BRIEF CLINICAL UPDATE

Management of Portal Vein Thrombosis in Cirrhotic Patients

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Cirrhosis is a widespread condition that causes significant morbidity and mortality worldwide. In 2017 global estimates included 112 million cases of compensated cirrhosis and 10.6 million cases of decompensated cirrhosis. Cirrhosis is caused by multiple etiologies, including: alcohol, fatty liver disease, hepatitis B and hepatitis C. Cirrhosis can lead to multiple life-threatening complications, and about 1.43 million died from cirrhosis in 2019.[1]

Cirrhosis leads to significant dysregulation of coagulation. Focus is often placed on increased bleeding risk, due to multiple factors including increased portal pressures, thrombocytopenia and platelet dysfunction, and diminished production of liver pro-coagulant factors. However, it is now understood that cirrhosis patients may have simultaneously hypercoagulability. The mechanism of hypercoagulability may be explained in part by increased levels of endothelial-derived von Willebrand factor as well as diminished production of liver-derived anticoagulant factors.[2] This may explain why some cirrhotic patients develop thrombotic complications, including portal and hepatic vein thromboses.

Portal vein thrombosis can involve partial or complete occlusion of the portal vein trunk. It is much more common in patients with cirrhosis than in the general population. Estimates of incidence and prevalence of portal vein thrombosis within the cirrhotic population varies widely. Some variance is due to differences in classification, ranging between 1.3%-9.8%. Prevalence of portal vein thrombosis in the general population is 0.7-1 out of 10,000.[3] It is usually diagnosed through imaging, including ultrasound, computed tomography, or magnetic resonance. It may be categorized by duration of presumed onset. Acute or recent portal vein thrombosis occurs within 6 months, and chronic portal vein thrombosis persisting beyond 6 months.[4]

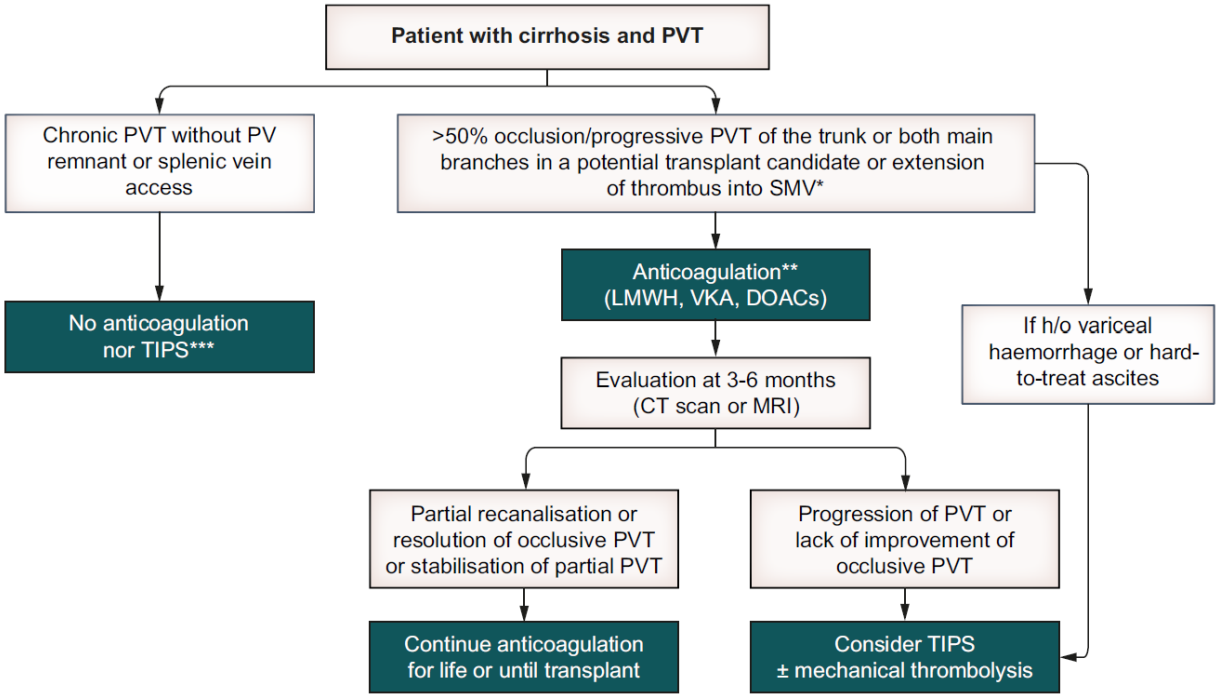
The presentation of portal vein thrombosis may vary from patient to patient. First, thrombosis can be categorized as minimally occlusive (obstructing <50% of original lumen), partially occlusive (obstructing >50% of the original lumen), or completely occlusive. It may also be described as having undergone cavernous transformation if the original portal vein is no longer seen and numerous tortuous collateral vessels have developed. Patients can also be symptomatic or asymptomatic; with symptoms including abdominal pain, fever, or dyspepsia.

Portal vein thrombosis in cirrhosis effect on mortality is unclear. There is strong correlation between presence of portal vein thrombosis and severe portal hypertension. However, the causal relationship is less obvious. It is not known whether portal vein thrombosis is merely a consequence and sequela of worsening cirrhosis, or whether it causes the disease to become more severe. Nery et al, prospectively followed 1243 patients with cirrhosis without portal vein thrombosis for a mean of 47 months. Portal veins were routinely assessed by ultrasound; along with other prognostic factors in cirrhosis such as levels of prothrombin, bilirubin, albumin, and creatinine and presence of ascites, hepatic encephalopathy, and variceal bleeding. The study concluded that although portal vein thrombosis is associated with severe liver disease, there was no evidence that development of portal vein thrombosis causes progression of disease.[5] Another trial was contradictory. A randomized controlled trial done by Villa et al examined 70 patients with cirrhosis and patent portal veins. Patients who were randomized to receive prophylactic enoxaparin or no treatment. They reported a statistically significant decrease in incidence of portal vein thrombosis in the treatment group. They also reported a statistically significant decrease in progression to decompensation as well as in mortality in the treatment group, without significant increase in bleeding.[6] Whether these outcomes indicate improved prognosis specifically from prevention of portal vein thrombosis or from the general treatment of the hypercoagulable state associated with cirrhosis is not certain. The meaning and implication of portal vein thrombosis in cirrhosis is still not well-understood.

If portal vein thrombosis is complicated by intestinal ischemia, urgent treatment is warranted. However, intestinal ischemia tends to occur less often in patients with cirrhosis secondary to the presence of established porto-systemic collaterals. Given conflicting data surrounding portal vein thrombosis in cirrhosis, the decision to treat in the absence of intestinal ischemia is not straightforward. This decision should be evaluated on a case-by-case basis with consideration of multiple factors.

The possibility of future liver transplantation is a more compelling reasons to treat portal vein thrombosis. Having a patent portal vein at the time of liver transplant reduces the risk of the transplant surgery, as reconstruction of the portal vein complicates surgery. Large transplant database studies have shown more complications and decreased survival in patients with portal vein thrombosis at time of transplant surgery.[4] Trials investigating whether treatment of portal vein thrombosis prior

to transplant improves outcomes have not been published, and clear treatment guidelines have not been established. A treatment algorithm was developed by Senzolo M, et al.[7] (Figure 1 below.)



If decision is made to treat, there are a few different accepted treatment options. With medical therapies, most studies on treatment of portal vein thrombosis use either low molecular weight heparin (LMWH) or vitamin K antagonists (VKA). Given baseline hypercoagulability in cirrhosis and difficulty monitoring VKA levels, LMWH has usually been chosen as the treatment of choice. Direct oral anticoagulants (DOACs) can also be considered. However, many of the initial trials evaluating the efficacy and safety of DOACs excluded patients with cirrhosis. Therefore, there is extremely limited data on DOACs in patients with cirrhosis.

Interventional vascular procedures can also be considered as treatment for portal vein thrombosis. Pharmacological thrombolysis has been tried, with significant associated morbidity and mortality. Recanalization rates are similar to patients treated with medical anticoagulant therapies alone. Portal vein recanalization followed by TIPS (PVR-TIPS) has also been tried in patients with chronic portal vein thrombosis prior to liver transplant, with suggestion of improved post-transplant outcomes.

Conflicting data regarding the treatment of portal vein thrombosis in patients with cirrhosis still exists. Management decisions regarding portal vein thrombosis remain complex. Treatment needs to be individualized depending on multiple patient factors. These include their level of symptoms, overall severity of cirrhosis, and eligibility for liver transplantation. A multi-disciplinary approach involving several specialties may be warranted to determine the best treatment plan.

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