An early decision of transjugular intrahepatic portosystemic shunt may be considered for non-malignant and non-cirrhotic portal vein thrombosis with ascites: a concise review of the theoretical possibility and practical difficulty

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Portal vein thrombosis (PVT) is rarely encountered in the absence of abdominal malignancy or cirrhosis [1]. At the acute stage of PVT, most patients present with abdominal pain of sudden onset or persistently progressing during a short-term period [1]. Provided that the thrombus is extended into the mesenteric venous arch, intestinal ischemia and infarction can occur [2]. Under the circumstances, appropriate treatments should be timely given. Otherwise, an emergency surgical resection of the bowel is inevitable for intestinal infarction. Once multiple organ dysfunction or failure is complicated in these patients, in-hospital mortality approaches approximately 50% [3]. In the absence of portal recanalization, cavernous collateral vessels develop around the obstructed segment of the portal vein [4]. In the stage of cavernous transformation of the portal vein (CTPV), the most common clinical presentation is variceal bleeding, which can often be tolerated because of well-preserved liver function. Ascites and biliary symptoms are also seen in a minority of patients.

Given the high rate of portal vein recanalization and the low incidence of major complications previously reported in several case series [5, 6], the current American Association for the Study of Liver Diseases (AASLD) practice guidelines recommend that anticoagulation therapy for at least 3 months should be initiated just after the diagnosis of acute PVT is established [7]. However, a prospective, multi-center, cohort study showed a relatively low recanalization rate of 38% in patients with acute PVT receiving the immediate use of anticoagulation [8]. More importantly, a significantly inverse correlation between portal vein recanalization and the presence of ascites in the study suggests that alternative therapeutic options should be actively explored. Additionally, the presence of ascites is closely associated with increased mortality in non-malignant and non-cirrhotic patients with PVT [9, 10]. The prognostic value of ascites is further validated by a recent study indicating that the presence of ascites at diagnosis of PVT is the only independent predictor of survival (hazard ratio (HR) = 5.1, p = 0.03), and the cumulative 5- and 10-year survival rates are significantly lower in patients with ascites than those without (83% and 42% vs. 95% and 87%) [11]. Our retrospective case series also demonstrated that the presence of ascites is an independent predictor of death in non-malignant

and non-cirrhotic patients with CTPV (HR = 10.729, p = 0.033) [12]. Taken together, the presence of ascites is considered a predictor for the failure to recanalize the thrombosed portal vein by anticoagulation and poor prognosis in non-malignant and non-cirrhotic patients with PVT. Thus, a more effective therapeutic modality for portal vein recanalization should be adopted in such patients.

Transjugular intrahepatic portosystemic shunt (TIPS) refers to the non-surgical creation of a portosystemic shunt by placing a stent between a hepatic vein and an intrahepatic portal vein branch through the hepatic parenchyma, thereby effectively decreasing the portosystemic gradient. Since the first report of its clinical use in 1988 [13, 14], TIPS has been widely applied for complications of portal hypertension, such as recurrent variceal bleeding uncontrolled by medical and/or endoscopic therapy and refractory ascites requiring large volume paracentesis [15, 16]. Recently, more and more studies have focused on the application of TIPS in management of portal vein thrombosis [17–24], because it provides a more direct route to access the thrombosed site of the portal vein and a more effective modality to recanalize the occluded segments by local fragmentation of the thrombus and aspiration thrombectomy. As compared with other interventional modalities, the major advantages of TIPS in the treatment of PVT are also obvious in that the TIPS-induced acceleration of portal blood flow may prevent thrombus extension downstream into the intrahepatic portal venous branch and reduce intestinal ischemia or infarction caused by thrombus extension upstream into the superior mesenteric vein [25]. However, it should be noted that the technical difficulty of TIPS insertion is gradually increased with the development and aggravation of PVT [20–22]. Accordingly, the TIPS success rate would be greatly reduced if an early decision of TIPS was not put into practice in the setting of PVT.

We hypothesize that TIPS insertions may be performed in non-malignant and non-cirrhotic patients with PVT and concomitant ascites as early as possible. It can increase the rate of portal vein recanalization and maintain the long-term portal venous patency, thereby improving the survival by means of avoiding a series of sequelae of PVT, such as intestinal ischemia and infarction caused by thrombus extension into mesenteric venous arches, complications of portal hypertension secondary to chronic portal vein occlusion, and liver dysfunction produced by the interruption of portal blood flow.

Ideally, a multi-center, randomized, controlled trial comparing the outcome of TIPS versus anticoagulation is optimal to test the above-mentioned hypothesis. However, if multiple centers participated in this trial, the TIPS success rate would vary depending on the operators' experience in each center. Accordingly, the trial could be limited to a few centers with extensive experience to avoid the potential bias.

Whether TIPS can improve the survival and replace the role of anticoagulation in the treatment of PVT in non-malignant and non-cirrhotic patients with ascites is the core of our hypothesis and the primary objective of the future trial. However, it should be noted that a long-term follow-up is required because of the relatively excellent outcome of non-malignant and non-cirrhotic PVT patients. The secondary objectives may be to compare the rate of portal venous recanalization and safety between patients receiving anticoagulation and those undergoing TIPS. Common complications include anticoagulant-induced bleeding or thrombocytopenia and hepatic capsule perforation that complicates the course of TIPS creation, etc. In addition, as for the patients with successful TIPS insertions, the investigators should prospectively collect the data regarding the post-operative change of liver architecture and the incidence of hepatic encephalopathy, considering that the diversion of portal blood flow may result in a short supply of nutrition into the liver and excessive accumulation of toxic intestinal substances into the brain [25]. As for the patients without portal vein recanalization, the evolution of PVT (i.e. degree and extension of thrombus) and the incidence of variceal bleeding and splenomegaly should also be recorded.

Because the treatment strategy and outcome of PVT are very different among the patients with and without malignancy and liver cirrhosis [26, 27], abdominal malignancy and liver cirrhosis should be strictly excluded from the future trial. Patients with contraindications to anticoagulation or TIPS should also be excluded (for example, congestive heart failure, uncontrolled systemic infection or sepsis, etc.). Given the rarity of PVT in the absence of malignancy or liver cirrhosis, a long enrollment span may be warranted for an adequate number of samples.

In spite of these potential difficulties, clinicians and investigators should be encouraged to reassess the role of anticoagulation for PVT, and the treatment strategy of PVT should be stratified by the presence of ascites.

Conflict of interest

The authors declare no conflict of interest.

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