

# World Journal of *Clinical Cases*

*World J Clin Cases* 2021 October 26; 9(30): 8953-9319



**REVIEW**

- 8953 Endothelial progenitor cells and coronary artery disease: Current concepts and future research directions  
*Xiao ST, Kuang CY*

**MINIREVIEWS**

- 8967 Regulation of bone metabolism mediated by  $\beta$ -adrenergic receptor and its clinical application  
*Zhong XP, Xia WF*
- 8974 Tricuspid valve endocarditis: Cardiovascular imaging evaluation and management  
*Fava AM, Xu B*

**ORIGINAL ARTICLE****Case Control Study**

- 8985 Novel application of multispectral refraction topography in the observation of myopic control effect by orthokeratology lens in adolescents  
*Ni NJ, Ma FY, Wu XM, Liu X, Zhang HY, Yu YF, Guo MC, Zhu SY*

**Retrospective Cohort Study**

- 8999 Uncertainty in illness and coping styles: Moderating and mediating effects of resilience in stroke patients  
*Han ZT, Zhang HM, Wang YM, Zhu SS, Wang DY*

**Retrospective Study**

- 9011 Development and validation of a prognostic nomogram model for Chinese patients with primary small cell carcinoma of the esophagus  
*Zhang DY, Huang GR, Ku JW, Zhao XK, Song X, Xu RH, Han WL, Zhou FY, Wang R, Wei MX, Wang LD*
- 9023 Preliminary establishment of a spinal stability scoring system for multiple myeloma  
*Yao XC, Shi XJ, Xu ZY, Tan J, Wei YZ, Qi L, Zhou ZH, Du XR*
- 9038 Effect of intrauterine perfusion of granular leukocyte-colony stimulating factor on the outcome of frozen embryo transfer  
*Zhu YC, Sun YX, Shen XY, Jiang Y, Liu JY*
- 9050 "An integrated system, three separated responsibilities", a new fever clinic management model, in prevention and control of novel coronavirus pneumonia  
*Shen J, He Q, Shen T, Wu ZQ, Tan MM, Chen YL, Weng Q, Nie LM, Zhang HF, Zheng B, Zhang J*

**Clinical Trials Study**

- 9059** Single dose dexamethasone prophylaxis of postembolisation syndrome after chemoembolisation in hepatocellular carcinoma patient: A randomised, double-blind, placebo-controlled study  
*Sainamthip P, Kongphanich C, Prasongsook N, Chirapongsathorn S*

**Observational Study**

- 9070** Serum calcium, albumin, globulin and matrix metalloproteinase-9 levels in acute cerebral infarction patients  
*Zhong TT, Wang G, Wang XQ, Kong WD, Li XY, Xue Q, Zou YA*

**SYSTEMATIC REVIEWS**

- 9077** Neoadjuvant radiotherapy dose escalation for locally advanced rectal cancers in the new era of radiotherapy: A review of literature  
*Delishaj D, Fumagalli IC, Ursino S, Cristaudo A, Colangelo F, Stefanelli A, Alghisi A, De Nobili G, D'Amico R, Cocchi A, Ardizzoia A, Soatti CP*

**META-ANALYSIS**

- 9090** Clinical significance of breast cancer susceptibility gene 1 expression in resected non-small cell lung cancer: A meta-analysis  
*Gao Y, Luo XD, Yang XL, Tu D*

**CASE REPORT**

- 9101** Particular tumor of the pancreas: A case report  
*Zhu MH, Nie CF*
- 9108** Dynamic changes in the radiologic manifestation of a recurrent checkpoint inhibitor related pneumonitis in a non-small cell lung cancer patient: A case report  
*Tan PX, Huang W, Liu PP, Pan Y, Cui YH*
- 9114** Spontaneous rupture of a mucinous cystic neoplasm of the liver resulting in a huge biloma in a pregnant woman: A case report  
*Kośnik A, Stadnik A, Szczepankiewicz B, Patkowski W, Wójcicki M*
- 9122** Diagnosis and laparoscopic excision of accessory cavitated uterine mass in a young woman: A case report  
*Hu YL, Wang A, Chen J*
- 9129** Unusual cervical foreign body - a neglected thermometer for 5 years: A case report  
*Yang L, Li W*
- 9134** Long-term survival of a patient with pancreatic cancer and lung metastasis: A case report and review of literature  
*Yang WW, Yang L, Lu HZ, Sun YK*
- 9144** Synchronous diagnosis and treatment of acute myeloid leukemia and chronic lymphocytic leukemia: Two case reports  
*Chen RR, Zhu LX, Wang LL, Li XY, Sun JN, Xie MX, Zhu JJ, Zhou D, Li JH, Huang X, Xie WZ, Ye XJ*

- 9151** Conversion therapy of hepatic artery ligation combined with transcatheter arterial chemoembolization for treating liver cancer: A case report  
*Feng GY, Cheng Y, Xiong X, Shi ZR*
- 9159** Hemophagocytic lymphohistiocytosis secondary to composite lymphoma: Two case reports  
*Shen J, Wang JS, Xie JL, Nong L, Chen JN, Wang Z*
- 9168** Fatal visceral disseminated varicella-zoster virus infection in a renal transplant recipient: A case report  
*Wang D, Wang JQ, Tao XG*
- 9174** Choriocarcinoma misdiagnosed as cerebral hemangioma: A case report  
*Huang HQ, Gong FM, Yin RT, Lin XJ*
- 9182** Rapid progression of colonic mucinous adenocarcinoma with immunosuppressive condition: A case report and review of literature  
*Koseki Y, Kamimura K, Tanaka Y, Ohkoshi-Yamada M, Zhou Q, Matsumoto Y, Mizusawa T, Sato H, Sakamaki A, Umezu H, Yokoyama J, Terai S*
- 9192** Temporary pacemaker protected transjugular intrahepatic portosystemic shunt in a patient with acute variceal bleeding and bradyarrhythmia: A case report  
*Yao X, Li SH, Fu LR, Tang SH, Qin JP*
- 9198** Recurrent pyogenic liver abscess after pancreatoduodenectomy caused by common hepatic artery injury: A case report  
*Xie F, Wang J, Yang Q*
- 9205** Transient ventricular arrhythmia as a rare cause of dizziness during exercise: A case report  
*Gao LL, Wu CH*
- 9211** Successful management of infected right iliac pseudoaneurysm caused by penetration of migrated inferior vena cava filter: A case report  
*Weng CX, Wang SM, Wang TH, Zhao JC, Yuan D*
- 9218** Anterior abdominal abscess - a rare manifestation of severe acute pancreatitis: A case report  
*Jia YC, Ding YX, Mei WT, Xue ZG, Zheng Z, Qu YX, Li J, Cao F, Li F*
- 9228** Monteggia type-I equivalent fracture in a fourteen-month-old child: A case report  
*Li ML, Zhou WZ, Li LY, Li QW*
- 9236** Diagnosis and treatment of primary pulmonary enteric adenocarcinoma: Report of Six cases  
*Tu LF, Sheng LY, Zhou JY, Wang XF, Wang YH, Shen Q, Shen YH*
- 9244** Choroidal metastatic mucinous abscess caused by *Pseudomonas aeruginosa*: A case report  
*Li Z, Gao W, Tian YM, Xiao Y*
- 9255** Diagnosis and treatment of acute graft-versus-host disease after liver transplantation: Report of six cases  
*Tian M, Lyu Y, Wang B, Liu C, Yu L, Shi JH, Liu XM, Zhang XG, Guo K, Li Y, Hu LS*

- 9269** Hepatic portal venous gas without definite clinical manifestations of necrotizing enterocolitis in a 3-day-old full-term neonate: A case report  
*Yuan K, Chen QQ, Zhu YL, Luo F*
- 9276** Emergence of lesions outside of the basal ganglia and irreversible damage to the basal ganglia with severe  $\beta$ -ketothiolase deficiency: A case report  
*Guo J, Ren D, Guo ZJ, Yu J, Liu F, Zhao RX, Wang Y*
- 9285** Skeletal muscle metastasis with bone metaplasia from colon cancer: A case report and review of the literature  
*Guo Y, Wang S, Zhao ZY, Li JN, Shang A, Li DL, Wang M*
- 9295** Biopsy-confirmed fenofibrate-induced severe jaundice: A case report  
*Lee HY, Lee AR, Yoo JJ, Chin S, Kim SG, Kim YS*
- 9302** Missense mutation in *DYNC1H1* gene caused psychomotor developmental delay and muscle weakness: A case report  
*Ding FJ, Lyu GZ, Zhang VW, Jin H*
- 9310** Isolated hepatic tuberculosis associated with portal vein thrombosis and hepatitis B virus coinfection: A case report and review of the literature  
*Zheng SM, Lin N, Tang SH, Yang JY, Wang HQ, Luo SL, Zhang Y, Mu D*

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# Conversion therapy of hepatic artery ligation combined with transcatheter arterial chemoembolization for treating liver cancer: A case report

Guo-Ying Feng, Yu Cheng, Xiu Xiong, Zheng-Rong Shi

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## Abstract

### BACKGROUND

Hepatocellular carcinoma is an aggressive tumor, and its latency and lack of clinical symptoms mean that most patients are already in the late stage when diagnosed. Large tumor volume and metastasis are the main reasons for not attempting surgery. Portal vein embolization and associated liver partition and portal vein ligation for staged hepatectomy are commonly used in clinical practice to increase the volume of remnant liver to allow surgical resection; however, research in this area is currently lacking.

### CASE SUMMARY

A 48-year-old male patient with a history of viral hepatitis B for at least 30 years attended our center with a hepatic space-occupying lesion detected 3 d previously. Enhanced computed tomography scanning of the upper abdomen revealed a large mass in the right lobe of the liver, centered on the right posterior lobe, with the larger section measuring about 14 cm × 10 cm × 14 cm. He successfully underwent conversion therapy for a large right liver tumor after combined hepatic artery ligation and transcatheter arterial chemoembolization, and finally had an opportunity to undergo right hemi-hepatectomy and cholecystectomy. He remained asymptomatic with no obvious abnormalities on computed tomography scanning review at 2 mo after surgery.

### CONCLUSION

This case highlights new ideas and provides a reference for conversion therapy of

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large liver tumors.

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**Core Tip:** Portal vein embolization associated liver partition and portal vein ligation for staged hepatectomy, and transcatheter arterial chemoembolization (TACE) are commonly used in conversion therapy of advanced liver cancer. However, the therapeutic effects of portal vein embolization and TACE are limited, and associating liver partition and portal vein ligation for staged hepatectomy is associated with high morbidity and mortality. We therefore combined hepatic artery ligation with TACE, which has a longer treatment cycle and slower compensation of the contralateral liver compared with the above treatments but which may make R0 resection feasible with less surgical complications and with good postoperative recovery.

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## INTRODUCTION

Hepatocellular carcinoma (HCC) is an aggressive tumor, and its latent nature, together with the lack of obvious clinical symptoms means that most patients are already in the late stage of the disease when they are diagnosed. In these cases, the tumor may already be large and/or be accompanied by metastasis and invasion, leading to a mean survival time as short as 10 mo[1]. In patients with large liver tumors, insufficient remnant liver after surgery is one of the main reasons for not attempting surgery. Portal vein embolization (PVE)[2] and associated liver partition and portal vein ligation for staged hepatectomy (ALPPS)[3] are currently commonly used clinical procedures for increasing the volume of the remnant liver sufficiently to allow surgical resection. However, research in this area is still lacking. We report a case that highlights new ideas and references for conversion therapy of large liver tumors.

## CASE PRESENTATION

### Chief complaints

A 48-year-old man attended our center with a hepatic space-occupying lesion detected 3 d previously.

### History of present illness

The patient was found to have a hepatic space-occupying lesion detected by regular abdominal color Doppler ultrasound, with abdominal distension as the only manifestation.

### History of past illness

The patient had a history of viral hepatitis B for at least 30 years and had never received antiviral therapy.

### Personal and family history

No specific personal and family history.

**Physical examination**

No obvious abnormal physical signs.

**Laboratory examinations**

Initial laboratory examinations: The patient's alfa-fetoprotein (AFP) level was 5789.0 ng/mL. Blood analysis, blood biochemical parameters, prothrombin and partial thromboplastin times, d-dimers, arterial blood gas, and electrocardiogram were all normal.

At 93 d after the initial operation: AFP had reduced to 3119.0 ng/mL, and the indocyanine green 15-minute clearance rate was 4.0%.

At 2 mo after the initial operation: AFP was 9.2 ng/mL.

**Imaging examinations**

Pre-operative examination: Enhanced computed tomography (CT) scanning of the upper abdomen revealed a large mass in the right lobe of the liver, centered on the right posterior lobe, with the larger section measuring about 14 cm × 10 cm × 14 cm. The right hepatic vein mostly ran along the edge of the lesion, and the right hepatic vein and right portal vein were affected by pressure (Figure 1). The total liver volume was 3103.959 cm<sup>3</sup>, and the left hemi-liver volume was 662.376 cm<sup>3</sup>.

At 53 d after the initial operation: Repeat enhanced CT scanning of the upper abdomen showed no significant changes in the patient's left or right liver (Figure 2), with a total liver volume of 3002.174 cm<sup>3</sup> and a left liver volume of 846.648 cm<sup>3</sup>. CT angiography indicated that the tumor was mainly supplied with blood *via* the middle hepatic artery, with a smaller contribution from the left hepatic artery.

At 93 d after the initial operation: Repeat enhanced CT scan of the upper abdomen revealed a large soft tissue mass in the right lobe of the liver, with dot-like or sheet-like high-density shadows, slightly smaller than previously. Other imaging findings were similar to previously (Figure 3). The total liver volume was 2526.944 cm<sup>3</sup> and the left liver volume was 780.415 cm<sup>3</sup>.

At 2 mo after the initial operation: Enhanced CT of the upper abdomen revealed a small amount of fluid in the operation area and no obvious abnormalities (Figure 4).

**Pathological examinations**

At 98 d after the first stage of surgery: Postoperative pathological examination revealed a moderately differentiated HCC with extensive necrosis, microvascular invasion grade M0, and the surrounding liver tissue with chronic hepatitis, G2S3.

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**FINAL DIAGNOSIS**

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The final diagnosis of the presented case was moderately differentiated HCC.

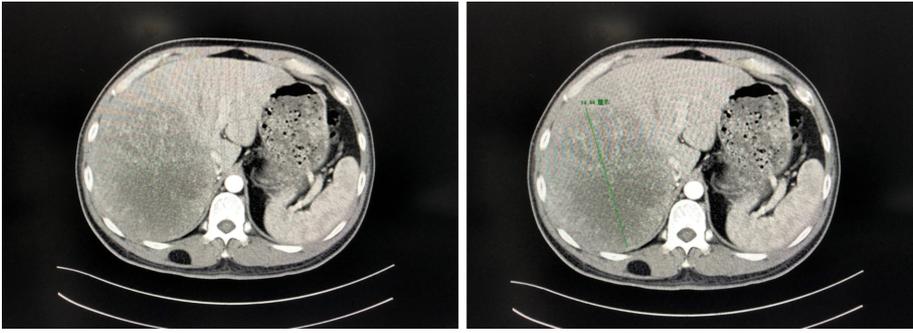
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**TREATMENT**

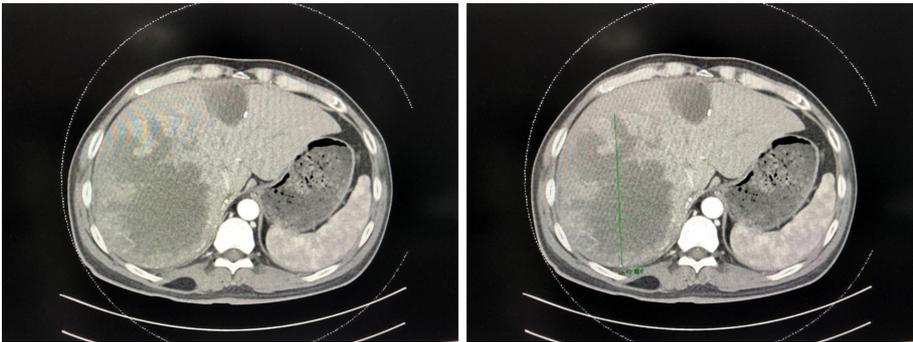
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The patient was Child-Pugh grade A. Considering that the left hepatic volume was only 21.34% of the total liver volume, we planned liver partition and portal vein ligation to prepare for hepatectomy. However, it was difficult to expose the portal vein during surgery, resulting in bleeding, and intraoperative ultrasound detected suspicious lesions in the left liver, resulting in a switch to liver partition and right hepatic artery ligation. The patient developed Dindo-Clavien grade I complications after surgery and was discharged from hospital awaiting review.

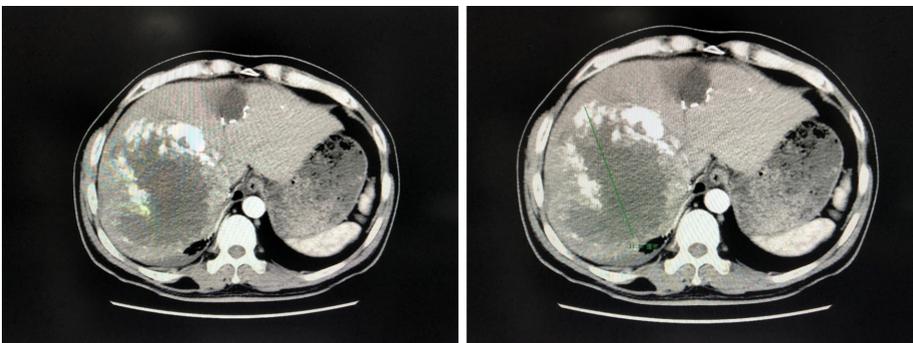
The patient returned to our center 53 d after his initial operation for reexamination. The volume of the left liver did not increase as expected. We therefore performed transcatheter arterial chemoembolization (TACE) 56 d after the first operation to limit the progression of the tumor. Intraoperative angiography showed that the right hepatic artery was ligated, and the right liver tumor was mainly supplied by the middle hepatic artery and to a lesser extent by the left hepatic artery *via* the collateral circulation (Figure 5A). He was treated with fluorouracil 750 mg + oxaliplatin 150 mg + pirarubicin 30 mg administered as a slow bolus, followed by iodized poppy seed oil and microspheres to embolize the branches of the middle and left hepatic arteries, respectively (Figure 5B). The patient recovered well and was discharged to await further review.



**Figure 1** Pre-operative enhanced computed tomography scan of the upper abdomen. A large mass in the right lobe of the liver, centered on the right posterior lobe, with the larger section measuring about 14 cm × 10 cm × 14 cm. The right hepatic vein mostly ran along the edge of the lesion, and the right hepatic vein and right portal vein were affected by pressure.



**Figure 2** At 53 d after the initial operation. No significant changes in patient's left or right liver.



**Figure 3** At 93 d after the initial operation. A large soft tissue mass in the right lobe of the liver, with dot-like or sheet-like high-density shadows, slightly smaller than previously. Other imaging findings were similar to before.

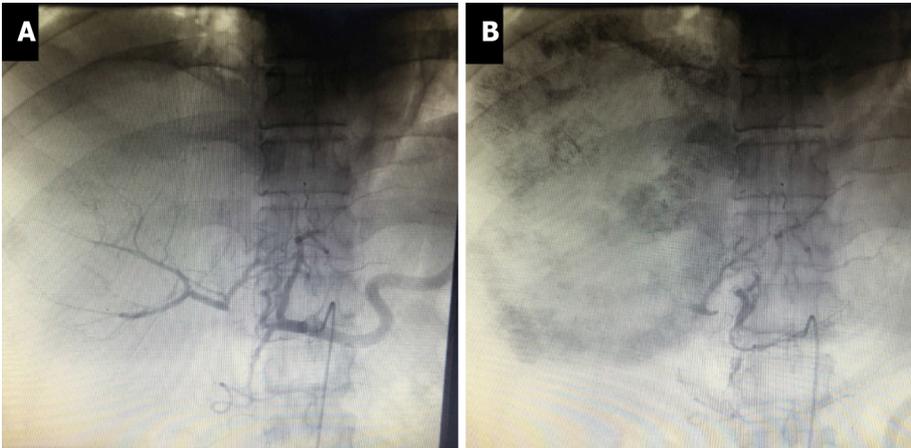
CT scans at 93 d after the first stage of surgery indicated that the left liver volume had increased to 30.88% of the total liver volume. The patient was still Child-Pugh grade A. He therefore underwent right hemi-hepatectomy and cholecystectomy 98 d after the first stage of surgery (Figure 6A-C).

## OUTCOME AND FOLLOW-UP

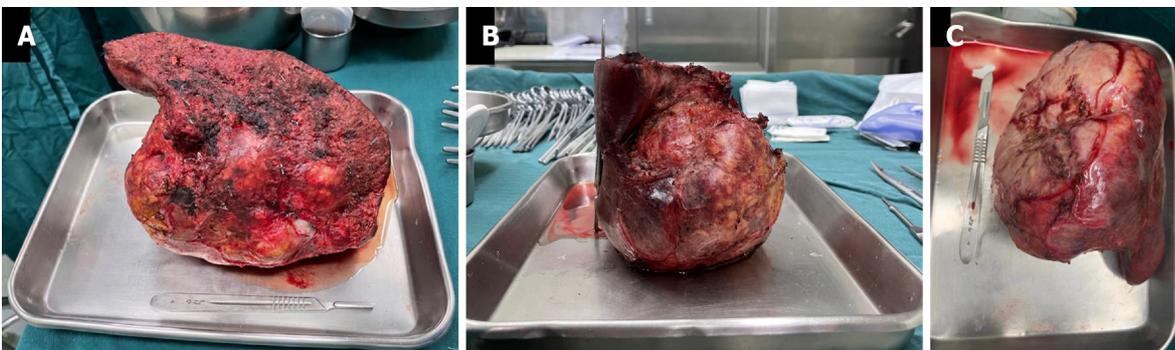
The patient had a relatively uneventful postoperative clinical course. Dindo-Clavien grade I-II complications occurred after surgery, and he was discharged 113 d after the primary operation. The patient returned to the hospital for review 2 mo later. He was asymptomatic, and enhanced CT of the upper abdomen found no obvious abnormalities. The patient remained satisfied with the results and continued to be reviewed at our center as planned.



**Figure 4** At 2 mo after the initial operation. A small amount of fluid in the operation area and no obvious abnormalities.



**Figure 5** Hepatic angiography before and after intervention. A: The right hepatic artery was ligated, and the right liver tumor was mainly supplied by the middle hepatic artery and to a lesser extent by the left hepatic artery *via* the collateral circulation; B: The tumor-supplying branches of the middle and left hepatic arteries were embolized.



**Figure 6** Postoperative right liver and right liver tumor specimens. A: Incisal margin view; B: Left side view; C: Diaphragmatic face view.

## DISCUSSION

Conversion therapy of HCC is a recent area of interest. TACE involves injecting chemotherapeutic drugs and embolic agents into the tumor-supplying blood vessels

*via* the hepatic artery to cause tumor necrosis. It is the first-choice standard non-surgical treatment for liver cancer and can effectively control tumor progression and increase the opportunities for liver resection and transplantation[4]. The problem of insufficient remnant liver volume can be addressed in several ways, including PVE, portal vein ligation (PVL), and ALPPS, which aim to limit the growth of the liver tumor on the affected side whilst enabling the healthy side of the liver to obtain sufficient portal vein blood flow and nutrients, reducing the volume of the affected-side liver and tumor, increasing the remnant liver volume after surgery, and improving the surgical resection rate and safety.

ALPPS was initially used in patients with liver metastases from colon cancer and has since been increasingly used for treating liver cancer. It provides a reasonable chance of complete resection for patients with initially unresectable primary liver tumors[5]. As a surgical technique, ALPPS can cause liver hypertrophy on the contralateral side in a shorter period of time compared with PVE or PVL. During this period, the patient's condition progresses less, and more than 90% of patients can undergo secondary radical hepatectomy[6-8]. However, ALPPS is associated with high morbidity and mortality[9]. The procedure has thus not been widely used for the treatment of HCC, and further studies are needed to assess its safety relative to PVE [8].

PVE and PVL involve blocking the branches of the affected hepatic portal vein through surgery and intervention, respectively. Previous studies[10] found no significant difference in safety and future liver remnant hypertrophy rate between PVE and PVL, while its minimally invasive nature suggests that PVE should be considered the preferred strategy. Because PVL is often implemented in ALPPS, the current literature mostly compares the advantages and disadvantages of PVE and ALPPS. In a comparison between ALPPS and PVE, the ALPPS group had a greater increase in future liver remnant and a higher completion rate of second-stage surgery, but PVE had lower morbidity and mortality rates after the second stage[11].

TACE utilizes the characteristics of liver cancer, including nourishment mainly by the hepatic artery. The injection of embolic agents such as iodized oil, microspheres, and chemotherapeutics, such as cisplatin and fluorouracil, *via* the hepatic artery leads to necrosis of liver cancer tissues, thereby allowing some tumors to be downgraded sufficiently to allow radical resection. The possibility of surgery has greatly improved the prognosis of patients with advanced liver cancer, and it has been widely used for the treatment of these patients. However, issues such as the choice of indications and number of preoperative TACE procedures require more evidence.

As one of the main blood vessels of the liver, the hepatic artery accounts for 50% of the liver's oxygen supply, with an average of 25% of the hepatic blood flow. Unlike many other organs, the blood supply to normal liver cells is mainly *via* venous blood distributed by the branches of the portal vein, with only 10%-35% of the blood supply of normal liver cells provided by the hepatic artery. However, malignant cells in the liver are mainly supplied by the branches of the hepatic artery, and the number of arteries around liver tumor tissues is three to four times higher than the number of veins[12]. We therefore suggest that even blocking only the hepatic artery supplying blood to the affected side of the liver tumor during surgery can achieve good results in terms of restricting tumor growth and, to a certain extent, restricting the growth of the affected side of the liver. Compared with ALPPS and PVE conversion therapies, the current treatment strategy can produce satisfactory results with relatively minor surgery. The degree of one-stage surgery required is much less than that with ALPPS, by only dissecting and ligating the branch of the hepatic artery that supplies blood to the tumor, without breaking the liver. Experienced surgeons can even complete the operation laparoscopically, potentially reducing the likelihood of postoperative liver failure[13] and improving the chances of a smooth recovery after the first-stage operation. Even though hepatic artery ligation combined with TACE may have less effect on the tumor than ALPPS, its effect is better than that of PVE alone. The effect of this strategy in terms of increasing residual liver volume is not obvious, compared with ALPPS and PVE. However, despite the current lack of evidence, the strategy warrants further research in terms of surgical operability and safety, especially when combined with TACE to re-embolize the tumor blood vessel branch.

Notably, although the current minimally invasive surgical technique has been applied to patients with Child-Pugh grade B liver cancer with good results[13,14], we do not recommend its implementation in patients with liver cancer of Child-Pugh grade B or below. The risk of postoperative liver failure remains high in patients with advanced giant liver tumors and liver decompensation, even if second-stage TACE is not considered immediately and only minimally invasive surgery is used to ligate the hepatic artery. In addition, the benefits of TACE in patients with Child-Pugh grade B

remain controversial[15]. As for ALPPS, the current conversion treatment plan is thus currently only reproducible in patients with huge liver tumors, whose liver function is sufficient to compensate.

## CONCLUSION

After first-stage liver partition and right hepatic artery ligation combined with second-stage TACE, the proportion of the current patient's left liver volume to total liver volume increased from 21.34% to 30.88%. Liver tumor R0 resection was then completed in the third stage, with no surgical complications and good postoperative recovery. The treatment was therefore considered to be relatively successful. However, the long treatment cycle and slow compensation of the contralateral liver still represent shortcomings compared with ALPPS and PVE. In addition, the unplanned nature of the first-stage operation means that this treatment still lacks good repeatability and evaluability. Nevertheless, the successful treatment of this patient demonstrated the effective, safe, and operable characteristics and suggests that this strategy might help provide a solution to the problem of insufficient residual liver volume after surgery and a reference for future treatment strategies.

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