



ORIGINAL ARTICLE

Utility of Doppler ultrasonography for predicting improvement of platelet count after transjugular intrahepatic portosystemic shunt

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Abstract

Objective. Portal pressure gradient (PPG) after transjugular intrahepatic portosystemic shunt (TIPS) <12 mmHg has been reported as the only factor predictive of increase in platelet count. As flow velocities measured on Doppler ultrasound are related to pressure gradient based on the Bernoulli equation, we used this parameter to predict increased platelet count after TIPS placement.

Methods. A total of 161 consecutive patients who underwent TIPS placement entered this retrospective study. The platelet count was measured before, one week after and one month after TIPS placement. Clinically significant thrombocytopenia was defined as platelet count $\leq 100\,000$. Pre- and post-TIPS PPGs were measured. The velocity of blood flow in the proximal, mid and distal TIPS stent was measured using Doppler ultrasound, and the difference in the highest and lowest measured velocity was entitled flow velocity gradient (FVG), which was considered normal when ≤ 100 cm/s.

Results. In 121 patients with pre-TIPS thrombocytopenia, the mean platelet count one week and one month after TIPS placement increased 25.7×10^3 and 35.0×10^3 in 90 patients with $PPG \leq 12$ mmHg ($P=0.028$ and $P=0.015$), while there was no significant change in platelet count in patients with a $PPG > 12$ mmHg ($P=0.098$ and $P=0.075$). Platelets increased significantly when $FVG \leq 100$ cm/s ($n=95$) vs $FVG > 100$ cm/s ($n=26$) one week (37.0×10^3 vs 11.0×10^3 ; $P=0.005$ vs 0.07) and one month after TIPS placement (17.0×10^3 vs 5.2×10^3 ; $P=0.01$ vs 0.21).

Conclusion. $FVG > 100$ cm/s is not associated with increase in post-TIPS platelet count. On the other hand, findings suggestive of proper TIPS function ($FVG \leq 100$ cm/s and $PPG \leq 12$ mmHg) predict a significant increase in post-TIPS platelet count.

Key words: liver cirrhosis; transjugular intrahepatic portosystemic shunt; platelet count; Doppler ultrasound

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Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) is commonly used for the management of complications of portal hypertension in cirrhotic patients [1]. TIPS is a nonsurgical procedure that does not require general anesthesia and is therefore a very good option for many of the ill nonsurgical candidate cirrhotic patients [2].

The pathogenesis of thrombocytopenia in cirrhotic patients is controversial and probably multifactorial including hypersplenism [3]. The effect of placement of TIPS on platelet count in thrombocytopenic cirrhotic patients is controversial with some showing an increase in platelet count after TIPS placement [4], while others failed to demonstrate such a relationship [5,6]. Portal pressure gradient (PPG) <12 mmHg after TIPS placement has been reported as the only predictor of increase in platelet count [3]. As flow velocities measured on Doppler ultrasound are related to pressure gradient based on the Bernoulli equation, the purpose of this study was to evaluate the effect of TIPS placement on platelet count as well as see if flow velocity in TIPS measured by Doppler ultrasound can be used to predict platelet count after TIPS placement.

Materials and Methods

Patient population

After receiving an Institutional Review Board approval, we reviewed the electronic medical records of all adult patients (age ≥18 years) with cirrhosis who underwent TIPS placement from January 2006 through December 2008.

Inclusion criteria: (1) platelet count was measured one week before as well as one week and one month after TIPS placement; (2) Doppler ultrasound of the liver was performed within one week post-TIPS placement; (3) The largest diameter of the spleen based on computed tomography (CT) or ultrasound performed within one month before and after TIPS placement was recorded. Patients with history of prior TIPS placement, prior history of liver transplant or no Doppler ultrasound evaluation within the first week post TIPS placement were excluded from the study.

A total of 161 patients were included and comprised the final patient population. Demographic characteristics including age, sex and ethnicity were collected. Moreover, the indication for TIPS placement was gathered. A total of 10 patients underwent liver transplant within five days to six months after TIPS placement, and the platelet count one week after transplant and the spleen size within one month after liver transplant were recorded.

TIPS placement

Before TIPS placement, paracentesis was done as needed. From the right hepatic vein or hepatic segment of the inferior vena cava to the branch of the portal vein, direct portography was carried out followed by stent placement. An 8 or 10 mm Viatorr stent (Gore and Associates, Flagstaff, AZ) was used to bridge the right portal vein to the right hepatic vein. PPG before and after TIPS placement was measured.

Doppler ultrasound

Patients underwent Doppler ultrasound within one week post TIPS placement. The velocity of blood flow in the proximal, mid and distal portion of the TIPS was measured in centimeters per

Table 1. Indications for TIPS placement

Indication	Number (%)
(1) Refractory ascites	93 (57.8)
(2) Variceal bleeding	56 (34.8)
(3) Both 1 and 2	6 (3.7)
(4) Hepatic hydrothorax	6 (3.7)

second (cm/s). The difference in highest and lowest measured velocity was calculated and named flow velocity gradient (FVG). FVG ≤100 cm/s was considered normal, while values >100 cm/s were considered abnormal.

Statistical analysis

All measured data are presented as mean ± standard deviation (SD). Statistical Package for the Social Sciences (SPSS) version 17.0 (Chicago, IL) was used for data entry and statistical analysis. Independent sample t test was used to compare the mean platelet count and spleen size in different subgroups of patients before and after TIPS placement. A P value ≤0.05 was considered statistically significant.

Results

A total of 225 consecutive patients who underwent TIPS placement from January 2006 through December 2008 were evaluated. Sixty-four patients were excluded due to prior history of TIPS placement, prior history of liver transplant or absence of Doppler ultrasound evaluation within the first week after TIPS placement. A total of 161 patients remained in the study (48 females and 113 males). The mean age of the patients at the time of TIPS placement was 52.3 ± 13.9 years. Table 1 shows the indications for TIPS placement in our patient population.

The mean PPGs before and after TIPS placement were 18.1 ± 5.6 mmHg and 7.1 ± 3.8 mmHg, respectively. PPG after TIPS was ≤12 mmHg in 100 patients, suggestive of successful decompression of the portal venous system. A total of 127 patients had a flow velocity of ≤100 on Doppler ultrasound, among which 87 had a PPG ≤12 mmHg.

The platelet counts were measured before, one week and one month after TIPS placement. There was no significant increase in platelet number after TIPS placement when all patients were included (Table 2). The platelet count, however, showed more pronounced increase when 121 patients with clinically significant thrombocytopenia (defined as platelet ≤100 000) were included in the analysis but was still not statistically significant (Table 2). Platelet count increased significantly when PPG gradient was ≤12 mmHg (n=90), while there was no significant change in platelet count in pre-TIPS thrombocytopenia patients with a PPG >12 mmHg (n=31) (Table 2). Platelet count also increased significantly when FVG was ≤100 cm/s as compared with those with FVG >100 cm/s (Table 2). The platelet count in 10 patients who underwent liver transplant showed significant increase one month after transplant (Table 2).

The mean spleen size before TIPS placement was 15.9 cm and 16.2 cm (P=0.89) within one month after TIPS placement. The mean spleen size before TIPS placement in 10 patients who underwent liver transplant was 17.5 cm; within one month after TIPS placement, the mean spleen size was 18.2 cm (P=0.77) and 17.4 cm (P=0.86) one month after LT.

Table 2. Changes in platelet count one week and one month after TIPS placement in different subgroups of patients

	Change in platelet count ($\times 10^3$) 1 week after TIPS placement (P value)	Change in platelet count ($\times 10^3$) 1 month after TIPS placement (P value)
All patients (n=161)	3.4 (0.12)	7.5 (0.13)
Patients with clinically significant thrombocytopenia (n=121)	6.8 (0.09)	10.8 (0.18)
Patients with PPG ≤ 12 mmHg (n=90)	25.7 (0.028)	35.0 (0.015)
Patients with PPG > 12 mmHg (n=31)	7.8 (0.098)	6.3 (0.075)
Patients with FVG ≤ 100 cm/s (n=95)	37.0 (0.005)	17.0 (0.01)
Patients with FVG > 100 cm/s (n=26)	11.0 (0.07)	5.2 (0.21)
Patients who underwent liver transplant (n=10)	-7.7 (0.72)	61.4 (0.001)

Discussion

Thrombocytopenia is a common finding in the setting of hepatic cirrhosis and portal hypertension. The exact mechanism is not clearly understood, but splenomegaly and associated hypersplenism are probably contributory factors [3]. TIPS had a 90% success rate in decompressing the portal pressure and therefore decreasing the portal hypertension and its associated complications (e.g. splenomegaly and possibly hypersplenism) [7]. However the effect of TIPS placement on reversing thrombocytopenia is controversial.

In our study, the platelet count one week and one month post TIPS placement was not significantly changed (3.4×10^3 and 7.5×10^3 ; P values 0.12 and 0.13, respectively). However when the platelet count was compared before and after TIPS placement in the subset of patients with clinically significant thrombocytopenia ($\leq 100\ 000$), the changes were slightly more pronounced but still not statistically significant (6.8×10^3 and 10.8×10^3 ; P values 0.09 and 0.18, respectively). This is in accordance with the prior studies that did not demonstrate a significant increase in platelet count after TIPS placement [5,6] and suggests that the pathogenesis of thrombocytopenia in cirrhotic patients is multifactorial and cannot be justified only by portal hypertension and hypersplenism [4]. An alternative explanation is that TIPS is unable to release sequestered platelets in the spleen secondary to portal hypertension and hypersplenism [5].

In addition to PPG, which is measured during invasive procedures such as TIPS placement itself and portal venography (PPG ≤ 12 mmHg shows adequate decompression of the portal system and suggests proper function [3]), there are some noninvasive methods for evaluating TIPS function using Doppler ultrasound including flow velocity gradient (FVG) in the TIPS. It has been shown that a velocity gradient of > 100 cm/s is suggestive of TIPS malfunction [8]. On the other hand, based on the Bernoulli equation ($\Delta = 4 (v_1^2 - v_2^2)$, Δp is the pressure gradient across an area of stenosis and V_1 and V_2 are the flow velocity before and after the area of stenosis). Flow velocities measured on Doppler ultrasound (such as FVG) are related to pressure gradient (such as PPG) and can therefore potentially be used interchangeably for the evaluation of the TIPS function.

In our study there was a significant increase in platelet count in clinically significant thrombocytopenic patients (platelet $\leq 100\ 000$) who had a PPG ≤ 12 mmHg after TIPS placement (25.7×10^3 increase one week and 35.0×10^3 increase one month after TIPS placement (P value: 0.028 and 0.015, respectively), while this increase in platelet count was not significant in patients with PPG > 12 mmHg (7.8×10^3 increase one week and 6.3×10^3 increase one month after TIPS placement; P value: 0.098 and 0.075, respectively). Thus, increase in platelet count can be

expected in the thrombocytopenic patients who underwent successful TIPS placement with adequate decompression of the portal venous system. This is concordant with the study performed by Papp *et al* [3]. Using FVG as a noninvasive index of proper function of the TIPS, the same results were observed in our study. Again, in clinically significant thrombocytopenic patients, the platelet count increased significantly when the FVG was ≤ 100 cm/s as compared with those with a FVG > 100 cm/s (37.0×10^3 vs 11.0×10^3 one week post TIPS; P value: 0.005 vs 0.07; and 17.0×10^3 vs 5.2×10^3 one month post TIPS, P value: 0.01 vs 0.21).

Multiple studies, however, have shown that the platelet count shows significant improvement after liver transplant [9,10]. Our study also showed the same findings. In the 10 patients who underwent liver transplant, the platelet count increased from 75.9×10^3 before transplant to 145×10^3 after transplant (P=0.001). The effect of liver transplant seems to be multifactorial, but rapid increase in thrombopoietin after transplant seems to play a major role [11].

The effect of transplant on splenic size, however, is not as universal as its effect on the platelet count. Although many studies have proposed reversal of splenomegaly after liver transplant [10, 12–14], others have described subgroups of patients who demonstrated persistent splenomegaly after liver transplant [15,16]. This may be due to the more time-consuming process of splenomegaly reversal happening over a course of a few months, even in patients with no post-transplantation vascular complications [16]. Our study also showed that there is no significant reduction in the size of the spleen after transplant within one month after the liver transplant (18.2 vs 17.4 cm, P=0.86).

This study is limited by its retrospective nature. Also, we followed the post-TIPS platelet count for only one month. More delayed follow-up can be helpful for evaluating the durability of positive effects from TIPS placement on platelet count. Ideally, performing venography in all cases would be the best confirmation of the patency of TIPS and can therefore be helpful for confirming the findings on PPG and FVG. This was not done in our study but can be of significant value if performed in future studies.

In conclusion, although the pathogenesis of thrombocytopenia is multifactorial, portal hypertension and associated hypersplenism seem to have some roles. Using flow velocity gradient on Doppler ultrasound as a noninvasive tool can predict improvement in platelet count in a subgroup of patients with clinically significant thrombocytopenia. PPG, although needing an invasive procedure to be measured, can also be used to predict improvement or lack of improvement in platelet count after TIPS placement in this subgroup of patients. Liver

transplant causes a significant increase in platelet count while having no effect on spleen size, at least within the first month after transplant.

Conflict of interest statement: None declared.

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