ± 9843.87 yuan).

FLR before LPVL was between 299.87 and 636.42 (433.16 ± 103.64) and FLR after LPVL was between 372.36 and 820.63 (550.62 ± 123.19) (Table 2). Increase in FLR was between 10.86ml and 184.21ml (117.26 ± 48.46) (Table 2). By paired t test, we revealed that FLR after LPVL was significantly higher than that before LPVL ($P < 0.001$). The duration between LPVL and second-stage procedure was between 18 and 33 days (26.75 ± 4.58 days). Disease progression had not been recorded in any patients. Second-stage curative resection of HCC was successfully performed for all the patients including seven right hemihepatectomy, one right hemihepatectomy plus caudate lobectomy and one extended right posterior sectionectomy. Length of hospital stay after the second-stage surgery was between 5 days and 17 days (11.22 ± 4.08 days). Expense for the second-stage surgery was between 64788 and 102242 yuan (79667.05 ± 9977.04 yuan).

Table 2
Standard liver volume, preoperative FLR, postoperative FLR, increase in FLR and degree of FLR hypertrophy.

Volumetric data						
Patient#	Diagnosis	SLV (ml)	Pre op FLR (ml)	Post op FLR (ml)	Difference in volume(ml)	DOH(%)
1	HCC	1177	636.42	820.63	184.21	0.289
2	HCC	1061	354.42	460.45	106.03	0.299
3	HCC	1178	339.44	478.55	139.11	0.410
4	HCC	1299	528.81	539.67	10.86	0.021
5	HCC	1342	509.19	678.80	169.61	0.333
6	HCC	1319	415.06	559.39	144.33	0.348
7	HCC	1180	364.11	526.47	162.36	0.446
8	HCC	1167	299.87	372.36	72.49	0.242
9	HCC	1257	476.95	555.88	78.93	0.165
10	HCC	1088	407.33	513.96	106.63	0.262

Discussion

For HCC patients with insufficient FLR, occluding portal vein through either PVE or PVL has become a routine practice [10, 11]. After being occluded of portal vein of the to-be resected liver tissue, blood will be redirected into the FLR, which has shown to be capable of reducing risk of peri-operative liver failure and other related complications. Occlusion of portal vein is usually accomplished through the method of PVE that was initially designed and reported for carcinoma of bile duct by Makucchi et al in 1984[12, 13]. Then in 1986, it was reported by Kinoshita et al that like in hilar cholangiocarcinoma, PVE could be safely performed among patients with hepatocellular carcinoma [14]. Besides being performed in patients with

hepatocellular carcinoma and hilar cholangiocarcinoma, PVE has also been described among patients with liver metastasis from colorectal cancer [15–17]. Although many clinicians regard PVE as the preferred choice, some doctors have investigated the roles and efficiency of PVL in increasing future liver remnant[18–20].

The decision to ligate the portal vein or perform PVE is usually made according to results of preoperative volumetric calculation, especially FLR/SLV. PVE is accomplished through the contralateral or ipsilateral liver lobe by the transhepatic route. However, some patients who may be potential candidates for staged hepatectomy undergo laparoscopic assessment before PVE. The capability of PVL to ligate the portal vein and its potential to avoid subsequent PVE is its advantage. Unlike in western countries, most of the hepatectomy procedures in China are performed for patients with hepatocellular carcinoma. Additionally, most patients with hepatocellular carcinoma in China simultaneously suffered from liver cirrhosis, meaning that underlying liver function should be more cautiously taken into consideration. And after searching studies on PVL, we found that PVL had not been extensively studied among patients with HCC. The purpose of this study was to assess feasibility, safety and efficiency of PVL in patients with hepatocellular carcinoma.

Results of the present study revealed that LPVL was feasible, safe and efficient for patients with hepatocellular carcinoma. Of the ten patients with hepatocellular carcinoma receiving LPVL, none experienced surgery-related complications and all successfully underwent second-stage curative hepatectomy. Additionally, it was also demonstrated that LPVL could efficiently increase FLR of patients with hepatocellular carcinoma. In some patients with hepatocellular carcinoma, metastasis from the primary site to FLR is often detected by preoperative imaging examinations or intraoperative assessment, meaning capability of LPVL to ligate portal vein as well as to resect metastatic lesion in FLR is its another advantage. In this study, one patient was diagnosed with metastatic lesion within FLR, and this lesion was dealt with by intraoperative microwave ablation. And in this study, none of the patients experienced disease progression and all underwent second-stage hepatectomy. In some studies, not all the patients could undergo second-stage hepatectomy due to disease progression [21]. Therefore, more large-scaled studies are needed to evaluate the effects of LPVL on progression of HCC. Therefore, considering all these findings, we may draw the conclusion that LPVL is feasible, safe and efficient.

There are other potential advantages related to LPVL. Ligating the portal vein at the time of laparoscopy could potentially avoid subsequent PVE. Furthermore, some of PVE-related complications could be avoided by performing LPVL. According to some previously published studies, PVE was associated with some unique technique and liver related complications [24–26]. And in these studies, it was reported that incidence of PVE-related complications was between 12.8% and 15%[22–24]. Common PVE-associated complications include haemobilia, arterial puncture, haemoperitoneum, puncture site haematomas, pseudoaneurysm, subcapsular haematomas, pneumothorax, occlusion of main portal vein, migration of embolic material to FLR, arteriovenous and arterioportal fistulas.

And apart from these complications described above, some authors have also reported that in some patients, PVE could result in inappropriate increase of tumors in comparison with that of normal liver tissue [25, 26]. Elisa et al reported that for patients with functionally intact liver parenchyma, after PVE, the metastatic lesions grew more rapidly than normal liver tissues [25]. However, it remains unknown whether this phenomenon could also be observed among patients with hepatocellular carcinoma. The capability of LPVL to resect minimal tumor in the FLR as well as to ligate the portal vein at the same time could potentially reduce the risk of HCC progression. Another advantage of LPVL is that it does not prevent subsequent PVE if PVE is indicated. For 17% of patients with variations of the right portal vein anatomy, risk of failure to induce adequate hypertrophy after LPVL significantly increased, suggesting that for these patients, LPVL should be prudently recommended and subsequent PVE should be prepared. In the study by Are C et al, it was reported that two patients did not have adequate hypertrophy after LPVL and subsequent PVE lead to sufficient increase in FLR.

Results of this study reveal that LPVL is feasible, safe and associated with adequate hypertrophy of FLR. Patients with HCC who are candidates for curative surgery but prevented by inadequate FLR should be assessed for LPVL. LPVL could avoid subsequent PVE with some of its unique complications and could deal with minimal lesions in the FLR as well as ligate the portal vein. Therefore, by performing LPVL, we could potentially reduce the risk of HCC progression in FLR. Considering all these results, we may reach the conclusion that for some patients, LPVL is a feasible, safe and efficient approach to induce adequate volume of FLR and it could be adopted as a feasible alternative to PVE.

Conclusions

For carefully selected HCC patients, LPVL is safe, feasible and efficient in inducing hypertrophy of FLR, suggesting its potential as an alternative to PVE.

Abbreviations

HCC: hepatocellular carcinoma

FLR: future liver remnant

LPVL: laparoscopic portal vein ligation

PVE: portal vein embolization

ALPPS: associating liver partition and portal vein ligation for staged hepatectomy

SLV: standard liver volume

Declarations

Availability of data and materials

Data analyzed in this study are available from the corresponding authors upon reasonable requests.

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Authors' contributions

Yusheng Guo, Tailai An and Jiangang Bi designed this study. Yusheng Guo, Linsen Liu and Yan Wang collected the data. Jiangang Bi and Tailai An supervised this study. Yusheng Guo and Yan Wang performed statistical analysis. Yan Wang, Linsen Liu and Tianchong Wu performed 3-dimensional reconstruction and volume calculation. Tailai An and Yusheng Guo wrote the manuscript. Shiyun Bao, Yawei Wang and Jiangang Bi revised the manuscript. Yusheng Guo and Tailai An submitted this study. All the authors read and approved the final manuscript.

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Availability of data and materials

Data analyzed in this study are available from the corresponding authors upon reasonable requests.

Ethics approval and consent to participate

Our study was approved by the Ethics Committee of Shenzhen People's Hospital (NO. LL-KY-2021864).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Positions of trocars for LPVL.

SLV: 1178 ml
FLR: 339.44ml
FLR/SLV: 28.81%

A

SLV: 1178 ml
FLR: 478.55 ml
FLR/SLV: 40.62%

B

Figure 2

Three-dimensional reconstruction and volumetric assessment before LPVL and after LPVL for patient #3.

A: Three-dimensional reconstruction and volumetric assessment performed before LPVL for patient #3 revealed an inadequate FLR. **B:** Three-dimensional reconstruction and volumetric assessment performed after LPVL for patient #3 revealed an adequate FLR.

Figure 3

A1 Unenhanced CT scanning performed for patient #3 before LPVL . **A2**: Arterial phase of CT scanning performed for patient #3 before LPVL. **A3**: Portal venous phase of CT scanning performed for patient #3 before LPVL. **A4**: Delayed phase of CT scanning performed for patient #3 before LPVL. **B1**: Unenhanced CT scanning performed for patient #3 29 days after LPVL. **B2**: Arterial phase of CT scanning performed for patient #3 29 days after after LPVL. **B3**: Portal venous phase of CT scanning performed for patient #3 29 days after after LPVL. **B3**: Portal venous phase of CT scanning performed for patient #3 29 days after LPVL. **B4**: Delayed phase of CT scanning performed for patient #3 29 days after LPVL.