



Thrombosis after transjugular intrahepatic portosystemic shunt: an ominous sign?

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Transjugular intrahepatic portosystemic shunt (TIPS) is increasingly used for the treatment of complications of portal hypertension, especially variceal bleeding and ascites refractory to conventional therapy (1,2). Development of thrombosis after TIPS placement is an uncommon complication, which was reported to occur in only 3% to 10% of patients when bare stents were used in several large series (3-6). Thrombosis usually develops acutely either at the time the stent is being deployed or within several days of TIPS placement (2,6). The cause of the thrombosis may be leakage of bile into the shunt, hypercoagulable syndromes, stent mispositioning, suboptimal stent sites, or inadequate coverage of the TIPS tract with sufficient stent (2,7-12). The direct result of thrombosis development is occlusion of the TIPS device, blocking flow in the portal vein and directly resulting in the recurrence of the complication of portal hypertension in addition to potentially causing bowel ischemia as a result of venous congestion in cases of thrombosis extending into the splenic and mesenteric veins (7). Thrombosis can be identified by Doppler ultrasound and patency can be re-established by repeat catheterization (2,7). The development of acute thrombosis also can be effectively prevented by prophylaxis anticoagulation or using e-PTFE-coated stents (13,14). One randomized controlled trial (RCT) showed that use of phenprocoumon (an anticoagulant) was associated with a lower rate of complete occlusion within the first three months following TIPS placement (13). In the RCT by

Bureau (14), no early thrombosis was observed in the e-PTFE covered stent-graft group (n=39) as compared with three cases in the covered stent-graft group (n=41). A recent RCT also showed that early thromboses were less frequent in patients receiving covered stent TIPS compared with those receiving bare stents (10/67 in bare stent group *vs.* 3/63 in the covered stent group) (15).

In a recent issue of *Clinical and Applied Thrombosis/Hemostasis*, Yue-Meng *et al.* (16) reported their experience on thrombosis in a cohort of cirrhotic patients undergoing elective TIPS. In this study, the prevalence of thrombosis in cirrhotic patients undergoing elective TIPS was 26.7% (27/101), despite using prophylaxis anticoagulation (low-molecular-weight heparin then shifted to aspirin or clopidogrel) and ePTFE-covered stent. This value is unexpectedly higher than that reported in the literatures (3-6). Even though the authors declared this rate was similar to those without TIPS and compared their results with those without TIPS from beginning to end in their paper, it should be noted that development of portal vein thrombosis (PVT) in the presence or absence of TIPS was two distinct situations. In cirrhotic patients without TIPS, a prior decrease in portal blood flow velocity, in combination with a hypercoagulable state caused by cirrhosis and/or concomitant thrombophilic disorders, constitutes the main risk factors (17-19). Thus PVT is not an infrequent occurrence in patients with cirrhosis, with a prevalence ranging from 2% to 23% (20). However, the

most determined risk factor has been overcome after TIPS by increasing the blood velocity. Indeed, the reported PVT recurrence rate after TIPS in the study by Luca *et al.* is only 5% (21). The common causes of thrombosis development after TIPS placement have been discussed above. Therefore, this high prevalence of thrombosis after TIPS in this study, if the report is true, questions the radiologist skills, which is related to stent mispositioning and incorrect release of the stent (7,11,12,14,15,22). Previous studies have shown that deployment of a stent with the cephalic end extending to the hepato-caval junction and the caudal end parallel to the vascular wall of the portal vein is favorable in a TIPS procedure to decrease the risk of thrombosis and shunt dysfunction (10,12). In contrast, an uncovered hepatic vein is more susceptible to shunt thrombosis caused by turbulence and the shear stress of high-velocity blood flow (10-12).

Another interesting finding in this study is that thrombosis after TIPS seem to seldom cause shunt dysfunction as the portion of patients who developed thrombosis (27/101, 27%) was higher than that developed shunt dysfunction (21/101, 21%) and most shunt dysfunction was revealed to be shunt stenosis which seems caused by pseudointimal hyperplasia (16/21, 76%) (16). This low rate shunt dysfunction resulted from thrombosis questions the adverse impact of the thrombosis. In addition, it has been shown that shunting branch of portal vein and stent position is associated with shunt dysfunction, hepatic encephalopathy and survival after TIPS (12). Thus, whether the poorer clinical outcomes in TIPS-treated patients who developed thrombosis are due to their suboptimal stent sites or thrombosis is hard to say.

Furthermore, several aspects in the misuse of statistical methods in this study should be considered. Firstly, the authors compared the results in patients with and without thrombosis; however, other potential confounders were not adjusted. Second, as the development of thrombosis change over time, they should be included in a Cox model treating as time-dependent covariates after adjusting other potential confounders (23).

Collectively, considering the unexpected high incidence of thrombosis after TIPS and inappropriate statistical methods, the results of this study should be interpreted with some caution.

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