PORTAL VEIN THROMBOSIS

Thrombosis Canada
Thrombose Canada

OBJECTIVE:

To assist health care professionals in the management of portal vein thrombosis (PVT).

BACKGROUND:

The portal vein is one of the splanchnic veins, formed at the confluence of the superior mesenteric and splenic veins and carries blood from the gastrointestinal tract to the liver. PVT can occur in the main portal vein, in the left or right portal branches, and/or in the smaller, intrahepatic branches. PVT is an uncommon site of thrombosis, estimated to occur in 4 per 100,000 individuals. Risk factors include liver cirrhosis, abdominal surgery, abdominal malignancy, thrombophilia, myeloproliferative neoplasms (MPN), hormone use, local inflammation (such as pancreatitis), inflammatory bowel disease, or intra-abdominal infections.

Most patients with PVT are asymptomatic and the diagnosis is made on abdominal imaging for other reasons. The most common clinical manifestation of PVT is abdominal pain.

DIAGNOSIS OF PORTAL VEIN THROMBOSIS:

Abdominal imaging with computed tomography (CT) demonstrating a non-enhancing luminal filling defect in the portal vein or abdominal ultrasound demonstrating echogenic thrombus with absent Doppler flow in the portal vein is consistent with a diagnosis of PVT. Detection of incidental PVT is increasingly made in asymptomatic individuals who undergo abdominal imaging for another indication.

MANAGEMENT OF PORTAL VEIN THROMBOSIS:

The management of PVT is based on limited observational studies and expert opinion. Given the moderate/weak level of evidence, the risks and benefits of anticoagulation need to be carefully weighed considering individual patient circumstances.

- Anticoagulation is recommended for patients with symptomatic or extensive PVT and in those with extension of the PVT into the superior mesenteric vein in order to prevent portal hypertension and bowel ischemia/infarction. This is based on observational studies suggesting that patients with PVT treated with anticoagulation have a low (~2%) rate of bowel ischemia and decreased thrombus progression and extension. Recurrent thrombosis is common (~5%) in the absence of anticoagulation or if anticoagulants are discontinued.
- Patients with PVT who are potential candidates for liver transplantation should also be considered for anticoagulation since their prognosis may be improved as a result.
- The role of anticoagulation in patients with asymptomatic PVT is controversial. In patients with underlying malignancy, incidentally detected thrombosis appears to carry a similar prognosis to symptomatic thrombosis and is managed with anticoagulation. In a registry of patients with splanchnic vein thrombosis (majority having PVT and receiving anticoagulation) including

patients with liver cirrhosis and cancer, outcomes were similar between the symptomatic and asymptomatic patients.

- The role of anticoagulation in patients with portal vein thrombosis and cavernous transformation is very unclear. Cavernous transformation suggests a chronic thrombosis which is unlikely to extend or induce bowel ischemia; hence, the risks of anticoagulation may outweigh any benefits.
- Anticoagulant options in the acute phase include unfractionated heparin and low molecular weight heparin (LMWH). Heparin may be used if there is concern for imminent bleeding, with the option of discontinuing heparin in the presence of bleeding. LMWH is recommended in patients with PVT and cancer and may be preferred in patients with liver disease or thrombocytopenia. LMWH, given at less than full therapeutic doses, may be an option for patients with localized PVT and patients at high bleeding risk.
    - Data regarding the direct oral anticoagulants (DOACs) is limited to mostly case reports and case series describing their use. One small randomized clinical trial assessed rivaroxaban 10 mg twice daily versus warfarin predominately in patients with cirrhosis who had a surgically-provoked portal vein thrombus. Rivaroxaban use resulted in higher recanalization rates and lower rates of mortality and cirrhotic decompensations. Extrapolation of these results to other populations should be done with caution.
    - Long-term anticoagulation may be achieved with LMWH or warfarin (target INR 2.0-3.0). If warfarin is used, the pre-warfarin INR should be normal and patients should be carefully monitored.
- Active bleeding is an absolute contraindication to anticoagulation. This may occur in patients with bleeding from esophageal varices or tumour site bleeding. Anticoagulation of PVT is associated with increased rates of gastrointestinal bleeding. Attempts to decrease bleeding risk, including endoscopy and variceal banding in patients with liver disease or surgical resection of a known gastrointestinal cancer, should be completed prior to anticoagulation if feasible.
- Previous bleeding or the presence of esophageal varices alone should not be considered a contraindication to anticoagulation.
- Bleeding risk should be assessed against the potential benefits of anticoagulation. Bleeding is more common in patients with cirrhosis and in those with platelet counts of $<50 \times 10^9$/L. An assessment of the presence of ongoing risk factors for thrombosis can assist in determining optimal duration of anticoagulation.
- The role of thrombophilia testing in patients presenting with no clear etiology for PVT is uncertain. [See **Clinical Guides: Thrombophilia: Antiphospholipid Antibody Syndrome; Thrombophilia: Deficiencies in Protein C, Protein S, and Antithrombin; Thrombophilia: Factor V Leiden and Prothrombin Gene Mutation; Thrombophilia: Homocysteinemia and Methylene Tetrahydrofolate Reductase].**
- The role of testing for underlying MPN in patients presenting with no clear etiology for PVT has not been systematically evaluated. However, up to 30% of patients with non-cirrhotic, non-malignant PVT have an underlying MPN. In patients with PVT with no clear etiology and without characteristic hematological features of MPN, 15% may harbour the JAK2 V617F mutation. This suggests that testing for common mutations in MPN, such as JAK2 V617F, may

have utility in this group of patients since it may affect frequency of follow-up, potentially with respect to duration of anticoagulation and follow-up and treatment of the MPN.

DURATION OF THERAPY:

- The duration of anticoagulation in patients with PVT is uncertain and is largely extrapolated from data on lower extremity deep vein thrombosis. Treatment duration is based on the estimated thrombosis and bleeding risks, as well as individual informed patient preference. PVT occurring in the context of a reversible risk factor should generally be treated for 3 months. Patients who have an unprovoked PVT or an ongoing risk factor should be treated for at least 3-6 months, with consideration for long-term therapy with periodic reassessment of bleeding risk.

TRANSJUGULAR INTRAHEPATIC SHUNT (TIPS):

In patients with liver cirrhosis, portal hypertension and PVT, portosystemic shunt has been used as a treatment option. In a small, retrospective study involving 52 patients, thrombosis burden improved the most in patients treated with TIPS when compared to anticoagulation or no treatment. Further studies are needed to compare effectiveness of anticoagulation and TIPS. However, this treatment option maybe considered in patients with significant portal hypertension.

OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES:

- Cancer and Thrombosis
- Deep Vein Thrombosis (DVT): Treatment
- Thrombophilia: Antiphospholipid Antibody Syndrome
- Thrombophilia: Deficiencies in Protein C, Protein S, and Antithrombin
- Thrombophilia: Factor V Leiden and Prothrombin Gene Mutation
- Thrombophilia: Homocysteinemia and Methylene Tetrahydrofolate Reductase
- Unfractionated Heparin and Low-Molecular-Weight Heparin and Fondaparinux
- Venous Thromboembolism: Duration of Treatment
- Warfarin

REFERENCES:

Amitrano L, et al. Safety and efficacy of anticoagulation therapy with low molecular weight heparin for portal vein thrombosis in patients with liver cirrhosis. J Clin Gastroenterol. 2010;44(6):448-451.

Dentali F, et al. Natural history of mesenteric venous thrombosis in patients treated with vitamin K antagonists: a multi-centre, retrospective cohort study. Thromb Haemost. 2009;102(3):501-504.

Hanafy AS, et al. Randomized controlled trial of rivaroxaban versus warfarin in the management of acute non-neoplastic portal vein thrombosis. Vascul Pharmacol. 2019;113:86-91. doi:10.1016/j.vph.2018.05.002.

Intagliata NM, et al. Diagnosis, development and treatment of portal vein thrombosis in patients with and without cirrhosis. Gastroenterology 2019;156(6):1582-1599.e1.

Jasper H, et al. Myeloproliferative neoplasms in Budd-Chiari syndrome and portal vein thrombosis: a meta-analysis. Blood 2012;120:4921-4928.

Kearon C, et al. Antithrombotic therapy for VTE Disease. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2)(Suppl):e419S-e494S.

Plessier A, et al. Acute portal vein thrombosis unrelated to cirrhosis: a prospective multicenter follow-up study. Hepatology 2010;51(1):210-218.

Rajani R, et al. The epidemiology and clinical features of portal vein thrombosis: a multicentre study. Aliment Pharmacol Ther. 2010;32(9):1154-1162.

Riva N, et al. Clinical history and antithrombotic treatment of incidentally detected splanchnic vein thrombosis: a multicentre, international prospective registry. Lancet Haematol. 2016;3(6):e267-e275.

Zhan C, et al. Comparison of Non-Tumoral Portal Vein Thrombosis Management in Cirrhotic patients: TIPS Versus Anticoagulation Versus No Treatment. J Clin Med 2021;10(11):2316.

Date of version: 14November2021

Please note that the information contained herein is not to be interpreted as an alternative to medical advice from your doctor or other professional healthcare provider. If you have any specific questions about any medical matter, you should consult your doctor or other professional healthcare providers, and as such you should never delay seeking medical advice, disregard medical advice or discontinue medical treatment because of the information contained herein.