# The Best Management of Portal Neoplastic Thrombosis in Hepatocellular Carcinoma

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**Abstract:** Hepatocellular carcinoma (HCC) is the fifth commonest cancer worldwide. Vascular invasion of the portal vein is one of the most important prognostic factors for survival in HCC patients and the prognosis is generally poor. The optimal treatment for patients with HCC and portal vein tumour thrombus (PVTT) remains controversial. Although many therapeutic options have been proposed, surgical resection is the only hope of cure for such patients.

We present the case of a 74-year-old man diagnosed with a single HCC nodule with portal thrombosis in the right hepatic lobe in the setting of HCV-related liver cirrhosis. After a first approach with a loco-regional treatment not tolerated by the patient, a right hepatectomy proved the best option. One year later the patient is still free from disease.

**Keywords:** Hepatocellular carcinoma, Portal vein thrombosis, Liver resection.

## INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth common cancer worldwide and the third cause of cancer-related death [1]. Portal vein tumour thrombosis (PVTT) is one of the principal factors influencing the prognosis of HCC as it is linked to an increased risk of intrahepatic and systemic metastases and shorter survival [2, 3]. PVTT is found in about 40-90% of patients at the first diagnosis of HCC [4].

Cheng et al. divided PVTT into four types based on tumour site and extent: the segmental or sectoral branches of the portal vein (type I), the right/left portal vein (type II), the main portal vein trunk (type III), or the superior mesenteric vein (type IV) [5].

The prognosis of patients with PVTT is generally poor with a median survival of 2.7-4 months in untreated cases [6]. PVTT remains one of the major contraindications to liver transplantation in patients with HCC due to the scarcity of organs and the high rate of tumour recurrence. Hepatic resection represents the only therapeutic alternative in these patients [7]. However, there is still no universal consensus on the best treatment for HCC with PVTT.

We describe a patient with HCV-related HCC complicated by PVTT successfully treated by right hepatectomy and right portal thrombectomy.

## CASE REPORT

A 74-year-old man was found to have hepatocellular carcinoma (HCC) with PVTT ten years after being diagnosed with liver cirrhosis due to hepatitis C virus. A computed tomography (CT) scan in 2012 showed a 30 mm nodule of HCC in the subdiaphragmatic surface of the VIII hepatic segment, invasion of the portal segmental branches in the right lobe, but no disease in lymph nodes or any other sites. Laboratory tests were as follows: alpha-fetoprotein (AFP) 2527 ng/ml (n.v. 0-10), aspartate aminotransferase (AST) 93 U/L (n.v. 0-40), alanine aminotransferase (ALT) 95 U/L (n.v. 0-40), gamma-glutamyl transpeptidase (GGT) 165 U/L (n.v. 8-61). The patient underwent percutaneous ethanol injection, but it was not tolerated and he asked to suspend the treatment.

Because of the limited extent of the cancer, hepatic resection was the surgical management of choice. Right hepatectomy was performed with total removal of the portal thrombosis. Macroscopic examination of the tumour on the cut specimen showed a 4.5 × 3.5 cm yellowish necrotic lesion with a fibrous capsule. Microscopically, haematoxylin and eosin staining demonstrated the tumour consisted of a solid trabecular structure with extensive coagulative and colliquative necrosis. In addition, histopathological examination showed Edmondson G3 HCC, macroscopic and microscopic intra and peritumoral vascular thrombosis, and neoplastic thrombosis in the portal vein and its main perihilar branches.

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The development of ascites complicated the postoperative course but resolved during a two-week hospital stay.

Three months after surgery, laboratory data showed a substantial normalization of hepatic markers: GOT 48 U/L, GPT 38 U/L, GGT 64 U/L, AFP 6.47 ng/ml. Abdominal ultrasound and thoraco-abdominal-pelvic CT evaluation showed no disease progression. On the basis of the radical surgical resection and the patient's good clinical status, no adjuvant chemotherapy was administered to prevent HCC recurrence. After 16 months of follow-up, the patient is still free from disease.

## DISCUSSION

The potentially radical treatment options for patients with HCC include surgical resection, liver transplantation and loco-regional therapies depending on tumour staging and liver function. Both the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Disease (AASLD) guidelines consider hepatic resection the treatment of choice for patients with preserved liver function and resectable HCC [8, 9]. However, only 10-30% of cases of HCC patients are eligible for surgical treatment at the time of diagnosis [10, 11].

PVTT is a negative prognostic factor for hepatocellular carcinoma because of the increased risk of intrahepatic and systemic metastases, and the progressive deterioration of liver function. According to a US study, the median survival of patients with HCC and PVTT was 2.7 months if left untreated vs. 24.2 months for those without PVTT [6].

The management of HCC with PVTT is complicated and controversial. According to EASL/AASLD guidelines, these patients are only candidates for non-curative treatment due to their poor prognosis and the post-operative risk of liver failure [8, 9]. PVTT represents one of the principal contraindications to liver transplantation due to the risk of early recurrence and the shortage of donors [12]. Several studies show a high response rate after loco-regional treatment in patients with HCC and PVTT, but their median survival time is <12 months [13, 14, 15, 16].

Transcatheter arterial chemoembolization (TACE) is an alternative therapeutic option in patients with advanced HCC [8, 9] but PVTT is usually considered a contraindication. TACE may be performed in these patients if their liver function is sufficiently preserved but the long-term outcomes of HCC with PVTT are generally poor [17, 18]. Georgiades et al. Showed a median survival of 9.9 months in patients with HCC and PVTT undergoing TACE [19]. Peng et al compared the outcomes of 603 patients with HCC and PVTT treated with TACE or liver resection. They found a better median survival for HCC and PVTT undergoing surgery compared to TACE (20 vs. 13.1 months), especially for types I or II PVTT [20].

Considering the limitations of non-surgical management, liver resection represents the only radical treatment in HCC patients with PVTT.

Recent studies have shown favorable long-term survival after surgical resection in well-selected cases of HCC with PVTT. Shi et al. evaluated outcomes after partial hepatectomy with or without thrombectomy in 406 patients with HCC and PVTT. Patients with types I and II portal vein thrombosis had better overall survival (OS) than those with types III and IV [21]. The same findings were reported in a recent study by Chen et al. where HCC with PTVV extending into the main portal venous trunk had a worse median overall survival worse than patients with types I or II PVTT (3-year OS was 5.7% and 22.7%, respectively) [22].

Our report describes the case of a 74-year-old man diagnosed with a single nodule of HCC with PVTT in the right hepatic lobe. According to Cheng et al.'s classification of portal vein thrombosis, our patient had type II PVTT [5]. Given the location and extent of PVTT, he underwent right hepatectomy with total removal of the portal thrombosis. Three months after surgery, there was a substantial normalization of hepatic markers and abdominal CT did not show any progression of disease. One year later, the patient is still disease-free.

The location and extent of vascular thrombosis are the principal factors influencing the choice of therapy and the prognosis of patients with HCC [2, 3]. Thrombi in extrahepatic locations or in the suprahepatic veins warrant different treatment strategies with proven efficacy and safety.

Two patients with HCC and PVTT extending into the right atrium followed at our centre obtained a survival benefit (OS > 18 months) with good clinical condition after systemic treatment alone (sorafenib and

antiangiogenetic drugs). The current patient received an antithrombotic prophylaxis (low molecular weight heparin) to prevent venous thrombosis as the protocol for general surgical procedures.

Patients with chronic liver disease have an impaired production of natural anticoagulant proteins, potentially increasing the risk of thrombotic events. However, the efficacy and safety of pharmacological prophylaxis in these patients is still a matter of debate. Villa et al. demonstrated the safety and the efficacy of a treatment with enoxaparin to reduce risk of portal vein thrombosis in a cohort of cirrhotic patients without HCC: patients treated with anticoagulants performed better in terms of liver function and OS [23].

To our knowledge, no guidelines are available on the use of venous thrombosis prophylaxis in cirrhotic patients. A study by Vivarelli et al. showed that anticoagulant prophylaxis is a safe option in patients without oesophageal varices undergoing hepatic resection. However, prophylaxis should be avoided in patients with a high risk of bleeding [24].

The present case demonstrates that liver resection is justified in selected patients with types I and II PVTT and offers a good long-term outcome for resectable HCC. By contrast, the benefit of surgery is less clear when the PVTT extends into the main portal vein or beyond. Thrombectomy has been proposed as a feasible treatment option if the tumour thrombus does not infiltrate the portal venous wall [21] but did not improve the survival rate for these patients compared with TACE. Further clinical studies are required.

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