



Laparoscopic associating liver tourniquet and portal ligation combined rescue transhepatic arterial embolization for staged hepatectomy

A case report

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Abstract

Rationale: Staged hepatectomy is an important surgical method for large hepatocellular carcinoma (HCC). However, the insufficient future liver remnant (FLR) is still the major barrier in stage II hepatectomy. We herein reported a case of laparoscopic associating liver tourniquet and portal ligation combined rescue transhepatic arterial embolization (TAE) for staged hepatectomy.

Patient concerns: Laparoscopic associating liver tourniquet and portal ligation for staged hepatectomy (ALTPS) was performed for cirrhotic HCC in stage I. To stimulate the growth of FLR, a "rescue" TAE was initiated before stage II.

Diagnose: HCC with hepatitis B cirrhosis.

Outcomes: Two weeks later after TAE, the FLR achieved sufficient hypertrophy and stage II surgery was successfully performed. The patient was discharged 7 days after the second stage without serious complication. During the follow-up at postoperative 6 months, the patient underwent radiofrequency ablation, because contrast-enhanced ultrasonography showed 1 cm tumor recurrence in the remnant liver.

Lessons: Rescue TAE plays an important role to stimulate the increasing of FLR after ALTPS.

Abbreviations: AFP = alpha-fetoprotein, ALB = albumin, ALPPS = associating liver partitioning and portal vein occlusion for staged hepatectomy, ALT = alanine aminotransferase, ALTPS = associating liver tourniquet and portal ligation for staged hepatectomy, AST = aspartate transaminase, BW = body weight, Cr = creatinine, CT = computed tomography, FLR = future liver remnant, HABR = hepatic arterial buffer response, HCC = hepatocellular carcinoma, ICG = indocyanine green, INR = international normalized ratio, KGR = kinetic growth rate, PBL = portal branch ligation, PT = prothrombin time, PVE = portal vein embolization, PVL = portal vein ligation, RFA = radiofrequency ablation, SLV = standard liver volume, TAE = transhepatic arterial embolization, TBIL = serum total bilirubin.

Keywords: ALTPS, hepatic arterial buffer response (HABR), rescue, staged hepatectomy, TAE

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1. Introduction

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) can achieve rapid hypertrophy of the future liver remnant (FLR).^[1] In 2014, we introduced a modification of the ALPPS procedure, the laparoscopic anterior approach "associating liver tourniquet and portal ligation for staged hepatectomy (ALTPS)" (through the retrohepatic tunnel without the mobilization of the right liver).^[2] Although the technique was a useful technique, which could provide a less invasive modification of the ALPPS procedure with greater oncological efficacy, but sometimes the growth still was not enough after stage I. According to the International ALPPS registry, 70% of the tumors were colorectal metastases, and ALPPS increased the mean volume by 80% over 7 days.^[3]

In contrast, most of the cases were hepatocellular carcinoma (HCC) developing from chronic viral hepatitis in China. It is well known that a liver with chronic liver diseases has a lower regenerative and hypertrophying capacity. [4] Albert et al's report^[5] showed patients with HCC developing from chronic viral hepatitis only attained a volume increment by 48.7% over 6 days. Accordingly, we need to think about what could be applied to the patients when the operation of stage I failed to stimulate sufficient growth of the FLR?

Table 1
Perioperative clinical characteristics of the patient.

	AST, U/L	ALT, U/L	Alb, g/L	TBIL, μmol/L	Cr, μmol/L	PT, S	INR
Before operation	67	56	32.6	7.8	71.3	11.7	1.0
POD 1 (stage I)	765	734	28.4	18.7	74.1	11.9	1.1
POD 3 (stage I)	342	489	32.1	28.9	67.8	12.3	1.2
POD 7 (stage I)	84	97	33.7	19.8	58.7	11.6	1.3
POD 14 (stage I)	58	61	32.4	21.2	57.2	11.8	1.1
POD 1 (TAE)	432	521	31.2	26.2	68.2	13.2	1.3
POD 3 (TAE)	243	286	30.2	24.3	54.4	14.2	1.3
POD 7 (TAE)	79	84	31.1	18.8	60.2	12.3	1.2
POD 14 (TAE)	43	54	32.1	13.6	54.0	11.5	1.1

Alb = albumin, ALT = alanine aminotransferase, AST = aspartate transaminase, Cr = creatinine, INR = international normalized ratio, PT = prothrombin time, TAE = transhepatic arterial embolization, TBIL = serum total bilinubin.

Previous study has indicated that the loss of portal blood flow after portal vein ligation (PVL) is compensated by a HABR. Several studies suggested that the HABR play a very important role in blood-flow restoration and tumor growth after PVL. [6,7] Considering the important role of the HABR after PVL, if the FLR growth still was not enough after stage I, we imagined that HABR can be blocked by using transhepatic arterial embolization (TAE).

We herein reported a case that underwent "rescue" TAE for staged hepatectomy, because the liver hypertrophy gained with the first stage of the laparoscopic anterior approach ALTPS was insufficient for the serious cirrhosis.

2. Methods

2.1. Patient information

In September 2015, a 48-year-old male suffering from HCC with hepatitis B cirrhosis was admitted to the Sichuan Academy of Medical Sciences (Sichuan Provincial People's Hospital). The standard liver volume (SLV) of the patient according to West China Hospital's Formula of SLV of Chinese adult^[8] was 1368 mL [body height and body weight (BW) were 169 cm and 90 kg, respectively]. The Sichuan Provincial People's Hospital administration and the ethics committee authorized the surgery.

According to the Pugh-modified Child's score scale, the score was 6 (Child classification: grade A). Indocyanine green (ICG)

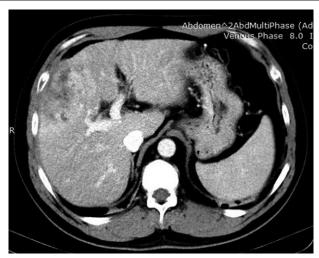


Figure 1. Computed tomography images before operation.

retention rate was 16% at 15 minutes. Laboratory tests showed increases in HBV-DNA $(6.9 \times 10^4 \text{ IU/mL})$, prothrombin time (PT), aspartate transaminase (AST), and alanine aminotransferase (ALT) (Table 1). Computed tomography (CT) shows 4 tumors in the right liver, no tumor in the left liver, and no tumor thrombus in the portal vein (Fig. 1). The tumor characteristics combined with a elevated alpha-fetoprotein (AFP) level, increasing to 2323.8 ng/L, with no evidence of splenomegaly or portal hypertension, were consistent with HCC. Considering that Ultrasonic Transient Elastography (Fibroscan, Denmark) showed the median value of stiffness was 24.7kPa, a liver biopsy of segments 2/3 was performed, indicating nodular cirrhosis and fatty liver (G 4, S 3, F 2). CT liver volumetry showed that if the right hemihepatectomy was required to be performed, the FLR (segments 2, 3, and 4 with volume of 415 mL) would likely be insufficient for postoperative recovery (FLR/SLV: 30%; FLR/BW: 0.46%), which indicated that the patient was inappropriate to receive radical resection of HCC.

2.2. Surgical procedures

Plans were made to use the laparoscopic anterior approach ALTPS procedure to induce rapid hypertrophy of the FLR. The patient underwent operation as previously described in detail. ^[2] In the first stage, using a totally laparoscopic technique, a tourniquet was placed around the parenchymal transection line on the Cantlie line via an anterior approaching through the retrohepatic tunnel for staged right hepatectomy, and the right portal vein was ligated. Laparoscopy showed apparent nodules on the liver surface (Fig. 2). Cholecystectomy was performed



Figure 2. Apparent nodules in the liver surface and the tourniquet was placed around the parenchymal transection line on the Cantlie line in stage I.



Figure 3. Right portal vein ligation in stage I.

firstly. Then, a 10 F catheter was positioned as a tourniquet around Cantlie line between the right and middle hepatic veins, using the hanging maneuver via an anterior approach through the retrohepatic tunnel (Fig. 2). The right portal vein was ligated (Fig. 3), and the right hepatic artery was freely dissected. The tourniquet was then passed in front of the right portal pedicle by using an Extra-Glissonian approach for preventing the occlusion of the right hepatic artery and right bile duct.

Two weeks after stage I of ALTPS, a CT scan revealed a 56% growth of the FLR (648 mL), but it was still only 47% of the SLV and 0.72% of the BW. As the patient suffered serious cirrhosis and fatty liver (G 4, S 3, F 2), this was found to be insufficient for resection. To further stimulate the growth of the FLR, "rescue" TAE (selective right hepatic artery embolization) was performed. Open right hemihepatectomy (stage II of ALTPS) was performed at 14 days after "rescue" TAE, which achieved sufficient hypertrophy of the FLR (Fig. 4A). The kinetic growth rate (KGR, as cc per day and % per day) in every week was calculated as mean volume increasing per day, assuming a linear growth model from the first stage to the second. [9] At the 3rd month after surgical operation of stage II, CT suggested a marked compensatory enlargement of the FLR (Fig. 4B).

3. Results

The perioperative clinical characteristics of the patient are shown in Table 1. Preoperative FLR was 415 mL, increasing to 621 mL (FLR/SLV: 45%; FLR/BW: 0.69%) at 7 days after the first stage, with 50% hypertrophy (Fig. 5A). In the first week after the first

stage, the KGR was 29.4 cc per day (7.14% per day). The FLR at 14 days after the first stage increased to 648 mL (FLR/SLV: 47%; FLR/BW: 0.72%), with 56% hypertrophy (Fig. 5B). In the second week after the first stage, the KGR was 3.9 cc per day (0.86% per day). The operative time of the first stage was 160 minutes. intraoperative blood loss was 60 mL, and the patient did not receive a blood transfusion. There was no tumor progression after the first surgical stage in the patient. Two weeks after stage I of ALTPS, "rescue" TAE was performed. CT showed obvious necrosis in the tumors after "rescue" TAE. The FLR at 7 days after the TAE increased to 716 mL (FLR/SLV: 52%; FLR/BW: 0.79%), with 73% hypertrophy (Fig. 5C). In the first week after the TAE, the KGR was 9.7 cc per day (2.43% per day). The FLR at 14 days after the TAE increased to 738 mL (FLR/SLV: 54%; FLR/BW: 0.82%), with 78% hypertrophy (Fig. 5D). In the second week after the TAE, the KGR was 3.1 cc per day (0.71% per day). The operative time of the second stage was 220 minutes, intraoperative blood loss was 400 mL, and the patient did not require a blood transfusion. No serious complication occurred. The patient was discharged 7 days after the second stage. The pathological diagnosis of the tumor was HCC. As of follow-up at postoperative 6 months, contrast-enhanced ultrasonography showed 1cm tumor recurrence in the remnant liver (AFP: 114.2 ng/L). The patient underwent radiofrequency ablation (RFA), and AFP decreased to 7.6 ng/L 1 month after RFA (perioperative FLR is shown in Fig. 6).

4. Discussion

Currently, resection of hepatic tumors has been performed worldwide in treating HCC.^[10] The possible shortage of FLR is the major problem in extended hepatectomy. Obtaining sufficient margins is the primary objective, postoperative liver decompensating and surgical failure should be also avoided at the same time. It has been shown that patients with cirrhosis but without portal hypertension require an FLR of at least 40% or 0.8% of BW.^[9]

In contrast to portal vein embolization (PVE), which enhances liver growth by approximately 20% to 35% in 30 to 45 days, the ALPPS technique allows the FLR growth of 40% to 160% in only 6 to 9 days. [1]

Robles et al^[11] introduced the ALTPS as a less invasive modification of the ALPPS procedure. In the first stage, the newly modified tourniquet in ALTPS could avoid liver splitting and reduce the invasiveness of the intervention. In the second stage of

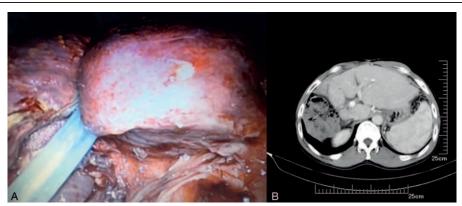


Figure 4. (A) The laparoscopic image in stage II, it has clearly showed that the right liver was shrink and the left liver achieved sufficient hypertrophy. (B) Computed tomography images at 3rd month after the operation of stage II.

Xu et al. Medicine (2017) 96:43

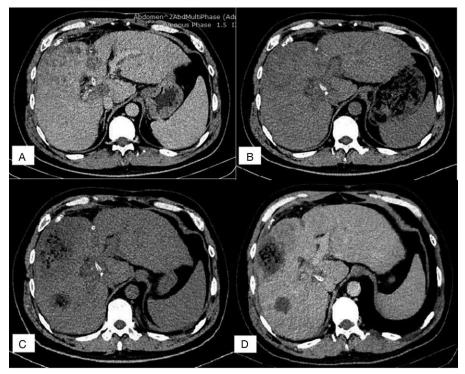
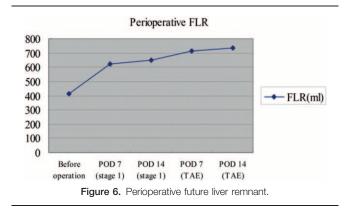


Figure 5. Computed tomography images after operation. (A) Computed tomography image on POD 7 (stage I). (B) Computed tomography image on POD 14 (stage I). (C) Computed tomography image on POD 7 (TAE). (D) Computed tomography image on POD 14 (TAE).

ALTPS, there is virtually no adhesion, and the transection of the parenchyma caused by the ischemia line of the tourniquet can proceed rapidly, with limited bleeding. Adequate hypertrophy of the FLR had been also achieved after 7 days by ALTPS technique. Recently, we have introduced laparoscopic anterior approach ALTPS. This technique could provide a less invasive modification of the ALPPS procedure with greater oncological efficacy. [2,11]

In China, most of the liver tumors were HCC developing from chronic viral hepatitis. A liver with chronic liver diseases has a lower regenerative and hypertrophying capacity. Sometimes the FLR growth would be not enough even after ALPPS. Several studies have indicated that the loss of portal blood flow after portal branch ligation (PBL) is compensated by HABR, which guarantees a rapid normalization of overall blood flow in the ligated lobe. ^[6,7]



Rocheleau et al's study¹⁶ showed left PVL produced a fully compensatory increase in right portal flow without significantly affecting total portal flow. Left hepatic artery flow increased by 210%, and right hepatic artery flow decreased by 67% after left PVL at 4 hours after surgery. At 7 days after surgery, left and right hepatic blood flow was similar to the result of the measurement at 4 hours, meanwhile HABR was still present. Because of the hypertrophy of the right lobes, hepatic blood flow was increased by 666% in each gram of liver tissue within 7 days. Therefore, the hepatic artery was the only source of blood perfusion, the portal artery and hepatic artery provided for the remnant left hepatic lobes with flow rates similar to the right lobes. [6]

In Kollmar et al's study, [7] they demonstrated that left PBL provoked a 50% reduction of the left hilar blood flow at day 3, however, it recovered to almost normal after 14 days. Assuming that the hepatic artery contributes 20% to 30% of the total blood flow to the normal liver, the left hilar blood flow is reduced by 50% on the third day after PBL, indicating that HABR has increased 2-fold with arterial blood flow. Because of the 60% decrease of the left lobe, this represents a 3.3-fold increase of arterial flow. On the 14th day after PBL, the total left hilar blood flow had returned to 90% of the control group, the arterial flow rate was increased by 4-fold compared to the controls, and 6.7fold as much as the loss of tissue quality. This is consistent with the results of Rocheleau et al's reports. [6] Moreover, some clinical studies suggested that, despite liver atrophy, tumors within the ligated lobe do not shrink in size but rather show acceleration of growth. [12,13] Experimental studies have shown that the loss of portal venous blood flow in the PBL is compensated by HABR, which ensures rapid normalization of total blood flow of the ligated lobe. [6] Thus, PBL caused only initial microcirculatory disturbances in liver atrophy, followed by HABR, microvascular remodeling, and hepatocellular proliferation. This may explain

the acceleration of tumor progression observed occasionally after PVL $^{[7]}$

Above-mentioned studies suggested that the HABR played a very important role in blood flow restoration and tumor growth after PVL. [6,7] Considering the important role of HABR after PVL, we imagined that stopping the HABR by TAE could be added as rescue technique, if the FLR growth still was not enough at 14 days after stage I. At 7 days after "rescue" TAE, CT showed obvious necrosis of the tumors in right liver and second rapid hypertrophy of the FLR after stage I. The phenomenon may be explained by stopping the HABR using "rescue" TAE.

TAE used as a rescue technique when ALTPS fails to stimulate sufficient growth of the FLR, which can be expected to be used to stimulate FLR growth and prevent tumor progression. We believe that TAE should be reserved as a rescue maneuver for patients after failed stage I, especially for patients with cirrhosis.

In addition, ALTPS is feasible with satisfactory short-term efficacy and safe for the treatment of HCC in cirrhotic patients. However, there are still some potential drawbacks and complications of the technique: The interval between the 2 stages may be extended, during which the tumor may grow or metastasize; Only a few special cases apply to this technique; Some large tumors may develop necrosis, which will cause liver abscess and affect the operation of stage II. We believe that a laparoscopic anterior approach for surgeons facile at advanced laparoscopic hepatobiliary surgery is a valid alternative to an open approach and might facilitate the second operation, because of oncological superiority and lack of adhesions. ^[2,5,14] Whether stage II is performed open or laparoscopically is up to surgeons' experience.

5. Conclusions

The HABR played a very important role after PVL. When the liver hypertrophy gained with the first stage of the laparoscopic anterior approach ALTPS was insufficient for the serious cirrhosis, TAE could be used as a rescue technique to stimulate

FLR growth and prevent tumor progression by stopping the HABR.

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