Editorial

Does non-malignant portal vein thrombosis affect outcomes of transjugular intrahepatic portosystemic shunt in patients with cirrhosis?

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Portal vein thrombosis (PVT) is no longer considered a contraindication for transjugular intrahepatic portosystemic shunt (TIPS). On the other hand, TIPS has shown to improve PVT (1) and reduce the risk of rebleeding as compared with endoscopic band ligation and propranolol albeit without providing a survival benefit (2,3). Also portal vein recanalization and TIPS in cirrhotics with chronic, obliterative PVT has increased the eligibility for liver transplantation and reduced the need for complex surgical grafts during transplantation (4,5).

Although TIPS is now successfully performed in patients with PVT, there are concerns about the influence of PVT on the long term outcomes of TIPS. Specific questions that arise are: (I) does the presence of PVT increase the risk of shunt dysfunction; (II) is the presence of PVT protective against hepatic encephalopathy (HE); (III) does PVT increase episodes of rebleeding and ascites post TIPS; and finally (IV) does it affect overall mortality? To address these questions, several studies (6-8) have reported their rates of overall survival, clinical relapse, shunt dysfunction and HE in patients with PVT undergoing TIPS. Although these reported outcomes appear to be comparable to those reported in patients with TIPS without PVT, direct comparison studies need to be performed. Such a study comparing post TIPS outcomes of patients with and without PVT was reported by Perarnau *et al.* (9). In this retrospective study, the authors found no statistical difference in the probability of survival at 1, 2 and 4 years, long-term shunt patency, episodes of acute HE, chronic HE, recurrent variceal bleeding and the cumulative probability to improve ascites scores between the PVT positive and negative groups.

In their retrospective study of the outcomes of TIPS for non-malignant PVT, Lv *et al.* (10) systematically studied and analyzed a large cohort of 1,171 patients over a 13-year period for the following outcome measures: (I) mortality; (II) clinical relapse; (III) shunt dysfunction; and (IV) overt HE. They found that there was no evidence that preexisting PVT was associated with an improved or worsened outcome after TIPS.

To reach this conclusion, the authors first adjusted the baseline characteristics of patients in the PVT positive and negative groups. Multiple variables that could influence the outcome of TIPS such as age, sex, cause of cirrhosis, liver function [Child-Pugh class, Child-Pugh score, Model for End-Stage Liver Disease (MELD) score, INR, serum total bilirubin, serum albumin, presence of ascites], presence of hydrothorax, splenectomy, previous HE, serum creatinine level, serum sodium level, indication for TIPS, type of stent (covered/uncovered), stent diameter (8 mm/10 mm) and portosystemic pressure gradient after TIPS were then systematically analyzed. For each of the four outcomes studied, a univariate analysis was performed. The individual

variables that demonstrate statistical significance were then subjected to a multivariate analysis and adjusted hazard ratios were determined. This analysis revealed that (I) increasing age, higher Child-Pugh class, and refractory ascites as indications for TIPS were independent predictors of mortality after TIPS; (II) increasing total bilirubin level, use of an uncovered stent (compared with a covered stent), and use of an 8-mm diameter stent (compared with a 10-mm stent) were independent predictors of clinical relapse; (III) decreasing INR, use of an uncovered stent, or use of an 8-mm diameter stent were independent risk factors for shunt dysfunction; and (IV) increasing age, INR, serum albumin level, and covered stent type were independent risk factors related to HE.

The most important finding of the study was that there was no significant difference in the cumulative incidence of death, HE, clinical relapse and first episode of shunt dysfunction at 1, 3 and 5 years between the PVT positive and PVT negative groups. These results were reproduced when multivariate analysis was repeated with adjustment of propensity scores and exclusion of patients with splenectomy before TIPS. In addition, sub group analysis of patients with different stages, degrees and extent of PVT did not reveal any statistical difference in the four outcomes as compared with patients without PVT.

This review by Lv *et al.* demonstrates on the basis of robust statistical analysis in a large cohort of patients that there is no statistical difference in the outcomes of TIPS in patients with and without PVT. The study design was well planned and appropriate statistical tests were performed to control for intergroup variability. The regression models used to calculate associations were appropriate for the given data set. The study ensured that redundant variables were not introduced in the final analysis. Also, proper control statistical tests were performed to rule out incorrect correlations.

The results of this study further support the utilization of TIPS in the management of non-malignant PVT in cirrhosis. This research would also be helpful in directing future studies towards comparison of TIPS with systemic anticoagulation in management of non-malignant PVT.

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