Conversion resection for patients with hepatocellular carcinoma and inferior vena cava tumor thrombus: a consecutive case series

Xiaoyun Zhang[1,2,3], Wei Peng[1,2], Chuan Li[1,2], Wusheng Lu[1], Zhiping Li[4], Jiayin Yang[1,2], Tianfu Wen[1,2]

[1]Department of Liver Surgery and Liver Transplantation Center, West China Hospital of Sichuan University, Chengdu, Sichuan 610041, China;
[2]Laboratory of Liver Transplantation, Frontiers Science Center for Disease-Related Molecular Network, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China;
[3]Laboratory of Pathology, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China;
[4]Department of Radiation Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China.

To the Editor: The incidence of hepatocellular carcinoma (HCC) with inferior vena cava tumor thrombus (IVCTT) is approximately 1.4%.[1] Owing to direct cancer cell dissemination into the systemic circulation, HCC-IVCTT is frequently associated with synchronous and metachronous extrahepatic metastasis. Without treatment, the median survival time is only 3 months for patients with HCC-IVCTT.

Systemic therapy and transcatheter arterial chemoembolization (TACE) are the options recommended by the Chinese treatment guidelines for patients with HCCIVCTT.[2] Tyrosine kinase inhibitors, such as lenvatinib, have been approved as first-line systemic therapies for advanced HCC.[3] In addition, radiation therapy (RT) sheds some light on the treatment of HCC with portal vein tumor thrombus, as it provides significantly better postoperative survival outcomes.[4] However, there are few scientific trials to support the effectiveness of combining TACE, lenvatinib and RT for the treatment of HCC-IVCTT.

Here, we present a case series of patients with initially advanced HCC-IVCTT who received conversion therapy with lenvatinib, TACE, and RT followed by R0 resection.

Strategy of conversion therapy: (1) TACE. TACE was performed through the femoral artery with the Seldinger technique with local anesthesia. After arteriography of the celiac trunk and superior mesenteric artery to visualize the arterial vascularization of the liver, body surface-dependent doses of the chemotherapeutic agents 5-fluorouracil (800–1000 mg) and epirubicin-adriamycin (30–40 mg) were injected. Subsequently, lipiodol (Lipiodol Ultra-Fluide; Andre Guerbet Laboratories, 22 avenue des Nations, Building Rimbaud, 93420 Villepinte, France) and polyvinyl alcohol foam embolization particles (Cook, Bloomington, IN, USA, 100–500 μm in diameter) were injected as selectively as possible into the hepatic segmental artery at the target tumor location. The embolization agent doses ranged from 5 to 30 mL and were determined based on the tumor location, size, and number.[5] (2) RT. Contrast-enhanced computed tomography (CT) scans were performed for radiotherapy planning with immobilization devices. A scan thickness of 3 mm was used. All patients received radiotherapy with a 6 MV linear accelerator using image-guided radiotherapy (40–60 Gy/5 fraction). The gross tumor volume of the tumor and IVCTT was determined by a CT scan that showed the position and size of the tumor and IVCTT. The adjacent tumor thrombus area was described as the clinical target volume (CTV). The planned target volume denoted the CTV and 0 to 4 mm margins for geometric uncertainties. The timing of radiotherapy was determined according to the patient's status and the physician's judgment.[6] (3) Hepatectomy. All procedures were performed by a senior surgeon (Professor T.F. Wen), who had >20 years of experience with living donor liver transplantation. In principle, hemihepatectomy or a more extended hepatectomy was performed to remove the involved main hepatic vein. Transection of the Glissonean pedicle and hepatic parenchyma preceded the removal of the IVCTT. Under the complete occlusion of hepatic vascular inflow, the IVC was clamped infrahepatically and suprahepatically. Total hepatic vascular exclusion (THVE) usually was required for only approximately 20 min. The IVC was resected partially if direct invasion was suspected and reconstructed if severe stenosis was anticipated when it was closed primarily.

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Correspondence to: Prof. Tianfu Wen, Department of Liver Surgery and Liver Transplantation Center, West China Hospital of Sichuan University, Chengdu, Sichuan 610041, China
E-Mail: wentianfu@scu.edu.cn

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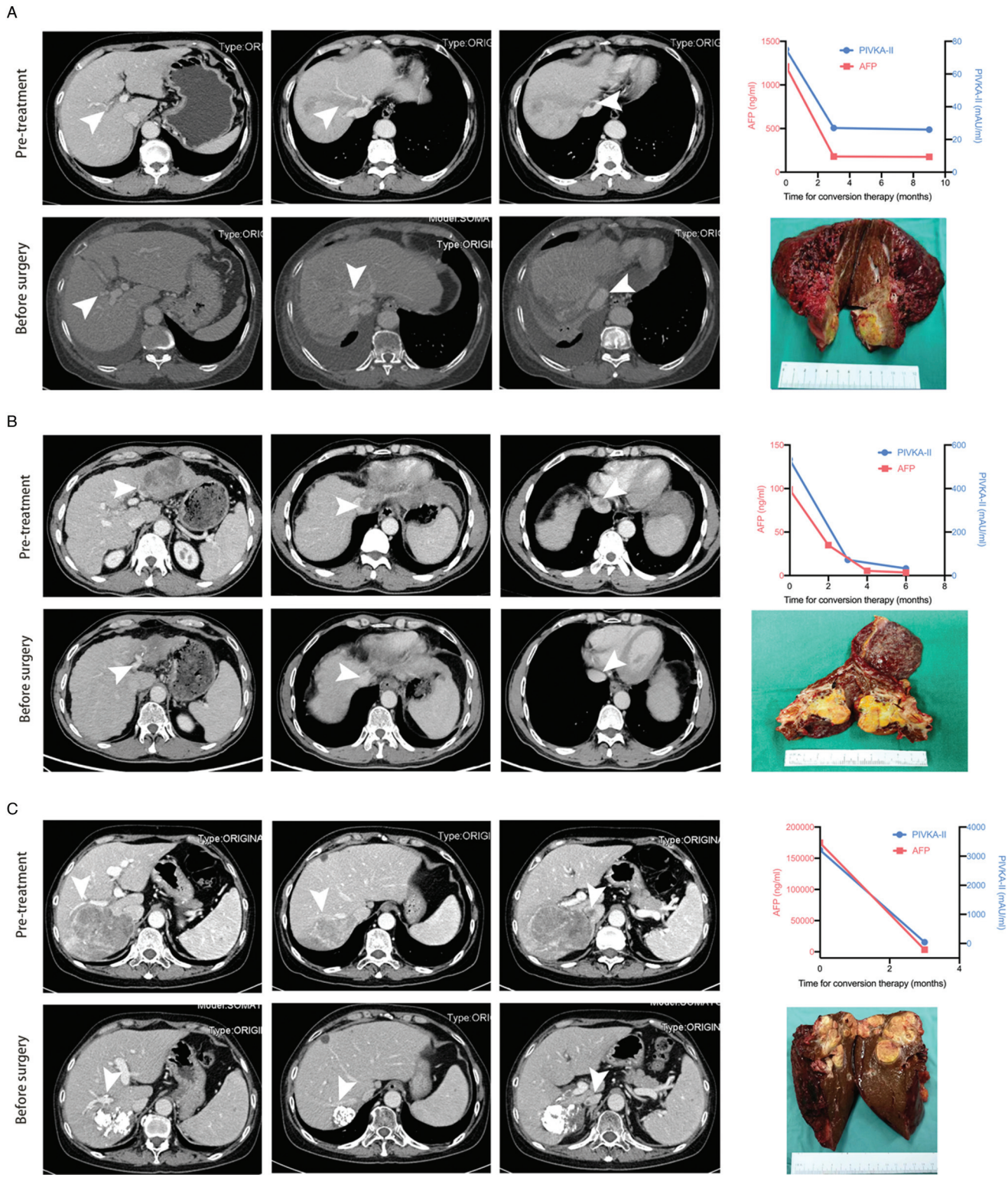

Figure 1: Conversion resection for patients with HCC and IVCTT. The imaging changes, the trend of tumor markers and postoperative specimens. (A) case 1; (B) case 2; and (C) case 3. HCC: Hepatocellular carcinoma; IVCTT: Inferior vena cava tumor thrombus. AFP: Alpha-fetoprotein; PIVKA: Protein induced by vitamin K absence.

Case 1 was a 64-year-old female who was diagnosed with HCC-IVCTT and portal vein tumor thrombus, PVTT (Vp2). After conversion therapy with TACE (1 time), lenvatinib (8 mg), and RT (40 Gy) for 266 days, the tumor diameter decreased from 5.9 to 4 cm, the alpha-fetoprotein (AFP) level decreased from 1210 to 175 ng/mL, and the protein induced by vitamin K absence-II (PIVKA-II) level decreased from 75 to 26 mAU/mL [Figure 1A]. More intriguingly, the IVCTT in case 1 vanished, and the patient achieved a complete response according to the modified

Response Evaluation Criteria in Solid Tumors (mRECIST). Finally, the patient underwent major resection and was spared from the usage of THVE because of the disappearance of the IVCTT.

Case 2 was a 48-year-old men who was diagnosed with HCC-IVCTT and PVTT (Vp3). After conversion therapy with TACE (1 time), lenvatinib (8 mg), and RT (48 Gy) for 149 days, the tumor diameter decreased from 7.6 to 4.8 cm, AFP level decreased from 99 to 3.52 ng/mL, and PIVKA-II level decreased from 534 to 33 mAU/mL. The IVCTT also vanished, and the patient achieved a partial response (PR) according to mRECIST [Figure 1B]. Finally, the patient also underwent major resection and was spared from the usage of THVE because of the disappearance of the IVCTT.

Case 3 was a 56-year-old woman who was diagnosed with HCC-IVCTT. After conversion therapy with TACE (1 time), lenvatinib (8 mg), and RT (43 Gy) for 98 days, the tumor diameter decreased from 8.9 to 6 cm, the AFP level decreased from 1,74,903 to 164 ng/mL, and the PIVKA-II level decreased from 3216 to 46 mAU/mL. The IVCTT shrank dramatically, and the patient achieved a PR according to mRECIST [Figure 1C]. Finally, the patient also underwent major resection and received shortened THVE (15 min) because of the shrinkage of the IVCTT.

The intraoperative bleeding was controllable for all three patients, and only case 3 required blood transfusion. No posthepatectomy liver failure was observed. Only case 1 experienced serious postoperative complications. Pleural effusion developed 2 weeks after liver resection, necessitating drainage. There was no recurrence or extrahepatic metastases in any of these three patients as of April 30, 2021. The overall survival time was from 4 to 16.4 months after surgery and 7.3 to 25.2 months after conversion therapy.

The treatment guidelines classified patients with HCC-IVCTT as advanced-stage and recommended systemic therapy and TACE as the primary treatment options. A recent Japanese nationwide survey showed that liver resection was associated with improved prognosis in selected patients.[1] Given the inordinate risk of recurrence as well as postoperative morbidity due to the complexity of THVE,[7] resection should be performed only for selected patients who can benefit sufficiently from the invasive procedure.

Conversion therapy before surgical resection can reduce the risk of perioperative complications and mortality. The 90-day mortality rate following resection of HCC-IVCTT is as high as 9.9%, which may be related to the use of THVE.[1] THVE is technically complicated and may cause liver failure or multiple organ dysfunction due to ischemia-reperfusion injury, circulatory instability and kidney and splanchnic venous congestion. However, two patients in our study avoided the use of THVE because of the disappearance of the IVCTT after conversion therapy, and the duration of THVE for another patient was shortened due to the shrinkage of the IVCTT. Thus, all patients had short postoperative hospital stays, and none experienced serious morbidity.

Conversion therapy aims to achieve tumor downstaging and provides patients with initially unresectable or borderline resectable malignancies a chance to receive curative resection. It is also a screening process for potential resection. In our study, these three HCC-IVCTT patients responded well to conversion therapy, and they also achieved good long-term survival after surgical resection. Therefore, response to conversion therapy may represent a selection criterion for HCC-IVCTT for surgical treatment.

Our research revealed a novel treatment method for patients with HCC-IVCTT. The patients achieved R0 resection after successful conversion treatment and had an excellent short- and long-term prognosis. The results show that conversion therapy is safe and feasible. Given the limitations and retrospective nature of this study, further prospective studies are needed to evaluate the long-term outcome of conversion resection for patients with HCC-IVCTT.

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Conflicts of interest

None.

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