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Received: November 29, 2020; Published: January 27, 2021

Abstract

TIPS is a well-established procedure for the management of portal hypertension in cirrhosis, common indications being refractory ascites and secondary prevention of variceal bleed. Pulmonary hypertension is present in a significant subset of cirrhotic patients and is a relative contraindication of TIPS. After placement of TIPS stent, pulmonary arterial pressure rises. It seldom needs stent reduction also.

We have presented a retrospective observational study comparing changes of pulmonary pressure before, immediately after and in long term follow-up after TIPS and factors influencing pulmonary pressure change after TIPS. Our secondary aim was to compare between echocardiography and catheter directed measurements in assessing pulmonary pressure.

Keywords: TIPS (Transjugular Intrahepatic Porto-Systemic Shunt); Pulmonary Pressure; Porto-Systemic Pressure Gradient; Echocardiography; Schwan-Ganz Catheter

Introduction

TIPS (Transjugular intrahepatic porto-systemic shunt) is a well-established method for the management of portal hypertension. The concept, evolution and development of it dated back to 1970s; however, it was in clinical use since 1990s. TIPS gained popularity in last decade because of technical advancement, leading to satisfactory outcome. Although TIPS does not have any absolute contraindication, but some relative contraindications do exist. One of them being severe pulmonary hypertension which might need TIPS reduction in selected cases. In addition, right heart pressure is a well-established predictor of mortality after TIPS. This single institute retrospective observational study was aimed to assess the changes of pulmonary pressure before and after TIPS. Secondary aim was correlation between echocardiography and catheter directed measurement in assessing pulmonary hypertension in setting of porto-systemic shunt.

Methodology

This is a single institute retrospective observational study. All the TIPS done between December 2017 and March 2020 at our center (23 patients) were included in this study. Main indication of TIPS being refractory ascites, esophageal or gastric variceal hemorrhage,

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refractory hydrothorax and HRS 2 (Hepatorenal syndrome). All the TIPS patients underwent echocardiography, EGD (esophago-gastroduodenoscopy), liver function test, complete blood count, international normalized ratio (INR), sodium, potassium and creatinine 1 - 7 days before procedure.

A tricuspid regurgitation jet (TR jet) was identified in parasternal long axis and parasternal short axis view. Doppler was used with sweep speed of 100 mm/s. The peak velocity was then measured (TR max). Subsequently, Bernoulli equation (P = 4[TRmax]2) was used to calculate pressure difference [1]. Right atrial pressure (RAP) is assumed by the size and distensibility of inferior vena cava (IVC) during inspiration at rest and during forced inhalation, and subsequently this value was added to the previously obtained pressure [2].

TIPS was done under general anesthesia by a single intervention radiologist in all cases. Right internal jugular vein was used in to secure an access, initially with 5F short sheath and finally with 10F long sheath of modified Roch-Uchida set. First, central venous pressure was monitored and then the pulmonary pressure was confirmed with Schwan-Ganz catheter before TIPS [3]. The same catheter was also used to measure porto-systemic pressure gradient. The porto-systemic pressure gradient was confirmed after portal puncture and parenchymal tract was dilated with a non-compliant balloon of 8mm (Mustang, Boston Scientific). TIPS shunt was created using a covered stent (Fluency[™] Endovascular stent graft, Bard) of 10 mm diameter. Length of it varied depending on length of parenchymal tract or whether shunts are made between portal evin and hepatic vein (TIPS) or directly between portal vein and IVC (DIPS). Finally, a 10 mm bare metal self-expandable stent (Wall stent[™], Boston Scientific) was used. Composite TIPS stent was dilated with the previously used 8 mm non-compliant balloon. After TIPS, porto-systemic pressure gradient was monitored and if it needs further reduction, then 10 mm balloon was also used in selected cases [4]. Finally, pulmonary arterial pressure was measured with Schwan-Ganz catheter directly and also with echocardiography at the same time. Echocardiography was repeated in follow-up to assess peak systolic pulmonary arterial pressure after 6-8 weeks of TIPS creation.

Follow-up data of 2 patients were not available. First one had an extrahepatic portal vein puncture leading to hemoperitoneum. Even after covering the rent in portal vein with long covered stent and all vasopressor support, he succumbed on day 2 following TIPS creation.

The other patient had budd-chiari syndrome (BCS). He was on oral Rivaroxaban 10 mg/ day dose, which was stopped 48 hours prior to TIPS. Post TIPS, intravenous unfractionated heparin infusion was used at the dose of 5000 IU twice a day with APTT monitoring. But he developed intracranial hemorrhage on right basal ganglion including internal capsule on day 2 following TIPS, associated with subfalcine and descending transtentorial herniation and finally died on day 5 following TIPS.

Result

From December 2017 through March 2020, 23 patients (15 males) of age 50.8 ± 13.5 (range 26 - 70) years underwent TIPS in our institute (Table 1). Indications for TIPS include refractory ascites (12), bleeding esophageal varices (5), bleeding gastric varices (3), refractory hydrothorax (1), Budd-Chiari syndrome (1) and sub-acute portal vein thrombosis (1) (Table 2). All patients underwent echocardiography day before, just after TIPS and a follow up at 6 - 8 weeks. Calculated peak pulmonary pressures were noted on echocardiography. Pre and post TIPS pulmonary pressures were also measured directly using swan-ganz catheter. Pre and post procedure pulmonary pressures as measured by swan-ganz catheter were 38 ± 6 mm of Hg and 46.8 ± 5.7 mm of Hg respectively. Post procedure there was significant not 'increase' (p < 0.001) in pulmonary pressure with mean increase of 8.7 [7.2 - 10.3 (95% CI)] mm of Hg (Table 3).

Total number of TIPS candidates	23	
Male	15	
Age	50.8 ± 13.5 years	

Table 1: Demographics of patient underwent TIPS.

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Total TIPS	N = 23	
Refractory ascites	12 (52.2%)	
Esophageal varix	5 (21.8%)	
Gastric varix	3 (13.1%)	
Refractory hydrothorax	1(4.3%)	
BCS	1 (4.3%)	
Subacute portal vein thrombosis	1 (4.3%)	

	Pre-TIPS units	Immediately after TIPS	6 - 8 weeks after TIPS
Catheter measurements	38 ± 6	46.8 ± 5.7	Not available
Doppler-Echocardiography	42.8 ± 8.2	52.2 ± 7.6	49.9 ± 6.9
Porto-systemic pressure gradient	24.7 ± 3.9	10.2 ± 2.4	Not available

Table 3: Systolic pulmonary arterial pressure measured with echocardiography and

 Schwan-Ganz catheter and porto-systemic gradient in mm of Hg.

As measured on echocardiography, the pre procedure systolic pulmonary pressure was $42.8 \pm 8.2 \text{ mm}$ of Hg which increased to $52.2 \pm 7.6 \text{ mm}$ of Hg with significant (p < 0.001) mean increase of 9.4 [7.9 - 10.8 (95% CI)] mm of Hg. Among 23 patients, 21 patients had a follow up echocardiography in 6 - 8 weeks. In the follow up echocardiography, mean pulmonary pressure was $49.9 \pm 6.9 \text{ mm}$ of Hg (Table 3). This was significantly higher (p = 0.001) by 6.8 [4.5 - 9.1 (95% CI)] mm of Hg as compared to pre procedure values. But when compared to the immediate post procedure values the mean difference was 2.5 (-0.04-5.1) mm of Hg, which just fall below the level of significance (p = 0.055).

All the patients had catheter-based measurement of the porto-systemic (PS) gradient just before and after the placement of the TIPS stent. The mean pre procedure PS gradient was 24.7 ± 3.9 mm. Immediately post procedure, the PS gradient showed a significant (p < 0.001) drop of 14.5 [12.8 - 16.2 (95% CI)] with post procedure PS gradient of 10.2 ± 2.4 mm of Hg (Table 3).

Pearson correlation was done to check correlation between the echocardiography and catheter derived pulmonary pressures. It showed good correlation (p < 0.001) for both pre (r = 0.74) and post (r = 0.75) TIPS measurements.

As mentioned previously, during follow up the pulmonary pressure remained significantly elevated as compared to baseline. Interestingly this difference of follow up and baseline pulmonary pressures showed a moderate but significant (p = 0.02) correlation with post TIPS PS gradient (r = 0.52); however, changes in pulmonary pressure did not have any significant correlation with reduction of PS gradient.

Discussion

TIPS is a well-established non-surgical option for the management of portal hypertension. It causes significant change in pulmonary pressure. In this study, there was significant increase in systolic pulmonary arterial pressure after TIPS with mean increase of 8.7 [7.2 - 10.3 (95% CI)] mm of Hg. It is consistent with the observation made by Van der linden., *et al* [5]. They documented a rise of mean pulmonary arterial pressure by 7.9 mm Hg (12.3 mm Hg to 23.2 mm of Hg). Arthur., *et al*. [6], showed 100% improvement (2 patient) in TIPS induced pulmonary hypertension after TIPS reduction indicating direct correlation between PS pressure gradient and systolic pulmonary arterial pressure.

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This observation of pulmonary hypertension was also noted in congenital extrahepatic porto-systemic shunt as noted by Kai-yang Lin [7] and Jeong-Eun Yi [8].

In our study, good correlation was noted between echocardiography and catheter-based measurement of systolic pulmonary arterial pressure. It is consistent with the finding obtained by Fuad., *et al.* [9], who had done it among liver transplant candidates. They found modest correlation between echocardiographic and catheter-based measurement (R = 0.58, p < 0.001) in liver transplant candidates (n = 31) compared with the control group (R = 0.74, p < 0.001, n = 49).

Sohail., et al. [10] also showed moderate correlation between echocardiography and catheter-based measurement of systolic pulmonary arterial pressure.

In a prospective study by Dan Yin., *et al.* [11], 397 pediatric patients with congenital heart diseases were included and they showed significant underestimation of systolic pulmonary pressure by echocardiography compared to that by catheter directed measurement.

Conclusion

Systolic pulmonary arterial pressure (sPAP) rises significantly after TIPS, which peaks at immediate post-TIPS period and persists in long term follow-up. Rise in sPAP shows moderate but significant correlation with post TIPS porto-systemic gradient. Good correlation is obtained between echocardiography and catheter-based measurement of sPAP in pre as well as post TIPS.

Conflict of Interest Disclosure

No conflict of interest.

Declaration of Funding Sources

No funding source.

Author's Contribution

Conception and design: Dr. Mousam Dey.

Analysis and interpretation of the data: Dr. Shambo Guha Roy.

Drafting of the article: Dr. Mousam Dey.

Critical revision of the article for important intellectual content: Dr. Simi Das, Dr. Kishalaya, Dr. Jabaranjan Hembram and Dr. Abhijit Chowdhury.

Final approval of the article: Dr. Mousam Dey, Dr. Shambo Guha Roy, Dr. Simi Das.

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