

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2023 September 27; 15(9): 1841-2097



Contents

Monthly Volume 15 Number 9 September 27, 2023

REVIEW

- 1841** Indocyanine green dye and its application in gastrointestinal surgery: The future is bright green
Lim ZY, Mohan S, Balasubramaniam S, Ahmed S, Siew CCH, Shelat VG
- 1858** Hepatic ischemia-reperfusion syndrome and its effect on the cardiovascular system: The role of treprostinil, a synthetic prostacyclin analog
Mouratidou C, Pavlidis ET, Katsanos G, Kotoulas SC, Mouloudi E, Tsoulfas G, Galanis IN, Pavlidis TE

MINIREVIEWS

- 1871** Advances and challenges of gastrostomy insertion in children
Bitar R, Azaz A, Rawat D, Hobeldin M, Miqdady M, Abdelsalam S
- 1879** Surgical decompression for the management of abdominal compartment syndrome with severe acute pancreatitis: A narrative review
Nasa P, Chanchalani G, Juneja D, Malbrain ML

ORIGINAL ARTICLE

Retrospective Cohort Study

- 1892** Excision of malignant and pre-malignant rectal lesions by transanal endoscopic microsurgery in patients under 50 years of age
Shilo Yaacobi D, Berger Y, Shaltiel T, Bekhor EY, Khalifa M, Issa N
- 1901** Safety and feasibility of modified duct-to-mucosa pancreaticojejunostomy during pancreatoduodenectomy: A retrospective cohort study
Sun Y, Yu XF, Yao H, Xu S, Ma YQ, Chai C

Retrospective Study

- 1910** Application of early enteral nutrition nursing based on enhanced recovery after surgery theory in patients with digestive surgery
Shao YR, Ke X, Luo LH, Xu JD, Xu LQ
- 1919** Autologous bone marrow infusion *via* portal vein combined with splenectomy for decompensated liver cirrhosis: A retrospective study
Liu BC, Cheng MR, Lang L, Li L, Si YH, Li AJ, Xu Q, Zhang H
- 1932** Application of multidisciplinary collaborative nursing with family care for enhanced recovery after surgery in children with inguinal hernia
Wang XM, Hou Q
- 1941** Preoperative and postoperative complications as risk factors for delayed gastric emptying following pancreaticoduodenectomy: A single-center retrospective study
Xie FL, Ren LJ, Xu WD, Xu TL, Ge XQ, Li W, Ge XM, Zhou WK, Li K, Zhang YH, Wang Z

- 1950** Efficacy of ileus tube combined with meglumine diatrizoate in treating postoperative inflammatory bowel obstruction after surgery
Yang W, Pu J
- 1959** Effect of internet multiple linkage mode-based extended care combined with in-hospital comfort care on colorectal cancer patients undergoing colostomy
Xu L, Zhou MZ
- 1969** Short- and long-term results of open *vs* laparoscopic multisegmental resection and anastomosis for synchronous colorectal cancer located in separate segments
Quan JC, Zhou XJ, Mei SW, Liu JG, Qiu WL, Zhang JZ, Li B, Li YG, Wang XS, Chang H, Tang JQ
- 1978** Prediction model of stress ulcer after laparoscopic surgery for colorectal cancer established by machine learning algorithm
Yu DM, Wu CX, Sun JY, Xue H, Yuwen Z, Feng JX
- 1986** Effect of two surgical approaches on the lung function and prognosis of patients with combined esophago-gastric cancer
Sun CB, Han XQ, Wang H, Zhang YX, Wang MC, Liu YN
- 1995** Clinical significance of serum oxidative stress and serum uric acid levels before surgery for hepatitis B-related liver cancer
Hou JX, Wang YB, Wu J, Ding GS, Wu Y, Wei LH, Wang F, Zhang ZM
- 2003** Multifactor analysis of the technique in total laparoscopic gastric cancer
Shi JK, Wang B, Zhang XS, Lv P, Chen YL, Ren SY
- 2012** Value of enhanced computed tomography in differentiating small mesenchymal tumours of the gastrointestinal from smooth muscle tumours
Nie WJ, Jing Z, Hua M
- 2021** Risk factors for myocardial injury during living donor liver transplantation in pediatric patients with biliary atresia
Wu YL, Li TY, Gong XY, Che L, Sheng MW, Yu WL, Weng YQ

Observational Study

- 2032** Comparative detection of syndecan-2 methylation in preoperative and postoperative stool DNA in patients with colorectal cancer
Song JH, Oh TJ, An S, Lee KH, Kim JY, Kim JS

Prospective Study

- 2042** Preoperative prediction of microvascular invasion in hepatocellular carcinoma using ultrasound features including elasticity
Jiang D, Qian Y, Tan BB, Zhu XL, Dong H, Qian R
- 2052** Quantitative evaluation of colorectal tumour vasculature using contrast-enhanced ultrasound: Correlation with angiogenesis and prognostic significance
Li MH, Li WW, He L, Li JF, Zhang SY

CASE REPORT

- 2063** Laparoscopy-assisted gastrectomy for advanced gastric cancer patients with situs inversus totalis: Two case reports and review of literature
Liu HB, Cai XP, Lu Z, Xiong B, Peng CW
- 2074** Acute flare of systemic lupus erythematosus with extensive gastrointestinal involvement: A case report and review of literature
Huang H, Li P, Zhang D, Zhang MX, Yu K
- 2083** Surgical management of gallstone ileus after one anastomosis gastric bypass: A case report
El Feghali E, Akel R, Chamaa B, Kazan D, Chakhtoura G
- 2089** Dual transformation therapy for giant hepatocellular carcinoma: Two case reports and review of literature
Gao Q, Zhu GZ, Han CY, Ye XP, Huang HS, Mo ST, Peng T

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Sung Uk Bae, MD, PhD, Associate Professor, Department of Surgery, Keimyung University Dongsan Hospital, Daegu 42601, South Korea.
sabiston0000@hanmail.net

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (WJGS, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, etc.

INDEXING/ABSTRACTING

The WJGS is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJGS as 2.0; IF without journal self cites: 1.9; 5-year IF: 2.2; Journal Citation Indicator: 0.52; Ranking: 113 among 212 journals in surgery; Quartile category: Q3; Ranking: 81 among 93 journals in gastroenterology and hepatology; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Rui-Rui Wu; Production Department Director: Xiang Li; Editorial Office Director: Jia-Ru Fan.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Peter Schemmer

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

September 27, 2023

COPYRIGHT

© 2023 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Dual transformation therapy for giant hepatocellular carcinoma: Two case reports and review of literature

Qiang Gao, Guang-Zhi Zhu, Chuang-Ye Han, Xin-Ping Ye, Hua-Sheng Huang, Shu-Tian Mo, Tao Peng

Specialty type: Surgery

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Akbulut S, Turkey;
Martín Del Olmo JC, Spain

Received: May 30, 2023

Peer-review started: May 30, 2023

First decision: July 4, 2023

Revised: July 12, 2023

Accepted: August 1, 2023

Article in press: August 1, 2023

Published online: September 27, 2023



Qiang Gao, Guang-Zhi Zhu, Chuang-Ye Han, Xin-Ping Ye, Hua-Sheng Huang, Shu-Tian Mo, Tao Peng, Department of Hepatobiliary Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning 530000, Guangxi Zhuang Autonomous Region, China

Corresponding author: Tao Peng, PhD, Chief Doctor, Department of Hepatobiliary Surgery, The First Affiliated Hospital of Guangxi Medical University, No. 6 Shuangyong Road, Nanning 530000, Guangxi Zhuang Autonomous Region, China. pengtaogmu@163.com

Abstract

BACKGROUND

In the translational therapy of giant hepatocellular carcinoma (HCC), hepatic arterial infusion chemotherapy (HAIC) combined with anti-PD-1 immunotherapy and tyrosine kinase inhibitors (TKI) after laparoscopic portal vein ligation (PVL) is extremely rare. This is a dual conversion therapy that combines surgery and oncology. Here, we report two cases of successful surgical completion after dual conversion therapy.

CASE SUMMARY

We report that a 54-year-old man and a 69-year-old woman were diagnosed with primary HCC combined with hepatitis B cirrhosis (case 2 also combined with fatty liver) on physical examination. Due to the insufficient residual liver volume assessed before surgery, laparoscopic right PVL was performed, followed by HAIC combined with anti-PD-1 immunotherapy and TKI. Finally, surgical resection was successfully completed, and pathology confirmed that the tumor was mostly necrotic (90%) in one case, and no live tumor tissue was found in the other case.

CONCLUSION

In the process of surgical transformation, our treatment plan takes into account the control and transformation of oncology at the same time, which is expected to provide more opportunities for radical hepatectomy and improve the prognosis of patients with large liver cancer.

Key Words: Giant hepatocellular carcinoma; Laparoscopic right portal vein ligation; hepatic arterial infusion chemotherapy; Anti-PD-1 immunotherapy; Tyrosine kinase inhibitor; Case report

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: There have been many clinical studies on translational therapy for giant hepatocellular carcinoma, but simply seeking surgical transformation always carries the risk of tumor progression. There's a combination of control and transformation in oncology either immunotherapy, targeted therapy, or a combination of both. In addition, we added hepatic arterial infusion chemotherapy to seek better prognosis. In addition to the success of surgical transformation in the 2 patients reported by us, the postoperative pathology also suggested good oncology control and transformation. This treatment regimen is promising to provide more opportunities for radical hepatectomy and better prognosis for patients with large liver cancer.

Citation: Gao Q, Zhu GZ, Han CY, Ye XP, Huang HS, Mo ST, Peng T. Dual transformation therapy for giant hepatocellular carcinoma: Two case reports and review of literature. *World J Gastrointest Surg* 2023; 15(9): 2089-2097

URL: <https://www.wjgnet.com/1948-9366/full/v15/i9/2089.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v15.i9.2089>

INTRODUCTION

The incidence and mortality rate of hepatocellular carcinoma (HCC) are comparable, making it one of the most common malignant tumors worldwide. According to global cancer statistics data in 2020, there were 600000 new cases of HCC worldwide, with over half of the cases occurring in China[1,2]. Surgical resection remains the first choice for HCC treatment, but the recurrence rate after surgery can be as high as 70%[3]. Some HCC patients may not be suitable for extensive liver resection due to insufficient future liver remnant (FLR) volume[4]. According to the results of the BRIDGE study, 64% of liver cancer patients in China are diagnosed at CNLC-Stage II and III [Barcelona Clinic Liver Cancer (BCLC) Stage B and C], with a median survival period of approximately 2 years[5,6]. Most patients in the advanced stages are not suitable for surgical resection and should receive mainly local and systemic treatments. In recent years, non-surgical treatments for liver cancer have made significant progress. Drug therapy, especially the combination of anti-angiogenic drugs and immune therapy, can achieve an objective response rate of about 30% and a median survival period of around 20 mo in the treatment of advanced or unresectable liver cancer[7-9].

The reasons for unresectability of liver cancer can be divided into two levels. One level is unresectability from a surgical perspective, including patients who cannot tolerate surgical trauma due to their overall condition, cannot tolerate liver dysfunction, or have insufficient FLR volume, which is considered unresectable from a surgical perspective. The other level is technically resectable, but the postoperative efficacy is not better than non-surgical treatment, which is considered unresectable from an oncological or biological perspective. The goal of conversion therapy is to eliminate these two reasons and achieve conversion from unresectable to resectable liver cancer[10]. The main methods of surgical conversion therapy for insufficient FLR volume include associating liver partition and portal vein ligation for staged hepatectomy (ALPPS), portal vein ligation (PVL), and portal vein embolization (PVE), but there is still a risk of tumor progression while the residual liver volume is growing. In our previous clinical study of 30 cases of conversion resection with insufficient FLR volume in HCC using PVL combined with apatinib (anti-VEGFR2) and camrelizumab (anti-PD1), the median preoperative estimated FLR/standard liver volume (SLV) was 32.9% (19.1%-39.9%). According to mRECIST, 4 cases (13.3%) achieved complete response (CR) and 8 cases (26.7%) achieved partial response (PR). Twenty-three cases (76.7%) met the criteria for second-stage surgery, and 20 of them (66.7%) completed second-stage liver tumor resection. Double conversion therapy had better clinical outcomes than simple surgical conversion. However, the control of tumors after PVL in our systemic therapy (objective response rate of 40%, disease control rate of 76.7%) was comparable to that of targeted immunotherapy. Considering the promising results of local combined systemic therapy in tumor control, we added hepatic arterial infusion chemotherapy (HAIC) on the basis of PVL combined with targeted immunotherapy.

Here, we report two cases of successful treatment of large liver cancer patients at our center. After PVL, the patients underwent HAIC combined with targeted immunotherapy, and finally successfully completed right hepatectomy.

CASE PRESENTATION

Chief complaints

Case 1: A 54-year-old Chinese male was admitted to the Department of Hepatobiliary Surgery due to upper abdominal discomfort for 2 wk.

Case 2: A 69-year-old Chinese woman was admitted to the hepatobiliary surgery clinic for 20 d due to physical examination.

History of present illness

Case 1: The patient reported right upper abdominal discomfort without obvious inducement more than half a month ago, presenting intermittent dull pain, each lasting 1-2 min.

Case 2: The patient reported a solid space occupying lesion in the liver during abdominal computed tomography (CT) examination 20 d ago.

History of past illness

Case 1: Hepatitis B cirrhosis for more than 30 years without systematic treatment.

Case 2: Hepatitis B cirrhosis for more than 30 years without systematic treatment; He had a history of fatty liver 3 years ago and was treated regularly with drugs.

Personal and family history

The patient denied any family history of malignant tumours.

Physical examination

There were no positive signs in either.

Laboratory examinations

Case 1: Laboratory tests indicated that AFP was 876.62 ng/mL and PIVKA-II was 12943.43 mAU/mL. Liver function, blood routine, prothrombin time, and international normalized ratio were all within normal ranges. AFP and PIVKA-II were 6.16 ng/mL and 114.89 mAU/mL before right hemihepatectomy.

Case 2: Laboratory tests showed no abnormalities.

Imaging examinations

Case 1: The outer edge of the liver was not smooth, and the proportion of each lobe was disordered. Irregular masses with slightly low density were seen in S5, 6, and 8 segments of the liver, with the size of about 6.7 cm × 6.5 cm × 7.5 cm, complete capsule and small difficult vessels were seen, and the density was not uniform. After enhancement, three stages of scanning were performed: The lesion enhancement was obvious in the arterial stage, but decreased in the portal and equilibrium stages, and the density was lower than that of liver parenchyma. Diagnosis: S5, 6, 8 segments of liver occupying, massive liver cancer was considered. Cirrhosis of the liver ([Figure 1A and B](#)). The preoperative SLV was estimated to be 1370.52 mL, and the FLR was estimated to be 418.39 mL using a three-dimensional CT reconstruction system. FLR/SLV was 30.5% ([Figure 1C](#)).

Case 2: A round mixed low-density mass with a size of 8.0 cm × 7.5 cm × 6.2 cm was seen in the right lobe of liver (S7/8 segment), with a clear margin. The third stage of enhancement scan showed that the edge of the disease showed continuous enhancement, mainly marginal enhancement, with a density slightly lower than that of open parenchyma, and patchy non-enhancement lesions were still seen in the equilibrium stage. The remaining hepatic parenchyma density was normal and no abnormal enhancement was observed. Diagnosis: right lobe of liver mass, primary liver cancer (mixed type?) was considered ([Figure 2A and B](#)). The preoperative SLV was estimated to be 913.5 mL, and the FLR was estimated to be 310.59 mL using a three-dimensional CT reconstruction system. FLR/SLV was 34% ([Figure 2C](#)).

FINAL DIAGNOSIS

Case 1

Combined with the patient's medical history, the final diagnosis was HCC (CNLC Ib stage, BCLC A grade, Child-Pugh A grade); hepatitis B cirrhosis.

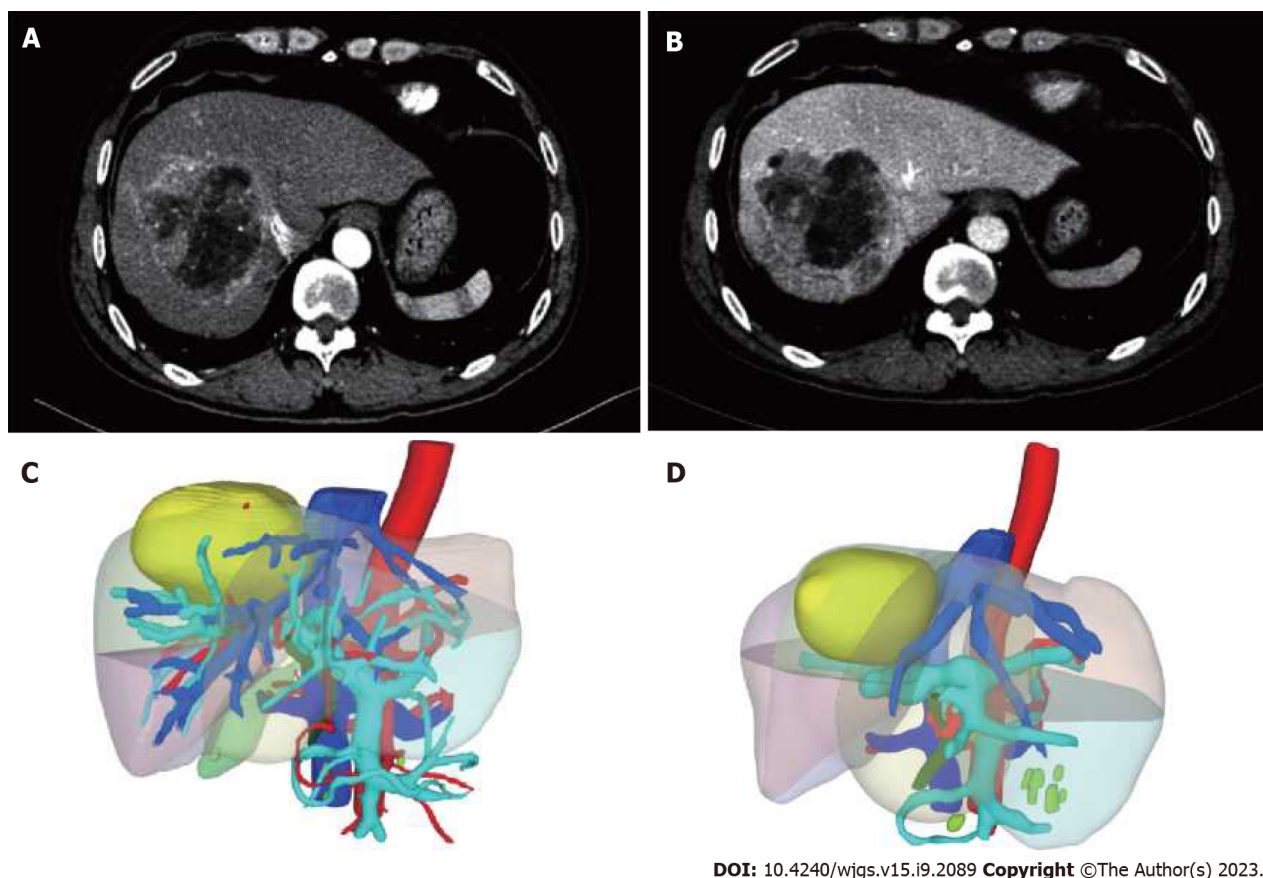
Case 2

Combined with the patient's medical history, the final diagnosis was HCC (CNLC Ib stage, BCLC A grade, Child-Pugh A grade); hepatitis B cirrhosis; fatty liver.

TREATMENT

PVL

Both patients in this series underwent complete laparoscopic right PVL surgery. The surgical steps were as follows: The patient was placed in a supine position, and pneumoperitoneum was established with trocar placement. Intraoperative ultrasound was used to confirm the location and boundaries of the tumor. The right portal vein branch near the first porta hepatis was dissected within the Glisson's sheath, and then titanium clips or No. 7 sutures were used for ligation. An electrocautery hook was used to mark the ischemic line on the liver surface ([Figure 3](#)). Case 1 and case 2 completed PVL on July 12 and 29, 2022, respectively.



DOI: 10.4240/wjgs.v15.i9.2089 Copyright ©The Author(s) 2023.

Figure 1 Image data of case 1. A: Arterial phase; B: Portal stage; C and D: 3D imaging before and after treatment.

HAIC combined with targeted immunotherapy

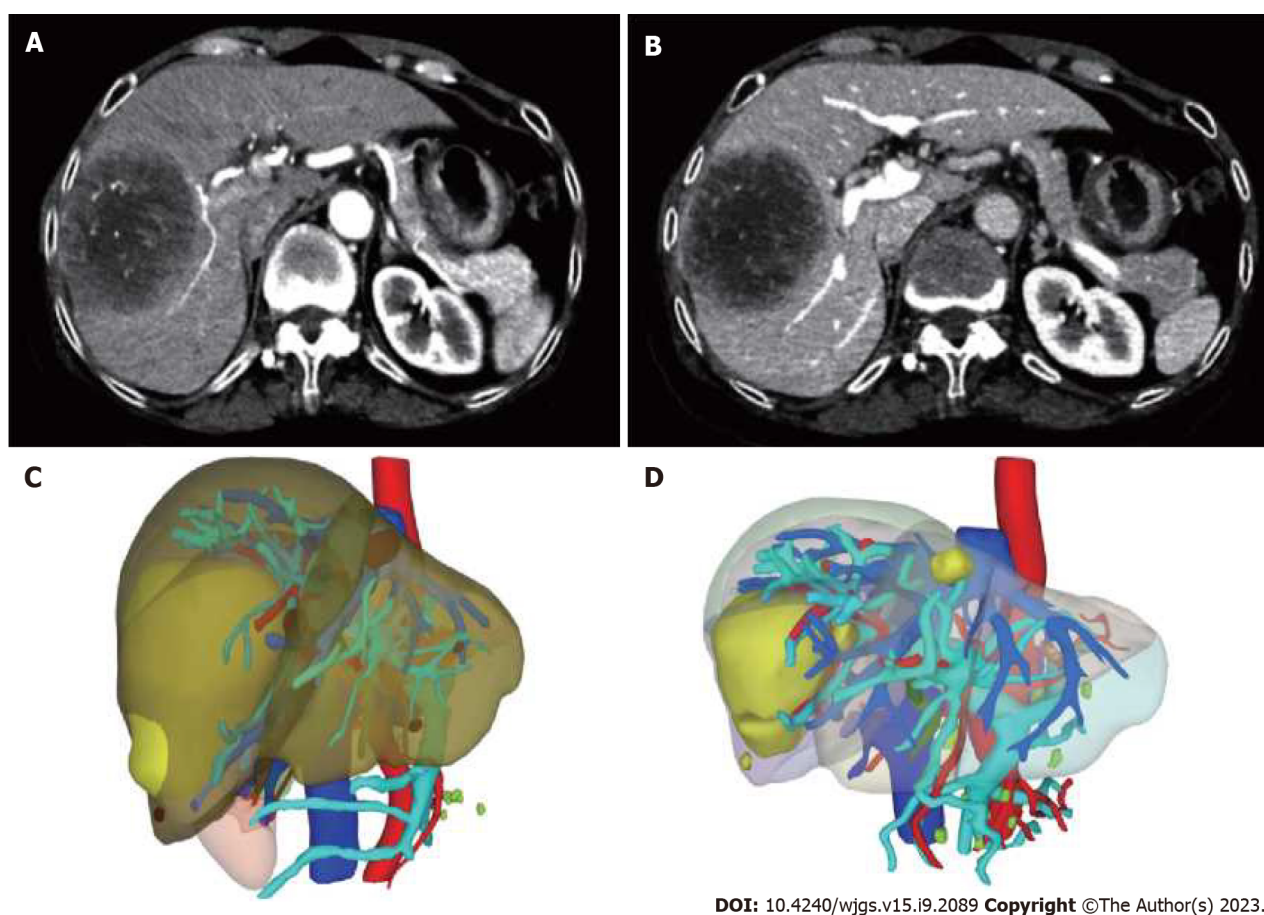
Case 1: The patient underwent a total of 4 cycles of HAIC combined with targeted immunotherapy, using the FOLFOX regimen for 46 h. The microcatheter is pushed into the hepatic artery and the drug is transfused through the hepatic artery. Oxaliplatin, 130 mg/m² before 2 h on day 1, calcium folinate, 400 mg/m² from 2-3 h on day 1, fluorouracil 400 mg/m² at 3 h on day 1, 2400 mg/m² over 24 h. On the following dates: July 15, 2022; August 8, 2022; September 6, 2022; and October 13, 2022. Bevacizumab was administered intravenously at a dose of 200 mg on July 18, 2022; August 11, 2022; September 9, 2022; and October 16, 2022. In addition, the patient received oral lenvatinib starting from July 18, 2022, until prior to surgery. After discontinuation of the medication for four weeks, the FLR to SLV ratio was reevaluated and found to be 60.5% (Figure 1D). Right hemihepatectomy was performed on November 25, 2022.

Case 2: On August 12 and September 16, 2022, the patient received HAIC treatment using the same protocol as before. On September 19, Carfilzomib was administered intravenously at a dose of 200mg. After a four-week drug holiday, the FLR/SLV was re-evaluated and found to be 47% (as shown in Figure 2D). On October 26, right hepatectomy was performed to remove the right half of the liver.

Right hemihepatectomy

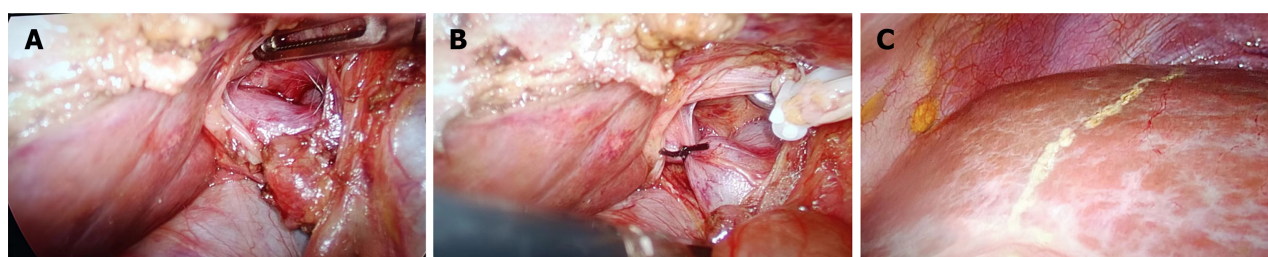
Case 1: During the initial surgical exploration, left liver hypertrophy was easily observed (Figure 4). After separation of adhesions, right hepatic pedicle was dissected intrafascially. Then, the liver parenchyma was continuously separated along the previously marked ischemic line using an ultrasonic knife. The right hepatic vein was transected with a stapling closure device until complete removal of the diseased liver. There were no major complications during the postoperative recovery period. Histopathological examination of the tumor confirmed that the majority of the tumor was necrotic (90% necrosis), with some residual viable tumor tissue at the periphery. The tumor was classified as HCC grade II, with a nodular pattern, with approximately 40% of tumor cells showing clear cell changes and approximately 40% of tumor cells showing macrovesicular fatty changes. Fibrous tissue proliferation with foam cell and multinucleated giant cell reactions were observed, along with deposition of hemosiderin and infiltration of lymphocytes. No satellite nodules or neural bundle invasion were observed, and the microvascular invasion was graded as MO. There was no tumor involvement in the liver capsule or surgical margins. The surrounding liver tissue showed chronic hepatitis changes, with a CS grade of C3S3 (Figure 5A).

Case 2: The postoperative pathological examination revealed extensive necrosis with no residual viable tumor tissue. Fibrous tissue proliferation with abundant lymphocyte and plasma cell infiltration, hemosiderin deposition, and foam cell reaction were observed around the necrotic tissue, consistent with changes after interventional treatment. Microvascular



DOI: 10.4240/wjgs.v15.i9.2089 Copyright ©The Author(s) 2023.

Figure 2 Image data of case 2. A: Arterial phase; B: Portal stage; C and D: 3D imaging before and after treatment.



DOI: 10.4240/wjgs.v15.i9.2089 Copyright ©The Author(s) 2023.

Figure 3 Complete laparoscopic right portal vein ligation surgery. A: Dissection of the right branch of the portal vein within the Glisson's sheath at the first porta hepatis; B: Occlusion with titanium clip or ligation with No. 7 silk suture; C: Marking of the ischemic line on the surface of the liver with an electrocautery hook.

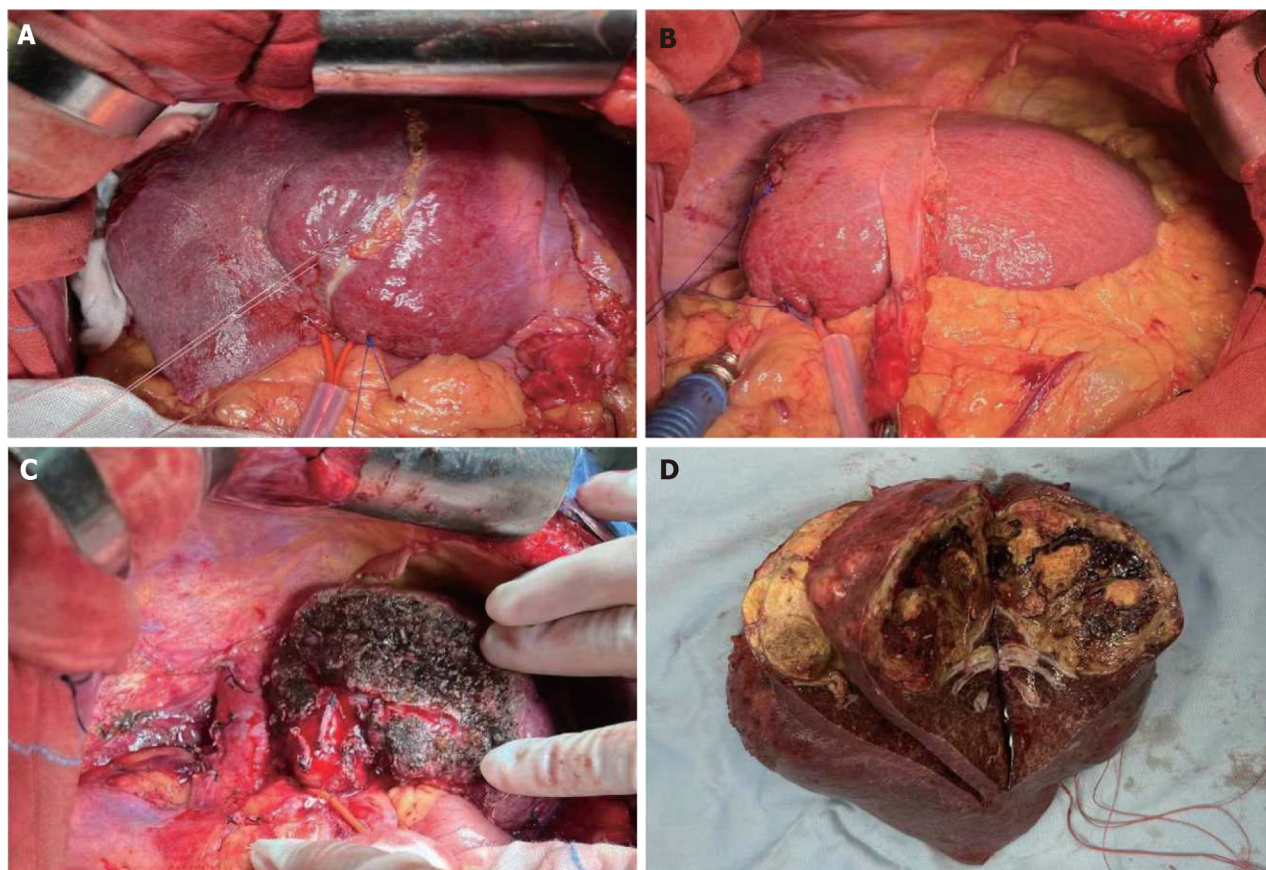
invasion and nerve bundle invasion could not be assessed due to the absence of viable tumor components. There was no tumor involvement in the liver capsule or surgical margins. The surrounding liver tissue showed chronic hepatitis with a grade of G2S2 (Figure 5B).

OUTCOME AND FOLLOW-UP

Cases 1 and 2: As of July 2023, the patient is still alive and has no recurrence.

DISCUSSION

Currently, international centers have similar criteria for determining the required liver reserve function for safe liver



DOI: 10.4240/wjgs.v15.i9.2089 Copyright ©The Author(s) 2023.

Figure 4 Right hemihepatectomy. A: Intraoperative exploration revealed hypertrophied left lobe of the liver and a marked ischemic line; B: Postoperative left lobe of the liver; C: Surgical section; D: Tumor specimen.

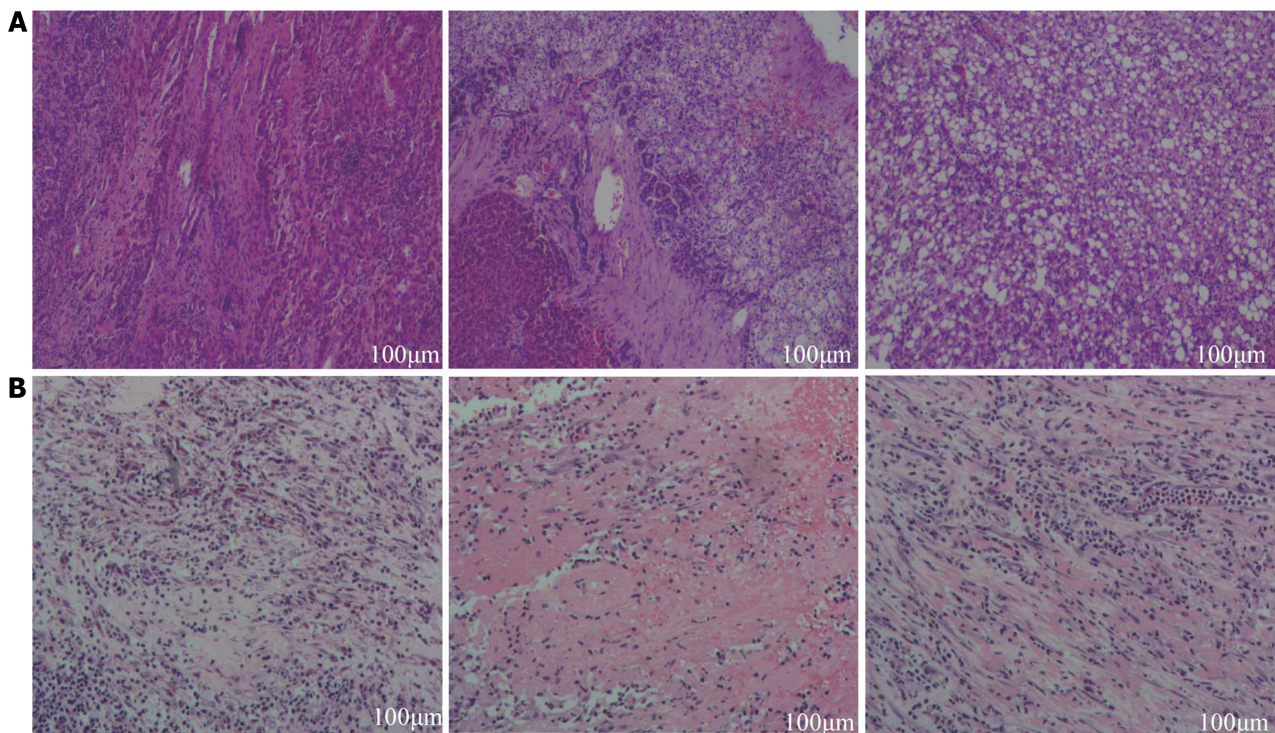
resection, which includes normal liver function (Child-Pugh Class A) with a retention rate of indocyanine green at 15 min (ICG-R15) of 20% to 30%; patients with chronic liver disease or liver parenchymal damage (including cirrhosis, severe fatty liver, and liver damage related to chemical drug treatment) require a FLR to SLV ratio of > 40%; for patients with impaired liver function, a higher FLR is required (e.g., ICG-R15 of 10% to 20%, and patients with chronic liver disease and cirrhosis require FLR/SLV > 50%)[10,11]. Insufficient FLR is an important criterion for unresectable liver cancer, and the goal of conversion therapy is to achieve a sufficient FLR.

In 1990, Makuuchi *et al* [12] reported the first series of PVE in 14 patients with hilar cholangiocarcinoma, demonstrating the safety and feasibility of this technique in reducing postoperative liver failure. PVE has been used in clinical practice for a long time, with a conversion success rate of 60% to 80% and a complication rate of 10% to 20%. The time required for residual liver hypertrophy after PVE is relatively long (usually 4 to 6 wk, during which time tumor progression may occur). In addition, more than 20% of patients may lose the opportunity for surgery due to tumor progression or insufficient volume of residual liver hypertrophy[13-15]. This has prompted exploration of alternative techniques. There is no significant difference in the induction of FLR hypertrophy between PVE and PVL (relative increase in FLR volume: PVE 43.2%, PVL 38.5%). The induction of FLR hypertrophy with PVL also takes 4 to 8 wk. However, the resection rate with PVL is higher than with PVE, resulting in significantly fewer patients who have to cancel surgery due to insufficient FLR hypertrophy. There is no statistically significant difference in the incidence of postoperative complications and mortality between the two techniques[16,17].

In 2012, ALPPS was first described as a surgical technique for increasing FLR in patients with liver tumors[18]. It is a more radical method of portal vein occlusion and elimination of collateral vessels from FLR to the diseased segment, resulting in faster and more extensive FLR enhancement. ALPPS can induce FLR hypertrophy of up to 47% to 192% within 1-2 wk, which is much higher than PVE. Due to the short interval between the two-stage surgeries, it can minimize the risk of tumor progression, with a tumor resection rate of 95% to 100%[19]. The main limitation of this technique is its high morbidity and mortality rates. Compared to PVE, the 90-d mortality rate remains at 8%-9%[20], and both mortality and morbidity rates are increased[21]. These findings were initially attributed to increased invasiveness of the surgery and subsequent bile leakage, with bile leakage occurring in 20% of the cases reported by Schnitzbauer *et al* [18].

When the tumor volume is too large, involves critical ducts, or cannot achieve an R0 resection, tumor reduction through anti-tumor treatment can be achieved before surgery to further improve long-term outcomes. Treatment options include local therapy, systemic therapy, and combination therapy[11].

In clinical practice, there is no consensus on which systemic treatment regimen to choose for potentially resectable liver cancer patients. Based on current clinical research data on first-line systemic treatment for liver cancer, lenvatinib has a



DOI: 10.4240/wjgs.v15.i9.2089 Copyright ©The Author(s) 2023.

Figure 5 Histopathological image. A: Case 1; B: Case 2.

higher objective response rate (ORR) than sorafenib[22]. Combination targeted therapy and immunotherapy (targeted immunotherapy combination)[7,8,23,24], represented by lenvatinib combined with pembrolizumab, nivolumab combined with ramucirumab, and bevacizumab, and atezolizumab combined with cetuximab, has an ORR > 20% for treating unresectable liver cancer, with stronger potential for conversion. Zhu *et al*[25] reported a conversion resection rate of 23.8% in 101 cases of initially unresectable liver cancer patients treated with PD-1 inhibitors combined with tyrosine kinase inhibitors (TKIs)[25]. Zhu *et al*[26] reported a conversion resection rate of 15.9% in 63 cases of initially unresectable liver cancer patients treated with PD-1 inhibitors combined with TKIs. At the 2022 Annual Meeting of the American Association for the Study of Liver Diseases, we reported the effectiveness and safety of hepatic portal vein ligation (PVL) combined with apatinib (anti-VEGFR2) + camrelizumab (anti-PD1) (also known as double A combination) in treating insufficient FLR volume HCC. According to mRECIST, among them, 4 cases (13.3%) achieved CR, 8 cases (26.7%) achieved PR, 11 cases (36.7%) had stable disease (SD), and 7 cases (23.3%) had progressive disease (PD), with an ORR of 40% and a disease control rate (DCR) of 76.7%. This is a dual conversion regimen that considers both surgical and oncological aspects. The results of this study suggest that PVL combined with apatinib and camrelizumab may become a potential treatment option for insufficient FLR volume HCC.

In Asia, particularly in Japan and South Korea, HAIC has been used to improve the prognosis of advanced HCC and has been incorporated into treatment guidelines[27]. In a randomized phase III study (9810) announced at ESMO 2020, the surgical conversion rate of unresectable HCC with HAIC (oxaliplatin, fluorouracil, and folinic acid) was 23.8% in the HAIC group compared to 11.5% in the transarterial chemoembolization group ($P < 0.004$). Furthermore, the study also found that the ORR of advanced HCC treated with HAIC plus targeted therapy and immune therapy according to mRECIST criteria was 67.6%[28]. The results of clinical studies by Luo *et al*[29] and Zhang *et al*[30] at their respective centers, using HAIC in combination with targeted immunotherapy for advanced liver cancer, were encouraging, with objective tumor response rates of 57.2% and 96%, respectively, and good safety profiles. These studies demonstrate that combined systemic and local treatment can lead to better tumor response, providing new options for future HAIC-based conversion therapies.

In the two cases reported in our study, the main feature was the increase in FLR volume after PVL combined with systemic and local treatment. FLR increased by 30% and 13% in case 1 and case 2, respectively, with time intervals of 17 wk and 12 wk, respectively. Postoperative pathology confirmed that the majority of the tumor in case 1 had necrotized (90% necrosis), and the tumor in case 2 had completely necrotized, with both cases showing good recovery during follow-up. Dual conversion in terms of surgical and oncological outcomes was achieved, indicating that PVL combined with HAIC and targeted immunotherapy is a safe and effective dual conversion treatment approach.

CONCLUSION

Our treatment approach aims to achieve surgical conversion while also addressing tumor control and conversion,

offering potential opportunities for curative liver resection in patients with advanced HCC and improving their prognosis. However, research in this area is limited at present. Further studies are needed to confirm the safety, feasibility, and efficacy of our approach.

FOOTNOTES

Author contributions: Gao Q, Zhu GZ, and Han CY contributed to data curation and writing of the original draft; Ye XP and Huang HS contributed to data curation; Mo ST, and Peng T contributed to manuscript review and editing; all authors have read and approved the final manuscript.

Informed consent statement: Informed written consent was obtained from the patient for the publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to disclose.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Guang-Zhi Zhu 0000-0001-5958-7289; Xin-Ping Ye 0000-0002-9200-1312; Hua-Sheng Huang 0000-0003-1112-5071; Tao Peng 0000-0001-6133-7078.

S-Editor: Yan JP

L-Editor: A

P-Editor: Cai YX

REFERENCES

- 1 Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]
- 2 Cao M, Li H, Sun D, Chen W. Cancer burden of major cancers in China: A need for sustainable actions. *Cancer Commun (Lond)* 2020; **40**: 205-210 [PMID: 32359212 DOI: 10.1002/cac2.12025]
- 3 General Office of National Health Commission. Diagnosis and Treatment Guidelines for Primary liver Cancer (2022 edition). *Linchuang Gandanbing Zazhi* 2022; **38**: 288-303 [DOI: 10.3969/j.issn.1001-5256.2022.02.009]
- 4 Chan A, Zhang WY, Chok K, Dai J, Ji R, Kwan C, Man N, Poon R, Lo CM. ALPPS Versus Portal Vein Embolization for Hepatitis-related Hepatocellular Carcinoma: A Changing Paradigm in Modulation of Future Liver Remnant Before Major Hepatectomy. *Ann Surg* 2021; **273**: 957-965 [PMID: 31305284 DOI: 10.1097/SLA.0000000000003433]
- 5 Park JW, Chen M, Colombo M, Roberts LR, Schwartz M, Chen PJ, Kudo M, Johnson P, Wagner S, Orsini LS, Sherman M. Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. *Liver Int* 2015; **35**: 2155-2166 [PMID: 25752327 DOI: 10.1111/liv.12818]
- 6 Zhou J, Sun H, Wang Z, Cong W, Wang J, Zeng M, Zhou W, Bie P, Liu L, Wen T, Han G, Wang M, Liu R, Lu L, Ren Z, Chen M, Zeng Z, Liang P, Liang C, Yan F, Wang W, Ji Y, Yun J, Cai D, Chen Y, Cheng W, Cheng S, Dai C, Guo W, Hua B, Huang X, Jia W, Li Y, Liang J, Liu T, Lv G, Mao Y, Peng T, Ren W, Shi H, Shi G, Tao K, Wang X, Xiang B, Xing B, Xu J, Yang J, Yang Y, Ye S, Yin Z, Zhang B, Zhang L, Zhang S, Zhang T, Zhao Y, Zheng H, Zhu J, Zhu K, Shi Y, Xiao Y, Dai Z, Teng G, Cai J, Cai X, Li Q, Shen F, Qin S, Dong J, Fan J. Guidelines for the Diagnosis and Treatment of Hepatocellular Carcinoma (2019 Edition). *Liver Cancer* 2020; **9**: 682-720 [PMID: 33442540 DOI: 10.1159/000509424]
- 7 Finn RS, Ikeda M, Zhu AX, Sung MW, Baron AD, Kudo M, Okusaka T, Kobayashi M, Kumada H, Kaneko S, Pracht M, Mamontov K, Meyer T, Kubota T, Dutkus CE, Saito K, Siegel AB, Dubrovsky L, Mody K, Llovet JM. Phase Ib Study of Lenvatinib Plus Pembrolizumab in Patients With Unresectable Hepatocellular Carcinoma. *J Clin Oncol* 2020; **38**: 2960-2970 [PMID: 32716739 DOI: 10.1200/JCO.20.00808]
- 8 Xu J, Shen J, Gu S, Zhang Y, Wu L, Wu J, Shao G, Xu L, Yin T, Liu J, Ren Z, Xiong J, Mao X, Zhang L, Yang J, Li L, Chen X, Wang Z, Gu K, Pan Z, Ma K, Zhou X, Yu Z, Li E, Yin G, Zhang X, Wang S, Wang Q. Camrelizumab in Combination with Apatinib in Patients with Advanced Hepatocellular Carcinoma (RESCUE): A Nonrandomized, Open-label, Phase II Trial. *Clin Cancer Res* 2021; **27**: 1003-1011 [PMID: 33087333 DOI: 10.1158/1078-0432.CCR-20-2571]
- 9 Yau T, Kang YK, Kim TY, El-Khoueiry AB, Santoro A, Sangro B, Melero I, Kudo M, Hou MM, Matilla A, Tovoli F, Knox JJ, Ruth He A, El-Rayes BF, Acosta-Rivera M, Lim HY, Neely J, Shen Y, Wisniewski T, Anderson J, Hsu C. Efficacy and Safety of Nivolumab Plus Ipilimumab in Patients With Advanced Hepatocellular Carcinoma Previously Treated With Sorafenib: The CheckMate 040 Randomized Clinical Trial. *JAMA Oncol* 2020; **6**: e204564 [PMID: 33001135 DOI: 10.1001/jamaoncol.2020.4564]
- 10 Sun HC, Xie Q, Jia WD, Zhao M, Liu XF, Bi XY, Li G, Bai XL, Ji Y, Xu L, Wang Z, Zhu XD. Chinese Expert Consensus on transformation

- Therapy for liver Cancer (2021 edition). *Zhongguo Shiyong Waikē Zazhi* 2021; **41**: 618-632 [DOI: [10.19538/j.cjps.issn1005-2208.2021.06.02](https://doi.org/10.19538/j.cjps.issn1005-2208.2021.06.02)]
- 11 **Zhao HT**, Bi XY, Zhao H, Sun YK, Zhou JG, Chen B, Zhang W. Chinese expert consensus on neoadjuvant and translational therapy for hepatocellular carcinoma. *Ganai Dianza Zazhi* 2022; **9**: 23-28 [DOI: [10.3969/j.issn.2095-7815.2022.01.002](https://doi.org/10.3969/j.issn.2095-7815.2022.01.002)]
 - 12 **Makuuchi M**, Thai BL, Takayasu K, Takayama T, Kosuge T, Gunvén P, Yamazaki S, Hasegawa H, Ozaki H. Preoperative portal embolization to increase safety of major hepatectomy for hilar bile duct carcinoma: a preliminary report. *Surgery* 1990; **107**: 521-527 [PMID: [2333592](https://pubmed.ncbi.nlm.nih.gov/2333592/)]
 - 13 **Aloia TA**. Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy: Portal Vein Embolization Should Remain the Gold Standard. *JAMA Surg* 2015; **150**: 927-928 [PMID: [26308668](https://pubmed.ncbi.nlm.nih.gov/26308668/) DOI: [10.1001/jamasurg.2015.1646](https://doi.org/10.1001/jamasurg.2015.1646)]
 - 14 **Piron L**, Deshayes E, Escal L, Souche R, Herrero A, Pierredon-Foulongne MA, Assenat E, le Lam N, Quenet F, Guiu B. [Portal vein embolization: Present and future]. *Bull Cancer* 2017; **104**: 407-416 [PMID: [2WJGS-15-189270](https://pubmed.ncbi.nlm.nih.gov/2WJGS-15-189270/) DOI: [10.1016/j.bulcan.2017.03.009](https://doi.org/10.1016/j.bulcan.2017.03.009)]
 - 15 **European Association for the Study of the Liver**; European Organisation for research and Treatment of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol* 2012; **56**: 908-943 [PMID: [22424438](https://pubmed.ncbi.nlm.nih.gov/22424438/) DOI: [10.1016/j.jhep.2011.12.001](https://doi.org/10.1016/j.jhep.2011.12.001)]
 - 16 **Jaeck D**, Oussoultzoglou E, Rosso E, Greget M, Weber JC, Bachellier P. A two-stage hepatectomy procedure combined with portal vein embolization to achieve curative resection for initially unresectable multiple and bilobar colorectal liver metastases. *Ann Surg* 2004; **240**: 1037-49; discussion 1049 [PMID: [15570209](https://pubmed.ncbi.nlm.nih.gov/15570209/) DOI: [10.1097/01.sla.0000145965.86383.89](https://doi.org/10.1097/01.sla.0000145965.86383.89)]
 - 17 **Isfordink CJ**, Samim M, Braat MNGJA, Almalki AM, Hagendoorn J, Borel Rinkes IHM, Molenaar IQ. Portal vein ligation versus portal vein embolization for induction of hypertrophy of the future liver remnant: A systematic review and meta-analysis. *Surg Oncol* 2017; **26**: 257-267 [PMID: [28807245](https://pubmed.ncbi.nlm.nih.gov/28807245/) DOI: [10.1016/j.suronc.2017.05.001](https://doi.org/10.1016/j.suronc.2017.05.001)]
 - 18 **Schnitzbauer AA**, Lang SA, Goessmann H, Nadalin S, Baumgart J, Farkas SA, Fichtner-Feigl S, Lorf T, Goralczyk A, Hörbelt R, Kroemer A, Loss M, Rümmele P, Scherer MN, Padberg W, Königsrainer A, Lang H, Obed A, Schlitt HJ. Right portal vein ligation combined with in situ splitting induces rapid left lateral liver lobe hypertrophy enabling 2-staged extended right hepatic resection in small-for-size settings. *Ann Surg* 2012; **255**: 405-414 [PMID: [22330038](https://pubmed.ncbi.nlm.nih.gov/22330038/) DOI: [10.1097/SLA.0b013e31824856f5](https://doi.org/10.1097/SLA.0b013e31824856f5)]
 - 19 **Popescu GA**, Alexandrescu ST, Grigorie RT, Stoica L, Apavaloie CA, Hrehoreț D. GOOD TO KNOW: The ALPPS Procedure - Embracing a New Technique. *Chirurgia (Bucur)* 2017; **112**: 332-341 [PMID: [28675369](https://pubmed.ncbi.nlm.nih.gov/28675369/) DOI: [10.21614/chirurgia.112.3.332](https://doi.org/10.21614/chirurgia.112.3.332)]
 - 20 **Sandström P**, Røskov BI, Sparrelid E, Larsen PN, Larsson AL, Lindell G, Schultz NA, Bjørneth BA, Isaksson B, Rizell M, Björnsson B. ALPPS Improves Resectability Compared With Conventional Two-stage Hepatectomy in Patients With Advanced Colorectal Liver Metastasis: Results From a Scandinavian Multicenter Randomized Controlled Trial (LIGRO Trial). *Ann Surg* 2018; **267**: 833-840 [PMID: [28902669](https://pubmed.ncbi.nlm.nih.gov/28902669/) DOI: [10.1097/SLA.0000000000002511](https://doi.org/10.1097/SLA.0000000000002511)]
 - 21 **Eshmuminov D**, Raptis DA, Linecker M, Wirsching A, Lesurtel M, Clavien PA. Meta-analysis of associating liver partition with portal vein ligation and portal vein occlusion for two-stage hepatectomy. *Br J Surg* 2016; **103**: 1768-1782 [PMID: [27633328](https://pubmed.ncbi.nlm.nih.gov/27633328/) DOI: [10.1002/bjs.10290](https://doi.org/10.1002/bjs.10290)]
 - 22 **Kudo M**, Finn RS, Qin S, Han KH, Ikeda K, Piscaglia F, Baron A, Park JW, Han G, Jassem J, Blanc JF, Vogel A, Komov D, Evans TRJ, Lopez C, Dutcus C, Guo M, Saito K, Kraljevic S, Tamai T, Ren M, Cheng AL. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. *Lancet* 2018; **391**: 1163-1173 [PMID: [29433850](https://pubmed.ncbi.nlm.nih.gov/29433850/) DOI: [10.1016/S0140-6736\(18\)30207-1](https://doi.org/10.1016/S0140-6736(18)30207-1)]
 - 23 **Finn RS**, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Kudo M, Breder V, Merle P, Kaseb AO, Li D, Verret W, Xu DZ, Hernandez S, Liu J, Huang C, Mulla S, Wang Y, Lim HY, Zhu AX, Cheng AL; IMbrave150 Investigators. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med* 2020; **382**: 1894-1905 [PMID: [32402160](https://pubmed.ncbi.nlm.nih.gov/32402160/) DOI: [10.1056/NEJMoa1915745](https://doi.org/10.1056/NEJMoa1915745)]
 - 24 **Ren Z**, Fan J, Xu J, Bai Y, Xu A, Cang S, Du C, Liu B, Li Q, Lu Y, Chen Y, Shao G, Guo Y, Chen Z, Yang Y, Chen M, Wang Y, Zhou H. LBA2 Sintilimab plus bevacizumab biosimilar vs sorafenib as first-line treatment for advanced hepatocellular carcinoma (ORIENT-32)2. *Ann Oncol* 2020; **31** Suppl 6: S1287 [DOI: [10.1016/j.annonc.2020.10.134](https://doi.org/10.1016/j.annonc.2020.10.134)]
 - 25 **Zhu XD**, Huang C, Shen YH, Xu B, Ge NL, Ji Y, Qu XD, Chen L, Chen Y, Li ML, Zhu JJ, Tang ZY, Zhou J, Fan J, Sun HC. Hepatectomy After Conversion Therapy Using Tyrosine Kinase Inhibitors Plus Anti-PD-1 Antibody Therapy for Patients with Unresectable Hepatocellular Carcinoma. *Ann Surg Oncol* 2023; **30**: 2782-2790 [PMID: [36178565](https://pubmed.ncbi.nlm.nih.gov/36178565/) DOI: [10.1245/s10434-022-12530-z](https://doi.org/10.1245/s10434-022-12530-z)]
 - 26 **Zhu XD**, Huang C, Shen YH, Ji Y, Ge NL, Qu XD, Chen L, Shi WK, Li ML, Zhu JJ, Tan CJ, Tang ZY, Zhou J, Fan J, Sun HC. Downstaging and Resection of Initially Unresectable Hepatocellular Carcinoma with Tyrosine Kinase Inhibitor and Anti-PD-1 Antibody Combinations. *Liver Cancer* 2021; **10**: 320-329 [PMID: [34414120](https://pubmed.ncbi.nlm.nih.gov/34414120/) DOI: [10.1159/000514313](https://doi.org/10.1159/000514313)]
 - 27 **Kokudo N**, Takemura N, Hasegawa K, Takayama T, Kubo S, Shimada M, Nagano H, Hatano E, Izumi N, Kaneko S, Kudo M, Iijima H, Genda T, Tateishi R, Torimura T, Igaki H, Kobayashi S, Sakurai H, Murakami T, Watadani T, Matsuyama Y. Clinical practice guidelines for hepatocellular carcinoma: The Japan Society of Hepatology 2017 (4th JSH-HCC guidelines) 2019 update. *Hepatol Res* 2019; **49**: 1109-1113 [PMID: [31336394](https://pubmed.ncbi.nlm.nih.gov/31336394/) DOI: [10.1111/hepr.13411](https://doi.org/10.1111/hepr.13411)]
 - 28 **Shi M**, Li Q, He M, Guo R. 9810 Hepatic arterial infusion chemotherapy (HAIC) with oxaliplatin, fluorouracil, and leucovorin (FOLFOX) vs transarterial chemoembolization (TACE) for unresectable hepatocellular carcinoma (HCC): A randomised phase III trial. *Ann Oncol* 2020; **31**: S688
 - 29 **Luo L**, Xiao Y, Zhu G, Huang A, Song S, Wang T, Ge X, Xie J, Deng W, Hu Z, Wen W, Mei H, Wan R, Shan R. Hepatic arterial infusion chemotherapy combined with PD-1 inhibitors and tyrosine kinase inhibitors for unresectable hepatocellular carcinoma: A tertiary medical center experience. *Front Oncol* 2022; **12**: 1004652 [PMID: [36237309](https://pubmed.ncbi.nlm.nih.gov/36237309/) DOI: [10.3389/fonc.2022.1004652](https://doi.org/10.3389/fonc.2022.1004652)]
 - 30 **Zhang J**, Zhang X, Mu H, Yu G, Xing W, Wang L, Zhang T. Surgical Conversion for Initially Unresectable Locally Advanced Hepatocellular Carcinoma Using a Triple Combination of Angiogenesis Inhibitors, Anti-PD-1 Antibodies, and Hepatic Arterial Infusion Chemotherapy: A Retrospective Study. *Front Oncol* 2021; **11**: 729764 [PMID: [34868921](https://pubmed.ncbi.nlm.nih.gov/34868921/) DOI: [10.3389/fonc.2021.729764](https://doi.org/10.3389/fonc.2021.729764)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

