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Short Communication

Splanchnic Venous Thrombosis in pancreatitis in non-cirrhotic patients with: Should we anticoagulate?

Esam Aboutaleb, Fatima Saleh, Mohammed Said Noor, Hemant Sheth

Ealing Hospital, London, UK

Abstract: Acute Splanchnic venous thrombosis complication of pancreatitis in non-cirrhotic patients is an uncommon scenario which carries significant morbidity and mortality. Should we anti-coagulate or not in such scenario? We will present evidences about management of such scenario from literature as well as current guidelines.
Keywords: Splanchnic, thrombosis, pancreatitis

INTRODUCTION

Acute Splanchnic venous thrombosis complication of pancreatitis in non-cirrhotic patients is an uncommon scenario which carries significant morbidity and mortality (Xu, W. *et al.,* 2015; & Ponziani, F. R. *et al.,* 2010). A debate remains regarding the decision on whether to anticoagulate these patients or not, and this review will highlight the current research aimed at demystifying this pertinent clinical question.

DISCUSSION

Splanchnic venous thrombosis happens in about 1-24% in patients diagnosed with acute pancreatitis (Nadkarni, N. A. *et al.,* 2013). About 17% of patients with acute pancreatitis develop pancreatic necrosis (Singh, V.K. *et al.,* 2011; & Van Santvoort, H. C. *et al.,* 2011). Among such 17% Splanchnic vein thrombosis happens in about half of them (Easler, J. *et al.,* 2014). Complications related to splanchnic venous thrombosis in contest of acute pancreatitis are rare and need further dedicated studies to evaluate. However, such complications carry risk of bowel infarction with significant risk of mortality (Xu, W. *et al.,* 2015; & Ponziani, F. R. *et al.,* 2010).

The mainstay of treatment in non-cirrhotic patients is supportive, while attempting to tackle the root cause of the thrombosis. Watchful waiting may accompany this, or an active approach may be undertaken: anti-coagulation. The aim of this is to prevent thrombus extension, while promoting recanalization of the existing thrombus (DeLeve, L.D. *et al.,* 2009).

The argument for anti-coagulation is that, in addition to a greater ability at hindering extension and encouraging recanalization, it will also therefore reduce the risk of portal hypertension and ischaemia or infarction and their sequelae (DeLeve, L.D. *et al.,* 2009). However, proponents of the least intrusive option point out the benign course of the splanchnic venous thrombosis in acute pancreatitis patients as well as considerable risks associated with anticoagulation, most obviously, the risk of bleeding, specifically intestinal or variceal. Heparin-induced thrombocytopenia (HIT), although this is more likely with unfractionated heparin which is not so widely-used nowadays, is also a possible complication (European Association for the Study of the Liver. 2016; & Hall, T.C. *et al.,* 2011). Harris and *et al.,* found that using anti coagulation in this cohort of patients is safe but without any significant difference in recanalization rates in

those with and without anti coagulation (Harris, S. *et al.,* 2013).

A 2009 multi-centre prospective study by Plessier *et al.,* supports the argument for anticoagulation in non-cirrhotic patients, given it is initiated in the early stages (within 30 days from date of diagnosis). This was based on a pool of 95 anticoagulated patients, of whom 39%, 80%, and 73% achieved recanalization of the portal, splenic, and superior mesenteric veins respectively, with recanalization ceasing beyond the sixth month of anticoagulant therapy. The risk of thrombus extension (0%), GI bleeding (9%), and intestinal infarction (2%). The overall mortality rate for the group being 2% (both patients of which died from causes unrelated to the thrombosis or anticoagulation). Overall, while anticoagulation promoted re-canalisation, it proved better at preventing extension and therefore infarction, if not spread to the mesenteric veins), with a considerably lower associated bleeding risk (Plessier, A. *et al.,* 2010).

A similar conclusion may be drawn from the retrospective study by Baril *et al.,*, which specifically examined the morbidity and mortality of patients with CT-proven PVT with pylephlebitis over a 3-year period. Of the 44 patients identified, 15 of them also had mesenteric vein thrombosis (Baril, N. *et al.,* 1996). Eighteen of the 44 patients had an underlying predisposition to thrombosis, due to clotting factor deficiency (6/18), malignancy (8/18), or AIDS (4/18). Of the 32 patients who were not anti-coagulated, 5 died, 3 of which were hypercoagulable, with the remaining 2 having normal clotting function. Of the 12 hypercoagulable patients who were not anticoagulated, 2 developed necrotic bowel. In contrast, of the 12 anticoagulated patients, who included 6 hypercoagulable patients, none developed bowel infarction or died.

A further case review of 100 relevant case reports since 1971 by Kanellopoulou *et al.,* in 2010, in which 81 had acute, and 19 had chronic, pylephlebitis, also demonstrated improved outcomes in those 35 patients treated with an anticoagulant, rather than with antibiotics alone. Comparative rates of complete recanalization (25.7% vs 14.8% (p>0.05)), no recanalization (5.7% vs 22.2% (p<0.05)), and death (5.7% vs 22.2% (p<0.01)), were more favourable in the former group (Kanellopoulou, T. *et al.,* 2010).

The following year, a systematic review of the available English-language literature on non-cirrhotic acute PVT cases over a 60-year period from 1950 was undertaken by Hall *et al.,*, which compounded the view that anticoagulation is preferable. Twenty-nine articles meeting the inclusion criteria comprised a total data set of 315 patients, of which 228 were anticoagulated, 12 were conservatively managed, and 71 were

thrombolysed. Early anticoagulation showed complete re-canalisation in 38% of cases and only partial re-canalisation in 14%, whereas in the conservatively managed group, re-canalisation was only seen in up to 16.7% (2/12) of patients, and was associated with minimal thrombus extension or a self-limiting cause. Thrombolysis, on the other hand, was associated with major complications in up to 60% of cases. The team concluded that rates of re-canalisation with anticoagulation were favourable, without a burdensome increase in morbidity (Hall, T. C. *et al.,* 2011).

CURRENT GUIDANCE

In 2009, De Leve *et al.,* published guidelines approved by the American Association for the Study of Liver Diseases (AASLD) recommending anticoagulation for at least 3 months to all patients with acute PVT. This should be LMWH in the first instance, followed by switching to oral preparations. In those without any contraindication, and extension of the thrombus into the mesenteric veins, long-term anticoagulation should also be considered. These recommendations were based on clinical trials & general agreement of benefit (DeLeve, L. D. *et al.,* 2009).

In 2012, the British Journal of Haematology published guidelines on the investigation and management of venous thrombosis at unusual sites on behalf of the British Committee for Standards in Haematology based on the available evidence. They recommended that while anticoagulation poses a high risk of bleeding in cirrhotic patients with acute or chronic PVT, one which usually outweighs the benefit, whether to anticoagulate remains a case-to-case decision to be made. On the other hand, in agreement with AASLD standards, anticoagulation therapy is recommended in cases of acute PVT without cirrhosis, with no significant evidence to suggest the appropriate time-course (Scully, M. *et al.,* 2012).

In line with this, the European Association for the Study of the Liver 2015, published a number of clinical guidelines regarding PVT. They also advise commencement of LMWH in those with no major contraindications to anticoagulation, with oral VKA being used in the long-term (target INR 2-3), but specify the duration, being at least 6 months. In order to minimise risk and complications from anticoagulation, it also suggested screening for HIT, as well as monitoring anti-Xa activity in pregnant women, patients with reduced renal function, and overweight patients, with a target of 0.5-0.8 IU/ml (European Association for the Study of the Liver. 2016).

CONCLUSION

Incidence of PVT in non-cirrhotic and normal clotting patients is rare and in need of more randomised controlled trials with large enough sample sizes from

which to make valid arguments, and thus shape future clinical practice with more definitiveness when deciding on treatment for these patients. We think decision to anti coagulate should be made case by case taking in considerations bleeding risk, functional status and patients' desires.

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