

## Role Of Neo-Adjuvant TIPS in Child Pugh Class A And B Cirrhotic Patients Undergoing Elective Intra-Abdominal Surgery

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### ABSTRACT

**BACKGROUND:** Portal hypertension is routinely diagnosed and managed among cirrhotic patients. While awaiting liver transplant a number of patients may require elective intra-abdominal surgery for alternative reasons. These patients are at increased risk of morbidity and mortality due to underlying portal hypertension which results in higher bleeding risk and poor wound healing.

**AIM:** To determine safety and efficacy of pre-operative prophylactic TIPSS in improving surgical outcomes.

**METHODS:** A retrospective chart review was performed for Child Pugh Class A or B patients who underwent prophylactic TIPSS procedure before elective intra-abdominal surgery at our institution over a span of 5 years.

**RESULTS:** A total of 9 patients satisfied the inclusion criteria. All underwent their respective surgical procedure within a mean of 2.5 months from the time of TIPSS placement. Average hospital stay post-surgery was 2.5 days and 30-day mortality was 0%. The surgery included- umbilical hernia repair with or without mesh (6/9), open nephrectomy (1/9), laparoscopic nephrectomy (1/9) and open cholecystectomy (1/9). There were no reported peri-operative complications including infection, bleeding or hepatic decompensation.

**CONCLUSION:** Preoperative portal decompression by using neo-adjuvant TIPSS is a safe and efficacious modality to decrease the morbidity and mortality for patients with Child Pugh Class A and B cirrhosis undergoing abdominal surgery.

**Key words:** Cirrhosis; Prophylactic TIPS; Abdominal surgery

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### INTRODUCTION

Portal hypertension is present in 60% of cirrhotic patients; it is the result of resistance to portal blood flow. Diagnosis can be made clinically and confirmed with hepatic venous catheterization to determine the hepatic venous pressure gradient (HVPG)<sup>[1]</sup>. Sinusoidal portal hypertension is found in most chronic liver diseases and is characterized by an increase in wedge hepatic venous pressure and a normal free hepatic venous pressure resulting in an increase of the HVPG. The normal value of this gradient is 5 mmHg. It is a strong

prognostic indicator in compensated and decompensated cirrhosis. Cross-sectional and prospective studies have indicated that features of portal hypertension complications are not seen until HVPG is at least 10 mmHg, therefore becoming clinically significant. An HVPG above 12 carries a higher risk of variceal bleeding. Increased mortality risk is seen when HVPG is above 16 mmHg, and values up to 20 mmHg have a low 1-year survival rate<sup>[2-3]</sup>.

Multiple studies throughout the years have attempted to predict the prognosis of patients with cirrhosis based on clinical and laboratory information. The two most commonly used models are the Child-Pugh classification and the Model for End Stage Liver Disease (MELD) score<sup>[4]</sup>. Garrison *et al* in 1984 evaluated 92 patients with cirrhosis undergoing surgery and determined the mortality risk increased as the Child Pugh Classification progressed, determining a mortality of 82% in Child-Pugh Class C<sup>[5]</sup>.

Transjugular intrahepatic porto-systemic shunt (TIPS) is an established procedure that has proven benefit in the treatment of patients who have complications of portal hypertension. Originally described by Röscher *et al* in 1969 and first performed by Richter *et al* in 1989. It is a percutaneous imaging-guided procedure in which a channel is constructed within the liver to reduce portal pressure by diverting blood from the portal to the systemic circulation, functioning as a side-to-side portocaval shunt<sup>[6]</sup>. The strongest evidence in favor of performing a TIPS procedure exists for the secondary prevention of variceal bleeding and also refractory ascites. Other uses include: refractory acute variceal bleeding, Budd-Chiari syndrome, hepatic veno-occlusive disease, hepatic hydrothorax, hepatorenal syndrome, and hepatopulmonary syndrome<sup>[7]</sup>.

General surgery procedures in patients with significant liver disease, cirrhosis and concomitant portal hypertension are associated with high mortality rates. Perioperative complications often are due to abdominal venous congestion and ascites present in patients with severe portal hypertension as well as severe hypoprothrombinemia and thrombocytopenia. Child-Pugh grades have been used to assess surgical risks, recent representative studies have reported mortality rates in cirrhotic patients undergoing abdominal surgery in the perioperative period as the following: 10% for Class A, 17-30% Class B and 63-82% Class C<sup>[8]</sup>. TIPS procedure is capable of reducing portal hypertension-associated complications leading to decreased intraoperative bleeding and perioperative complications in patients undergoing major extrahepatic surgery, but experience remains limited. With increasing prevalence of liver disease, improved survival and increasing liver transplant waiting times a growing number of patients with cirrhosis are likely to need surgical procedures<sup>[9]</sup>. Our aim was to study the role of neo-adjuvant TIPS in patients requiring elective intra-abdominal surgery as a method to decrease perioperative complications.

## STUDY DESIGN

**Study Location:** The study was conducted at the main hospital of Einstein Medical Center, Philadelphia, US.

**Study Duration:** The study involved reviewing medical charts of patients admitted to hospital over a span of 5 years (Jan, 2012 to Jan, 2016).

**Inclusion Criteria:** (1) Age  $\geq$  18 years old; (2) Cirrhotic patients Child Pugh Class A and B requiring TIPS placement before elective intra-abdominal surgery

**Data Collection:** Medical charts of all patients who satisfied the inclusion and exclusion criteria were retrospectively reviewed to collect information to confirm the indication for TIPS prior to elective intra-abdominal surgery. The following variables were obtained:

demographics including age, gender, race, BMI; pre-operative assessment including history of esophageal varices and bleeding history, presence of ascites and/or splenomegaly, baseline HVPG obtained from interventional radiology reports and pre and post TIPS HVPG, etiology of cirrhosis, HIV status, history of diabetes mellitus, use of immunosuppressive medications: type of intra-abdominal surgery and time lapse between TIPS and surgery; surgical outcomes including intraoperative and postoperative complications, infection, hepatic decompensation, change in MELD score pre-TIPS, post-TIPS and post-surgery; length of hospital stay and 30 day mortality. Postoperative complications were reviewed in the operative reports and subsequent progress notes of patient's hospital stay including variables such as infection -organ/system affected/etiology and severity, severity of hepatic decompensation if present and bleeding. Subsequent hospital visits were also reviewed to determine cause and mortality.

## Methodology

Medical charts were obtained from Medical Records and Radiology department. A total of 145 charts with ICD-10 code for TIPS during the time period of 2012 to 2016 were reviewed, with only nine patients meeting the inclusion criteria. Two patient information electronic systems were used, Cerner for lab work data as well as Interventional Radiology reports and Access Anywhere was used to obtain operative report, progress notes and post operative report follow up. The information was divided into 3 comparative tables, Table 1 which indicates demographics and significant past medical history, Table 2 which includes the pre-operative assessment and TIPS placement and Table 3 stating surgical outcomes. MELD sodium scores as well as Child Pugh scores were calculated for each patient based on the preoperative, post operative, pre TIPS and post TIPS labs.

## Statistical Analysis

Descriptive data was presented with numbers and percentages for categorical variables. The numbers obtained were analyzed using Mean, Medians and Range.

## RESULTS

Over a time span of 5 years at our tertiary medical center, nine patients with cirrhosis Child Pugh Class A and B met our inclusion criteria and are depicted in Table 1. Male gender was predominant in our population 66% (6/9) vs female 33% (3/9). Among race, Caucasian population was predominant over African American population 77% vs 22% respectively. The average BMI was 29.5 (overweight). Only 2 patients were noted to have positive HIV

**Table 1** Patient characteristics.

Patient	Age (years)	Gender	Race	BMI	HIV status	History of Diabetes Mellitus
	52	M	C	39	U	N
2	67	F	AA	35	N	N
3	58	M	AA	32	N	P
4	40	M	C	18.7	P	N
5	51	M	C	26	P	N
6	50	F	C	26	N	N
7	49	M	C	37	U	N
8	56	M	C	28	U	N
9	54	F	C	24	U	N

Gender M (male), F (female). Race C (Caucasian), AA (African-American). HIV status/ History of Diabetes: U (unknown), N (negative), P (positive).

**Table 2** Pre-operative assessment.

Patient	Esophageal varices		Ascites	Splenomegaly	Etiology of Cirrhosis	HVPG		Post TIPS complication	MELD score		Child Pugh Class	Time from TIPS to surgery (months)
	Present	Bleeding History				Pre TIPS	Post TIPS		Pre TIPS	Post TIPS		
1	P	A	A	P	HCV	22	10	Mild LFT elevation	10	10	7/B	2
2	A	A	A	A	EtOH	10	3	Mild LFTs elevation	7	9	6/A	1
3	P	A	P	P	HCV	20	3	None	14	13	8/B	1
4	A	A	A	A	EtOH	13	9	None	12	20	9/B	1
5	A	A	P	A	EtOH	18	3	None	8	8	6/A	7
6	A	A	A	P	HCV	14	8	None	26	27	9/B	4
7	P	A	A	P	EtOH	19	6	None	9	9	7/B	3
8	A	A	A	P	HCV	16	13	None	14	15	8/B	1
9	P	A	P	A	EtOH	42	9	None	8	10	7/B	3

P (present) A (absent): HCV (Hepatitis C virus), EtOH (alcoholic cirrhosis). LFTs(liver function test). Child Pugh Class score/class.

**Table 3** Surgical outcomes.

Patient	Surgical Procedure performed	Postoperative diagnosis	Estimated Blood Loss (ml)	Postoperative complications	MELD score Pre Sx	MELD score Post Sx	Length of hospital stay (Days)	30 day mortality
1	Primary repair of umbilical hernia	Umbilical hernia repair and cirrhosis	Minimal	None	8	10	4	0
2	Hand assisted laparoscopic left nephrectomy	Left renal mass, possible Renal Cell carcinoma, Cirrhosis of the liver	100	Slight rise in total bilirubin	9	15	3	0
3	Primary repair of umbilical hernia with reduction of contents	Umbilical hernia	5-10	None	11	13	1	0
4	Open right nephrectomy	Renal cell carcinoma	50	None	17	22	3	0
5	Umbilical hernia repair with mesh	Incarcerated umbilical hernia, cirrhosis, alcoholic cirrhosis	Minimal	None	11	8	2	0
6	Open umbilical hernia repair with primary closure	Incarcerated umbilical hernia	10	None	19	19	1	0
7	Open cholecystectomy	Symptomatic cholelithiasis with chronic cholecystitis, cirrhosis	500	None	9	11	7	0
8	Open Umbilical hernia repair	Umbilical hernia, large volume paracentesis	Minimal	None	19	16	1	0
9	Primary repair of umbilical hernia	Nonincarcerated umbilical hernia	Minimal	Mild Total bili elevation	9	9	1	0

ML: milliliters; Sx: surgery.

status (22%). Only 1 patient had history of diabetes mellitus. (11%) None of the patients were on immunosuppressive medications.

Placement of TIPS was performed for all patients by the hospital’s Interventional Radiology team; reports were reviewed in patient’s electronic chart. The outcomes for TIPS are shown in Table 2. TIPS placement for each of the nine patients was successful without procedure-related complications. The procedure was done in a standard fashion using a 10 x 60 mm covered stent (Viator PTFE) with post stent angioplasty. Post procedure only 2/9 (22%) patients had mild transaminitis, which resolved within a range of 2-3 days. There were no complications of hepatic encephalopathy or ascites. The mean time from TIPS procedure to surgery was 2.5 months. MELD sodium scores pre TIPS compared to Post TIPS were shown to increase post procedure in average of 1.6 points.

Pre operative assessment also depicted in Table 2 categorizes each patient according to their baseline liver function which includes: assessment of esophageal varices, ascites and splenomegaly before surgery based on prior imaging on patient’s records (ultrasound, endoscopy, CT scans); etiology of cirrhosis; HVPG; Child Pugh Score/Class. None of the patients had history of complications of variceal bleeding, 4/9 patients (44%) were found to have varices on upper endoscopy however no banding had been required. Ascites was evidenced on imaging in 3/9 patients (33%). Splenomegaly was noted in 5/9 (55%) of patients. The two main etiologies of cirrhosis were found to be alcohol-related in 5/9 (55%) and Hepatitis C related

cirrhosis seen in 4/9 (44%) of patients. Average HPVG pre TIPS was 19.3 and post TIPS was 7.1, average HVPG reduction 12 points. Among Child Pugh Classes the most prominent was Class B seen in 7/9 patients (77%) whereas 2 patients were Class A (22%).

Surgical outcomes are depicted in Table 3. The classification of surgery risk according to ACC/AHA divided the 9 patients into low risk surgery 6/9 (umbilical hernia repairs) and intermediate risk surgeries 3/9 (open cholecystectomy and nephrectomy). All patients survived surgery. Umbilical hernias in 6/9 patients were repaired successfully. Nephrectomies were successfully performed in 2 patients with diagnosis of Renal Cell Carcinoma. One successful open cholecystectomy was done due to symptomatic cholelithiasis. Intra operative blood transfusions were not reported in the surgical records nor were they required in the postoperative period. No complications were reported in the immediate postsurgical period or within the postoperative 30-day period (including infection or hepatic decompensation). Average length of hospital stay was 2.5 days. Umbilical hernia repair was the most common type of surgery required, 6/9 (66%). There was no reported mortality 30 days post surgery.

## DISCUSSION

TIPS procedure has been in use for more than 30 years to treat the complications of portal hypertension. Cirrhotic patients are already at a higher risk of morbidity and mortality compared to the general

population given their bleeding risk, infection risk and poor healing capacity. Preoperative portal decompression by TIPS in cirrhotic patients requiring extra-hepatic surgery can potentially reduce fatal outcomes in patients with well-compensated cirrhosis.

In regards to preoperative TIPS before abdominal surgery, experience remains limited. To our knowledge this approach has been described in 7 prior studies<sup>[4,6,9,10,11,12,13]</sup>. The first study to describe this in 2001 included seven cirrhotic patients requiring planned extra-hepatic intra-abdominal operations in which a “two-step” strategy” was applied performing TIPS in a time period ranging between 1-5 months prior to the planned procedure. In this patient cohort, TIPS was done without complications with decrease in respective HPVG, however intraoperative complications such as significant blood loss requiring transfusions was seen in 2 patients and one post operative death<sup>[10]</sup>. Another study described a two patients with Child Pugh C cirrhosis in which TIPS was used preoperatively to decompress the portal system before major intra-abdominal surgeries, both procedures were only notable for an estimated blood loss of 1.4L which was managed with transfusions, both recovered uneventfully.<sup>[11]</sup> Kim *et al* in 2009 reported their experience with six patients who had TIPS placed prophylactically within 22 days of surgery. Authors included all cirrhotic patients including Child Pugh A, B (64%) and C that underwent intra-abdominal or cardiothoracic surgery. All 6 patients were discharged with 0% one-year mortality<sup>[4]</sup>. Schlenker *et al* described 7 patients with cirrhosis Child Pugh A or B, largest group to our knowledge, were prepared for elective intra-abdominal surgery using TIPS within a mean of 13 days prior to surgery out of which 2 required blood transfusions, 3 experienced post operative complications such as wound infection, peritonitis, pneumonia and new ascites and only one patient died of liver failure 14 months post-surgery<sup>[9]</sup>. In a recent review by Jain *et al* which included 7 original studies with 24 cirrhotic patients who had elective TIPS before major abdominal surgery, 4.2% had poor wound healing, 4.2% had right heart failure and 12.5% had hepatic encephalopathy post-surgery<sup>[14]</sup>.

Our study analysis included nine patients with cirrhosis secondary to either alcohol or hepatitis C virus Child Pugh A and B. To our knowledge this is the largest group of patients studied using TIPS as a preparation for major abdominal surgery. TIPS placement was successful in all of the patients before their assigned elective intra-abdominal surgery done within a mean of 2.5 months prior to surgery. All of our patients survived the surgery with minimal blood loss; there were no reported infections, hepatic decompensation, need for transfusion, recurrent ascites or need for surgical re-intervention, with a 0% 30- day and 1 year mortality. The result of our positive outcomes combined with the previously described evidence supports the fact that pre-operative TIPS is a beneficial procedure in patients with cirrhosis in order to prevent morbidity and mortality associated with the invasive nature of surgery. Time from TIPS to surgery was different in our study (mean 2.5 months) compared to previous reports (22 and 13 days respectively) and plays an important role in optimizing the patient prior to surgery. Although, the hepatic venous pressure reduces immediately post TIPS, hemodynamic equilibrium and clinical effects takes time<sup>[15]</sup>.

Our study has few limitations. Only 9 patients were included in our study group, although to our best knowledge this is the largest group described in literature. Lack of comparison group limits our ability to demonstrate a reduction in morbidity and mortality. Unlike few previous studies, we did not include CPC cirrhotic patients in our study. Also, these patients were pre-selected by surgeons to preferably have a favorable outcome and thus there is an inherent bias in the final results. Despite all these limitations, our study does

add more evidence to the safety and efficacy of TIPS as a neo-adjuvant tool in pre-operative preparation of cirrhotic patients. Larger prospective studies with more heterogeneous population in terms of disease severity and nature of abdominal surgery will help us better define the evolving role of TIPS in this setting. Questions regarding the optimum timing of surgery post TIPSS and selection criteria of patients who are likely to benefit from it remains to be answered with more research in future.

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## Author contribution

Dr. Jain and Dr. Bandres share first authorship. Dr. Jain contributed to study design, literature review, interpretation of data and drafting of the manuscript. Dr. Bandres contributed to literature review, data collection and drafting of the manuscript. Dr. Mahmood contributed in acquisition of data. Dr. Feysa contributed to critical revision of the manuscript for important intellectual content.

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