Surgical Technique

The combination of extra-Glissonian pedicle ligation of the tumor-bearing area and traditional ALPPS: a novel modified ALPPS method

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Abstract: Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) can provide patients with large liver tumors the opportunity to undergo radical resection. However, tumor progression between the surgical stages and unsatisfactory hyperplasia of the residual liver reduces the second-stage resection rate and limit the application of ALPPS. We reported a novel modified ALPPS method that can accelerate tumor necrosis and hyperplasia of the residual liver and increase the second-stage resection rate. The data of patients who underwent the novel modified ALPPS procedure in our hospital between September 2021 and April 2024 were retrospectively analyzed. In addition to ligation of the right hepatic portal vein and liver partition during the first stage, we transected all the Glissonian pedicles of the tumor-bearing area to accelerate tumor necrosis. Ultimately, three patients underwent this novel modified ALPPS procedure. Second-stage resection was successfully performed in all these patients. Satisfactory hyperplasia was obtained in the residual liver before the second stage of surgery. The tumor-bearing area showed obvious necrosis and atrophy. The residual liver volumes of the three patients increased by 83%, 23%, and 49%, respectively. No postoperative complications or tumor recurrence was observed. This novel modified approach is safe and effective. This approach can prevent tumor progression between the surgical stages and promote compensatory liver proliferation.

Keywords: Modified associating liver partition and portal vein ligation for staged hepatectomy (modified ALPPS); liver cancer; tumor bearing area

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Introduction

Background

For most patients who suffer from liver cancer (including primary and metastatic liver cancer), liver resection is the priority treatment because it can significantly improve the prognosis (1). Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) is a treatment mainly for patients with large liver masses, insufficient residual liver volume after radical resection and a high risk of postoperative liver failure (2,3). However, several problems are encountered in this surgical process,

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such as unsatisfactory hyperplasia of the residual liver, tumor progression between the stages, liver failure, and abdominal infection, resulting in the patient's inability to successfully complete the second stage of surgery and undesirable survival times (4). ALPPS has been limited in its development due to its high complexity and high rate of postoperative complications, especially for tumor progression and a lack of an increase residual liver volume.

Rationale

The etiology of tumor growth between the stages has still not been elucidated, but hemodynamic alterations are currently considered to be the primary cause. ALPPS is a new procedure derived from portal vein ligation (PVL). Compared with traditional surgery, ALPPS can rapidly induce liver hyperplasia and hypertrophy, thereby reducing the incidence of postoperative residual liver volume insufficiency (5). At present, it is believed that the hyperperfusion of the residual liver after unilateral PVL is an important factor in promoting liver regeneration. The degree of liver growth is proportional to the degree of portal blood flow diversion (6). However, after PVL, changes in liver hemodynamics may also result in a tumor with a rich blood supply to provide the tumor with nutrients and cause tumor progression, ultimately preventing patients from completing the second stage of surgery (7).

Highlight box

Surgical highlights

- We modified the first-stage associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) procedure. Using this modified ALPPS method, necrosis of the tumor can be obtained and tumor progression can be avoided between two stages of ALPPS. The patient also achieved satisfactory liver hyperplasia and progressed safely to the next stage.

What is conventional and what is novel/modified?

- The conventional first-stage ALPPS procedure primarily involves ligating the right branch of the portal vein and separating the left and right liver lobes to get liver hyperplasia.
- Apart from the aforementioned steps, the modifications in novel method include that hepatic pedicles nourishing the tumor area were transected completely through the extra-Glissonean sheath.

What is the implication, and what should change now?

- Through the modified ALPPS, we have successfully circumvented issues of tumor progression and inadequate hypertrophy of the remnant liver. This enhancement has rendered ALPPS safer and more effective.

Objective

Therefore, how to address the above problems of ALPPS and increase the resection rate of the second stage has become a popular topic. Here, we first report a novel modified laparoscopic ALPPS method that can accelerate tumor necrosis and hyperplasia of the residual liver and increase the second-stage resection rate. With this novel approach, several of our patients underwent successful laparoscopic ALPPS in two stages. We present this article in accordance with the SUPER reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-691/rc).

Preoperative preparations and requirements

The data of patients who underwent liver resection between September 2021 and April 2024 at The First Affiliated Hospital of Chongqing Medical University were studied retrospectively. Clinical data (age, sex, liver function before and after the operation, complications, length of hospital stay after the operation, operative time, hemorrhage, ascites, and perioperative mortality) were collected. Eight of these patients underwent ALPPS (the baseline information is detailed in *Table 1*), and three patients underwent the novel modified ALPPS procedure. This study was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University (No. 2024.7.29/2024-083-01), and was conducted in accordance with the Helsinki Declaration (as revised in 2013). The procedure was performed by chief surgeon, assistant surgeon and scopist laparoscopically. All patients provided written informed consent to undergo surgery and the anonymous use of the data for research purpose.

Step-by-step description

Surgical procedures (the patient's position, the location of the trocar, and the method of blocking the hepatic hilum) have been described in our previously published articles (8). In the first stage of ALPPS, dissecting forceps were used to dissect the first hepatic hilum. The right portal vein was selected and clamped with a Hem-O-lock ligating clip (nonabsorbable, JNJ, Inc., New Jersey, USA). Parenchymal transection of the liver was performed with a harmonic scalpel (JNJ, Inc.) along the ischemic line and the middle

Table 1 The demographic data of 8 patients who underwent ALPPS

Characteristics	Value
Age (years)	47.50±8.91
Sex	
Male	8 (100.0)
Female	0
Pathology	
Hepatocellular carcinoma	7 (87.5)
Metastatic liver cancer	1 (12.5)
Tumor number	2.38±2.33
Tumor size (cm)	8.38±3.78
Tumor position	
Right liver	7 (87.5)
Both in right and left liver	1 (12.5)
First-stage surgery time (minutes)	204.38±45.63
First-stage surgery bleeding (mL)	218.75±99.78
Second-stage surgery time (minutes)	223.12±29.27
Second-stage surgery bleeding (mL)	362.50±74.40

Data are presented as n (%) or mean ± standard deviation. ALPPS, associating liver partition and portal vein ligation for staged hepatectomy.

hepatic vein. A Hem-O-lock ligating clip was used to clamp the vessels or bile duct. For the second stage of surgery, the right portal vein, right hepatic artery, and right hepatic duct were clamped with a Hem-O-lock ligating clip and disconnected. The perihepatic ligaments were dissected to complete the second stage of surgery (8,9).

Based on the traditional first-stage ALPPS, we increased the following steps. All the pedicles of the tumor-bearing area were analyzed and traced through imaging data before surgery [usually enhanced computed tomography (CT) or enhanced magnetic resonance imaging (MRI)]. Based on preoperative planning, we dissected the target hepatic pedicle along the Laennec membrane, and the Glissonean pedicle could be transected with little or no parenchymal damage through this extra-hepatic Glissonean dissection approach. Hepatic pedicles nourishing the tumor area were transected completely through the extra-hepatic Glissonean sheath in addition to the ligation of the right hepatic portal vein and liver partition during the first stage. We will present the treatment details of three patients who underwent the modified ALPPS procedure.

Patient 1

A 41-year-old male with a history of hepatitis B not taking medication regularly was admitted to the hospital with a "hepatic space-occupying lesion detected 3 days ago". The alpha fetoprotein (AFP) level was 130,539 ng/mL. CT showed a large mass in segments 5, 6 and 8 of the liver, approximately 10 cm × 5.6 cm × 6 cm in size, suggesting the possibility of hepatocellular carcinoma, and a cancerous thrombus in the right anterior and right posterior branches of the portal vein. The preoperative future liver remnant (FLR) volume was 515 mL, accounting for 32.8% of the total liver volume of 1,566 mL, and the tumor volume was 181 mL.

Considering the patient's portal vein cancerous thrombus, the patient underwent right hemihepatectomy. CT showed cirrhosis, so the low residual liver volume suggested a high risk of liver failure after right hemihepatectomy. Preoperative CT revealed that the tumor, although located in the right lobe of the liver, still had partial blood supply originating from segment 4, which nourished the tumor area. Therefore, the patient underwent modified ALPPS on June 30, 2022. As we had planned, the hepatic pedicles from segment 4 to the tumor-bearing area were dissected and ligated. The operation lasted 260 minutes, with 200 mL of blood loss.

The AFP concentration was 51,939 ng/mL on August 3, 2022. CT suggested a mass in the right lobe of the liver, with a size of 61 mm × 52 mm × 64 mm. The second calculation of the liver volume suggested that the FLR was 941 mL, accounting for 51.5% of the total liver volume of 1,824 mL, and the tumor volume was 151 mL, which decreased 16.5%. By comparison, the patient had a significant decrease in AFP levels and a 30 mL decrease in tumor volume. Necrosis and decreased activity of the tumor was seen on CT. The left lobe volume increased by 83%, and satisfactory hypertrophy was obtained, which allowed the patient to safely undergo the second stage of surgery on August 08, 2022. The surgical procedure is detailed in the "Step-by-step description" section. The duration of the operation was 225 minutes, with 300 mL of blood loss. The patient was followed up regularly at our center after surgery, and no recurrence or metastasis was observed as of April, 2024 (*Figure 1*).

Patient 2

The patient had a 20-year history of hepatitis B and was not taking medication regularly. The AFP level was 50.9 ng/mL, and the protein concentration induced by vitamin K

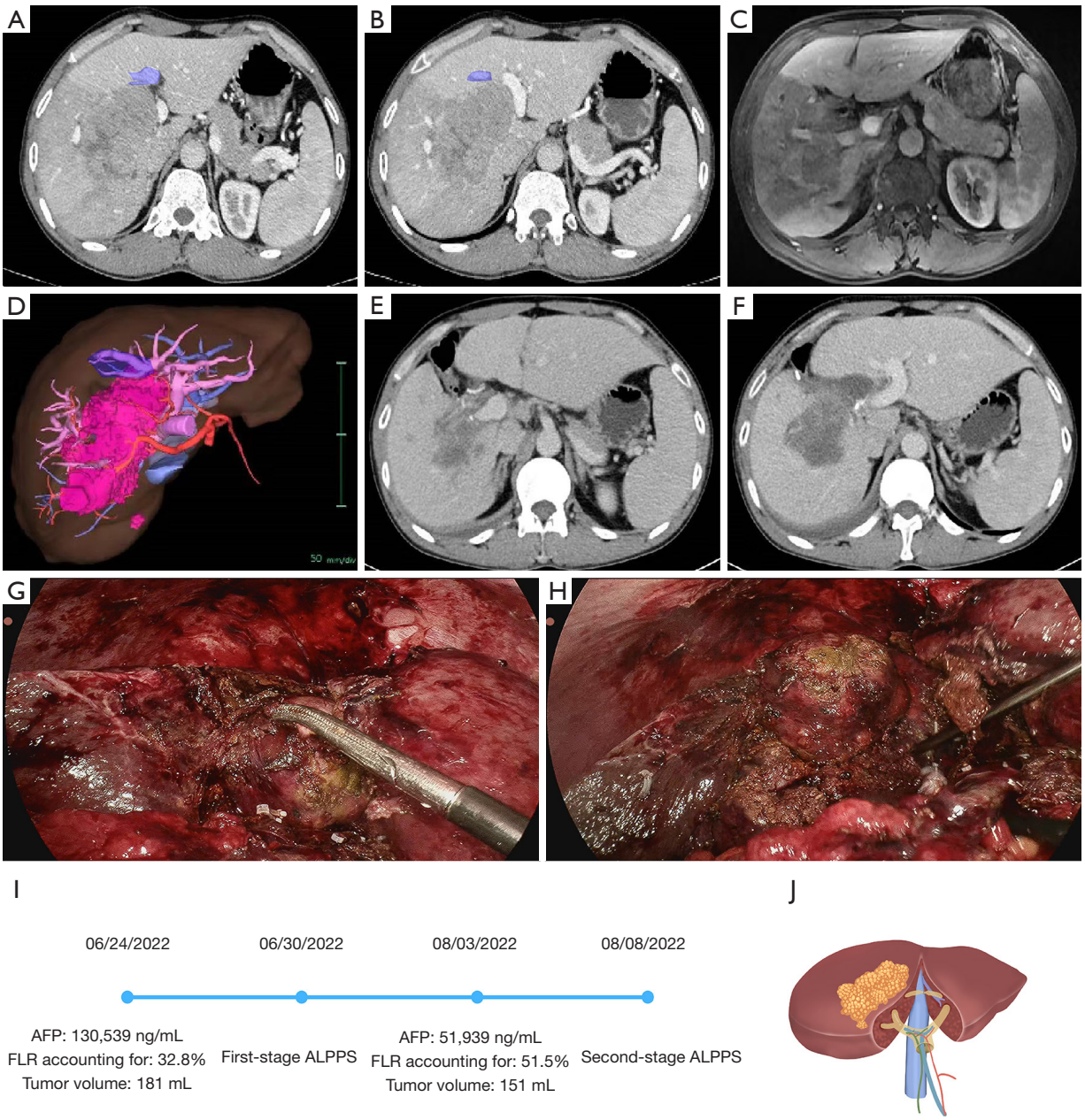


Figure 1 Clinical images for case 1. (A-D) First-stage preoperative CT and MRI images of the patient. (E,F) CT images before second-stage ALPPS. (G,H) Intraoperative images during second-stage ALPPS. (I) Clinical characteristics of the patient. (J) A brief overview of the surgical procedure during the first stage. (A,B,D, blue labeled) The tumor-bearing pedicle arising from the hepatic pedicle of segment 4. AFP, the alpha fetoprotein; FLR, future liver remnant; ALPPS, associating liver partition and portal vein ligation for staged hepatectomy; CT, computed tomography; MRI, magnetic resonance imaging.

absence or antagonist-II (PIVKA-II) was 1,247 mAU/mL. Enhanced CT of the upper abdomen revealed S8 tumors 30 mm × 22 mm in size and S5 tumors 25 mm × 17 mm in size. The left liver volume was 458 mL, accounting for 28% of the total liver volume of 1,634 mL, and the tumor volume was 11.9 mL.

The patient's tumor next to the inferior vena cava (IVC) was close to the right hepatic pedicle; thus, a right hemihepatectomy was required to secure the margins. Through preoperative evaluation, we found that the tumor

next to the IVC was mainly supplied by the paracaval (PC) Glissonian pedicle and the caudate process (CP) Glissonian pedicle. Eventually, the patient underwent surgery with the novel modified ALPPS procedure due to insufficient residual liver volume on September 4, 2023. Isolating the CP branch and PC branch and ligated them during the first-stage ALPPS. The operation lasted 280 minutes, with 300 mL of intraoperative blood loss.

Three weeks after surgery, the total liver volume was 1,573 mL, the left liver volume was 563 mL, and the tumor volume was 10.5 mL, which decreased 11.8%, for a residual liver volume of 35%. The AFP level decreased to 14.5 ng/mL, and the PIVKA-II level was 161.9 mAU/mL on September 20, 2023. Similarly, the patients' tumor volume, tumor markers, and tumor activity were significantly reduced. The left liver volume increased by 105 mL, which also allowed the patient to move to the next stage more safely. The patients underwent laparoscopic second-stage ALPPS surgery on September 24, 2023. The operation lasted 220 minutes, with 300 mL of intraoperative blood loss. No postoperative complications or recurrences were observed as of April, 2024 (*Figure 2*).

Patient 3

The patient was diagnosed with sigmoid colon cancer with liver metastases. The patient underwent radical sigmoid colon cancer surgery first. The carcinoembryonic antigen (CEA) level was 14.6 ng/mL on April 7, 2023. Enhanced CT of the upper abdomen suggested multiple intrahepatic metastases. The total liver volume was 2,037 mL, and the left liver volume was 728 mL, for a residual liver volume of 35%, and the tumor volume was 864 mL.

Careful analysis of the distribution of the patient's tumors revealed that the patient had two tumors approximately 2 cm in diameter in the left outer lobe, and most of the tumors were nourished by the right anterior Glissonean pedicle. Due to the unknown volume of the patient's left liver tumor, surgical resection of the left liver tumor combined with right hemihepatectomy was extremely risky. Left liver tumor resection and modified ALPPS were performed on April 14, 2023. The right anterior Glissonean pedicle was ligated in the process. Resection of the left liver tumor and separation of the liver parenchyma were subsequently performed. The surgery lasted 220 minutes, with 200 mL of blood lost (*Figure 3*).

Liver volume measurements were performed three weeks after the first surgery. The total liver volume was 2,207 mL, the left liver volume was 1,086 mL, and the tumor volume was 751 mL, which decreased 12.1%, for a residual liver volume of 49%. The patient's CEA level was 11.1 ng/mL. We also observed significant necrosis of the patient's tumor on the patient's CT images. The residual liver showed 49% growth despite the removal of two tumors. The patient underwent second-stage ALPPS surgery on May 16, 2023, with 170 minutes of surgical time and 300 mL of blood loss (*Figure 4*). No postoperative complications or recurrences were observed as of April, 2024. Patient 3's surgical procedure is detailed in *Video 1*.

Postoperative considerations and tasks

Assessment before the second-stage surgery following modified ALPPS procedure is crucial. Key aspects include changes in tumor size, activity, and alterations in left lobe liver volume. Our patients showed varying degrees of decreases in tumor markers and tumor activity after treatment. Marked tumor necrosis and decreased tumor volume were also observed on CT images. The residual volumes of the three patients increased by 83%, 23%, and 49%, respectively.

Tips and pearls

The challenge of the modified ALPPS technique lies in the interpretation of preoperative CT and MRI images, and the intraoperative dissection of the hepatic pedicle. Preoperatively, we need to develop an individualized surgical plan for each patient. Intraoperatively, we identify and clamp the major hepatic pedicle supplying the tumor bearing area.

Discussion

Surgical highlights

Tumor growth might be inhibited when the tumor blood supply is blocked (10). Therefore, we modified the traditional ALPPS method. The innovative aspect of our modified method is that in addition to ligating the right portal vein, we also perform extra-Glissonian pedicle ligation of the tumor-bearing area. With this method, we ultimately succeeded in inhibiting the activity of the tumor, causing necrosis and resulting in good proliferation of the residual liver.

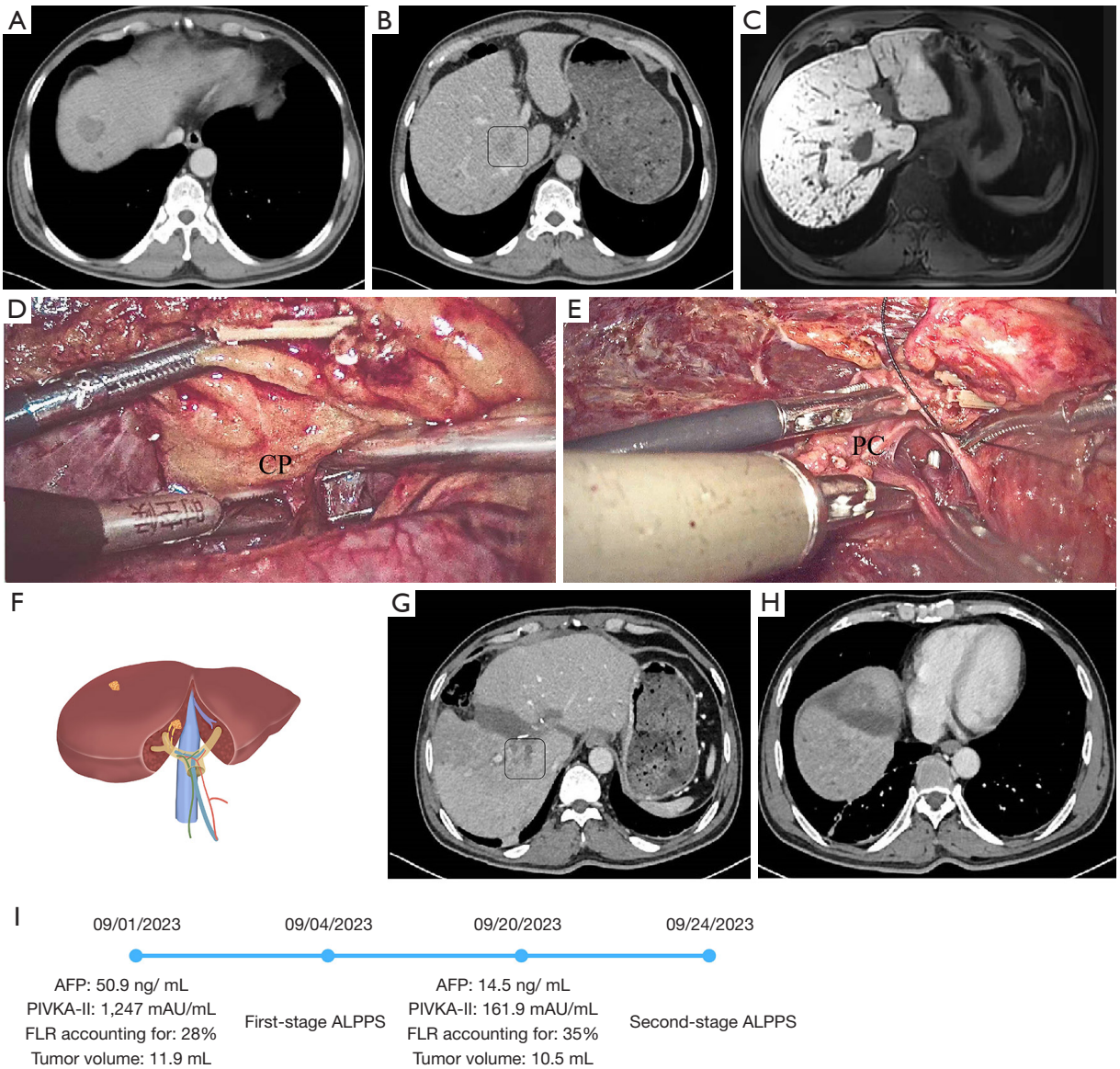


Figure 2 Clinical images for case 2. (A-C) Preoperative CT and MRI images of the patient. (D,E) Intraoperative images during first-stage ALPPS. (F) A brief overview of the surgical procedure during the first stage. (G,H) CT images before second-stage ALPPS. (I) The clinical characteristics of the patient. (B, square labeled) The PC tumor before surgery. (G, square labeled) The PC tumor after first-stage surgery and necrosis. CP, caudate process; PC, paracaval; AFP, the alpha fetoprotein; PIVKA-II, the protein concentration induced by vitamin K absence or antagonist-II; FLR, future liver remnant; ALPPS, associating liver partition and portal vein ligation for staged hepatectomy; CT, computed tomography; MRI, magnetic resonance imaging.

Strengths and limitations

Blockage of the artery is the main reason for the inhibition of tumor growth and development. The main source of nutrients for liver tumors is the artery in the hepatic pedicle. We chose to ligate both the right portal vein and the target hepatic pedicle of the tumor-bearing area. After ligation, the double blood supply of the portal vein and hepatic artery was lost, and the separation of the left and right halves of the liver also resulted in the inability of the tumor to establish collateral circulation with the left liver. In this way, we blocked the entire blood supply to the tumor-

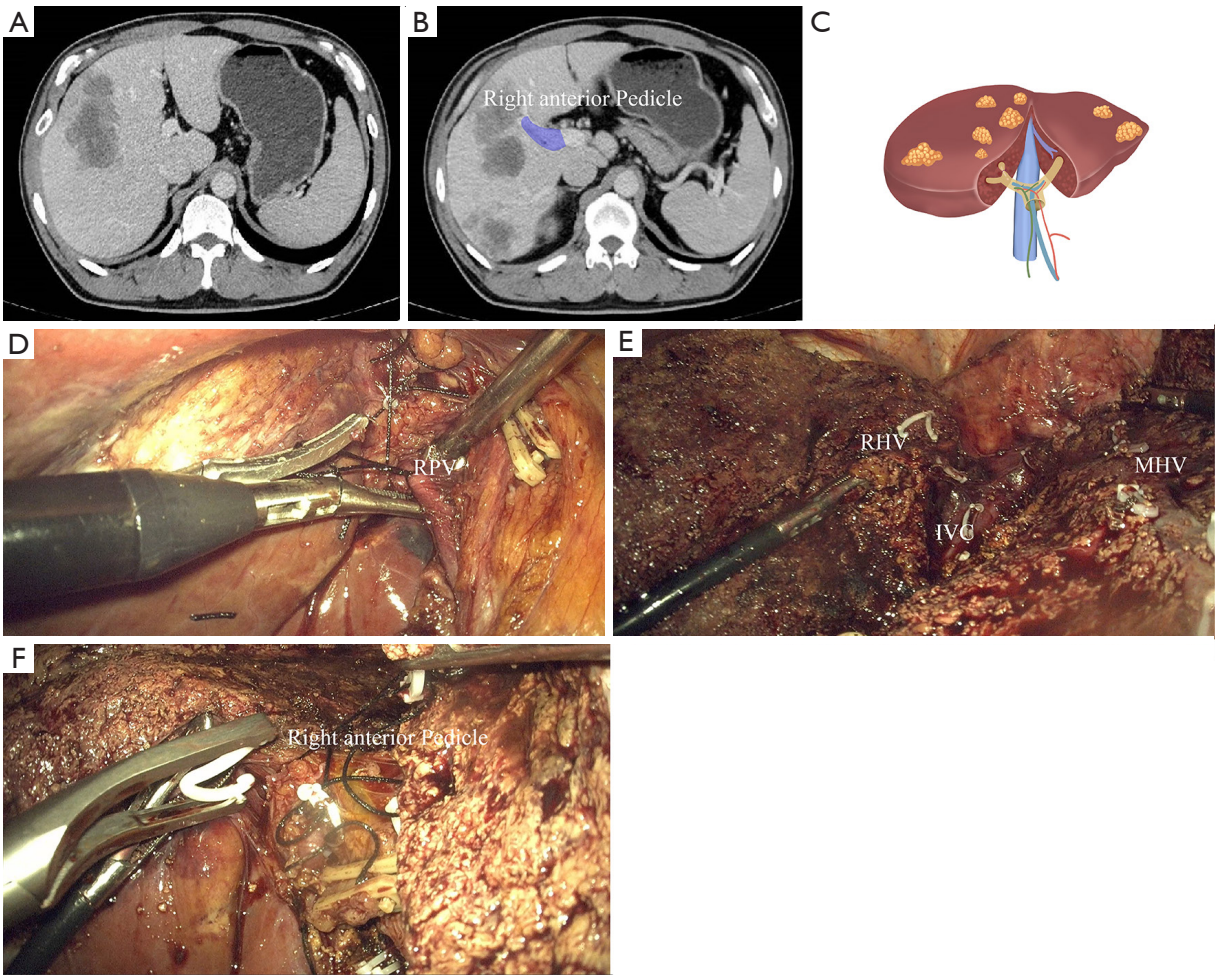


Figure 3 The first-stage surgery images for case 3. (A,B) The first-stage preoperative CT images. (C) A brief overview of the surgical procedure during the first stage. (D-F) Intraoperative images from the first-stage surgery. RPV, right portal vein; RHV, right hepatic vein; IVC, inferior vena cava; MHV, middle hepatic vein; CT, computed tomography.

bearing area. This blood supply blockade causes avascular necrosis and the atrophy of the tumor, which eventually leads to a decrease in tumor size and activity.

Arterial blockade may also lead to residual liver hyperplasia, but the reasons for this have not been clearly stated. Several experiments in mice have shown that simultaneous ligation of the portal vein and hepatic artery reduces mortality and is safer and more effective than PVL alone (11,12). According to retrospective studies, the combination of PVL and hepatic artery ligation can increase the residual liver volume more rapidly, safely and effectively (13,14). Ligation of the hepatic artery is safe and reliable. A satisfactory increase in residual liver volume was achieved in all three patients who received this treatment, which laid the foundation for patients to successfully undergo the second stage of surgery. On the one hand, faster hypertrophy of the residual liver volume allows the second stage of surgery to be performed earlier. On the other hand, efforts can be made to avoid tumor progression between the stages of surgery.

In addition, we ligated the bile ducts in the tumor-bearing area. Conventional ALPPS is usually performed without ligation of the bile duct. It has been suggested that ligation of the bile duct leads to hepatic atrophy of the right liver and causes compensatory hypertrophy of the residual liver, which is helpful for surgery. However, ligation of the bile duct may lead to a higher incidence of biliary complications (15). The benefits of bile duct ligation have also not been verified, so there is some controversy worldwide. The hepatic pedicle is relatively thick at the

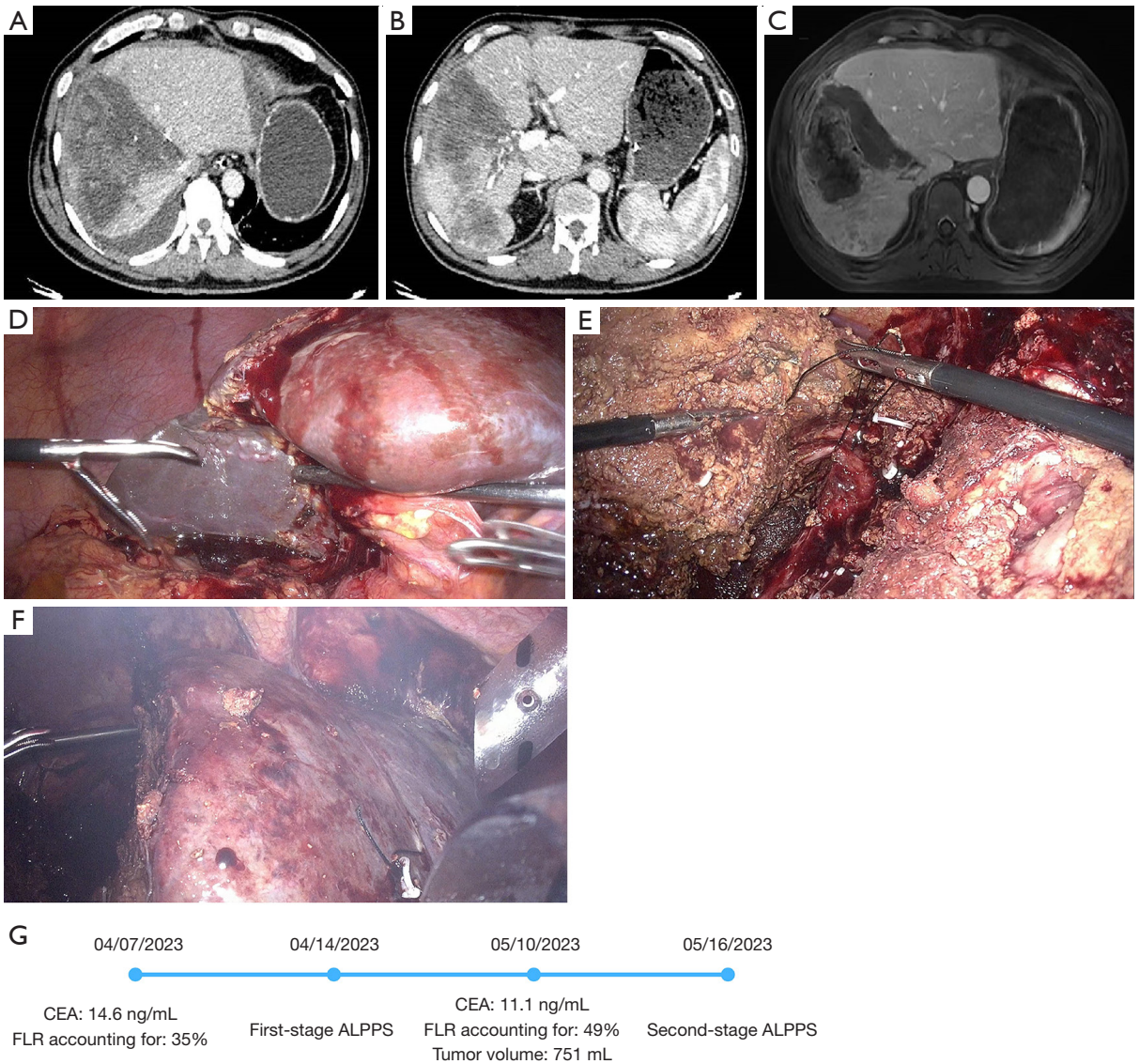
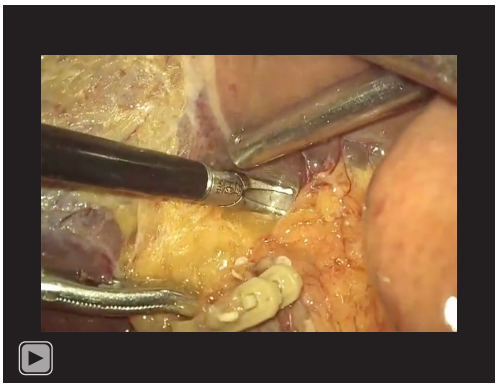


Figure 4 The second-stage surgery images for case 3. (A-C) Preoperative CT and MRI images of the patient. (D) The extent of ischemia in the right anterior lobe liver and the left lobe liver. (E) The degree of necrosis between the two livers. (F) The satisfactory hypertrophy of the left lobe liver. (G) Clinical characteristics of the patient. CEA, carcinoembryonic antigen; FLR, future liver remnant; ALPPS, associating liver partition and portal vein ligation for staged hepatectomy; CT, computed tomography; MRI, magnetic resonance imaging.

hepatic hilum and slowly becomes thinner as it enters the liver parenchyma. With a relatively small hepatic pedicle, intrathecal isolation of the bile duct is undoubtedly very difficult. This difficulty most likely leads to unwanted injury and hemorrhage. Therefore, ligation of the bile duct was chosen for our patients. In this way, tumor necrosis proceeded while promoting the proliferation of the residual liver. Finally, additional attention needs to be given to the biliary complications with this method. However, our three patients did not develop biliary-related complications.

The limitation of this novel modified method is the increased difficulty of the surgery. Preoperative evaluation of the vasculature of the tumor-bearing area is critical and requires surgeons to have extensive clinical experience in hepatobiliary surgery. In addition, ALPPS is a very complex surgery, and excellent surgical skills are required for



Video 1 Patient 3's surgical procedure.

surgeons to complete this procedure. Additionally, clinicians should be vigilant for surgery-related complications.

Comparison with other surgical techniques and researches

Apart from the modified steps, all other procedures involved in the first-stage ALPPS surgery remain identical to traditional ALPPS. In contrast to traditional ALPPS, our modified ALPPS offers advantages in preventing tumor progression and achieving satisfactory residual liver hypertrophy.

Implications and actions recommended

Our cases suggested that modified ALPPS can effectively prevent tumor progression between the stages of surgery. At the same time, the disappearance of all blood supplies can lead to faster and safer liver hyperplasia. Larger samples in clinical trials are needed to demonstrate the validity, safety, and feasibility of the novel modified ALPPS method.

Conclusions

We report a novel modified laparoscopic ALPPS method. The difference in this method lies in the extra-Glissonian pedicle ligation of the tumor-bearing area combined with traditional ALPPS. This approach may be helpful in reducing surgical complications and preventing tumor development between surgery stages. The patients showed satisfactory proliferation of the residual liver.

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None.

Footnote

Reporting Checklist: The authors have completed the SUPER reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-691/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-691/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University (No. 2024.7.29/2024-083-01), and was conducted in accordance with the Helsinki Declaration (as revised in 2013). All patients provided written informed consent to undergo surgery and the anonymous use of the data for research purpose.

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