Pressure gradients, laboratory changes, and outcomes with transjugular intrahepatic portosystemic shunts in pediatric portal hypertension

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Abstract

Introduction: Indications for TIPS are well described in adults and involve complications of PHTN. Complications from PHTN are associated with PSG of >12 mm Hg in adults. It is unclear if these parameters apply to children with PHTN.

Objective: To assess whether adult criteria for TIPS placement can be utilized in children, describe laboratory changes over time, and report outcomes.

Methods: We performed a retrospective review of 34 pediatric patients who underwent TIPS, examining indications, radiology, PSG reductions, laboratory changes, and outcomes.

Results: Most patients had PHTN due to parenchymal liver disease including congenital hepatic fibrosis (n = 5), biliary atresia (n = 5), cystic fibrosis–related liver disease (n = 3) and cavernous transformation of the portal vein (n = 6). Indications for TIPS included variceal bleeding, recurrent ascites, and maintenance of portal vein flow following thrombolysis. Variceal bleeding was observed in six children with PSG <12 mm Hg. Minor complications occurred in eight subjects. Continued bleeding occurred in one patient. Six patients were successfully bridged to transplantation, and three patients died secondary to end-stage disease. Standard laboratory tests stabilized after TIPS placement and hematocrit increased.

Conclusion: TIPS placement in pediatric patients was performed for complications of PHTN. Unlike adult series, a substantial proportion of our cases treated extrahepatic PHTN from cavernous transformation of the portal vein. Children presented with sequelae of PHTN with PSG below 12 mm Hg, below the adult standard. We found TIPS in pediatrics to be safe and effective with laboratory stabilization and improvement in hematocrit.
1 | INTRODUCTION

PHTN results from obstruction of blood flow through the portal venous system at any level. This obstruction can occur proximally in the portal venous system, within the hepatic sinusoids, or distally in the hepatic venous outflow tract. The etiologies are wide, ranging from thrombosis to malignancy to primary liver disease resulting in diminished blood flow through the liver. Portal hypertension can be complicated by variceal hemorrhage, ascites, hepatic encephalopathy, and splenic sequestration.\(^1\)\(^2\)

TIPS placement has become the standard of care for select adult patients in the treatment of complications from portal hypertension. This endovascular procedure has a high technical success with immediate reduction in PSG. The TIPS procedure has largely replaced surgical portosystemic shunts in adults as a result of improved short- and long-term clinical efficacy. Its indications and outcomes in the adult patient population are well-defined.\(^3\)\(^-\)\(^5\) PSG > 10 mm Hg can be associated with the formation of varices while >12 mm Hg predicts patients at risk for gastrointestinal bleeding and decompensation of liver disease according to the Baveno Consensus statements.\(^2\)\(^-\)\(^6\) TIPS can ameliorate these sequelae of portal hypertension by reducing PSG; however, it is cautiously considered in adults with high-risk 30-day mortalities such as a Model for End-Stage Liver Disease (MELD) Score >15-18.\(^3\)

There is a gap in consensus in the role of TIPS in pediatric patients with portal hypertension,\(^2\)\(^,\)\(^5\)\(^,\)\(^7\) attributable to limited literature, heterogeneity of disease, and the technical challenges inherent to small patients. There is also limited data on the use of PSG to identify children at risk from portal hypertension and literature such as the Baveno V Consensus Workshop on Methodology of Diagnosis and Therapy in Portal Hypertension recommends using adult guidelines while acknowledging the limitation of current literature.

The scope of training for interventional radiologists may lead to relative inexperience in either TIPS or pediatric interventional radiology.\(^8\) While existing results support the use of TIPS in pediatric patients with portal hypertension,\(^7\)\(^-\)\(^9\)\(^,\)\(^12\) the currently available case series are small and retrospective, ranging from 1 to 40 patients.\(^9\)\(^,\)\(^17\)\(^-\)\(^21\) Recently, Johansen et al published the largest single-center experience in 40 children and adolescents from Birmingham, UK,\(^22\) and again demonstrated safety and effectiveness. Our goal is to assess the applicability of adult standards in terms of indications and venous gradient measures to pediatric populations with portal hypertension to inform the development of age-specific standards and to describe our outcomes.\(^2\)\(^,\)\(^22\)

2 | METHODS

Local Institutional Review Board approved all research activities. Patients were retrospectively identified using an internal electronic health record system database search. Relevant clinical data were entered into a secured Research Electronic Data Capture database for further analysis. Data included initial baseline characteristics, demographics, vital signs, laboratory work, and procedural information as well as follow-up laboratory work for the following five visits after TIPS placement. Data were collected from January 1, 2004 to February 1, 2018.

Complications were stratified using the Society of Interventional Radiology Standards of Practice Committee guidelines.\(^23\) Major complications were defined as those that required significant therapy, hospitalization >48 hours, unplanned increase in the level of care or prolonged hospitalization, or caused permanent adverse sequelae including death. Minor complications were defined as those that required no or nominal therapy, no permanent consequence, and required no more than overnight admission for observation only.

Statistical analyses were performed in MATLAB 7.9 (Mathworks, Natick, MA). We sought to visualize dynamic changes in blood features after TIPS. This was aided by transforming the data of each blood measure into 10 logarithmic categories (>0-7d, >7-12, >12-22, >22-39, >39-68, >68-121, >121-214, >378-668, and >668-1180) for descriptive box plotting as shown in Figure 2.

2.1 | TIPS procedure

Patients with complications of portal hypertension are discussed in our multidisciplinary portal hypertension group, consisting of Hepatology, Interventional Radiology and Hepatobiliary Surgery to decide optimal management. Once endoscopic therapy is considered inadequate, shunt options are considered, and for prehepatic causes, Meso-Rex is usually the first choice. In the early phase of our program, splenorenal shunting was the preference in most cases; but, with the introduction of covered stents and growing experience

### What is known

- Indications and expected outcomes for TIPS in adults.
- PSG >12 mm Hg is a commonly used indication of clinically significant PHTN in adults.

### What is new

- TIPS has a role in both intrahepatic and selected cases of prehepatic portal hypertension in pediatric populations.
- PSG >12 mm Hg may not be an appropriate threshold for the risk of variceal bleeding in pediatric populations.

### Keywords

- gastrointestinal bleeding, liver, pediatric, portal hypertension, transjugular intrahepatic portosystemic shunt, varices
| Patient | Age, y | Weight, kg | Gender | Race | Underlying disease | Indication | Hct | WBC | Plt | ALT | Alb | NH3 | INR |
|---------|--------|------------|--------|------|-------------------|------------|-----|-----|-----|-----|-----|-----|-----|
| 1       | 12     | U          | M      | W    | Cystic fibrosis–related Liver disease | SGIB       | U   | U   | U   | U   | U   | U   | U   |
| 2       | 15     | 53.3       | F      | H    | Nodular regenerative hyperplasia | Ascites    | 30.4| 4.2 | 85  | 73  | 2   | U   | 1   |
| 3       | 11     | 25.3       | M      | W    | Congenital hepatic fibrosis | Ascites    | 22.9| 1.6 | 215 | 44  | 3   | 23  | 1.4 |
| 4       | 4      | 14.7       | F      | W    | Zellweger syndrome | SGIB       | 39.5| 14  | 124 | 52  | 2.9 | U   | 1.5 |
| 5       | 5      | 14         | F      | W    | Cavernous transformation of the portal vein | SGIB       | 32.6| 5.2 | 222 | 46  | 3.6 | U   | 1.1 |
| 6       | 4      | 18.8       | F      | W    | Fibrotic liver disease of unclear etiology | SGIB       | 32.7| 3.2 | 63  | 24  | 4.2 | 31  | 1.2 |
| 7       | 2      | 13         | F      | H    | Biliary atresia | SGIB       | 24.1| 5.4 | 99  | 165 | 2.3 | 32  | 1.2 |
| 8       | 17     | 76         | F      | W    | Autoimmune hepatitis | SGIB       | 34.8| 2.4 | 61  | 61  | 4   | U   | 1.3 |
| 9       | 18     | 62.4       | F      | W    | Nodular regenerative hyperplasia | SGIB       | 31.7| 11.5| 102 | 31  | 3.9 | U   | 1.3 |
| 10      | 6      | 17.1       | F      | A    | Congenital hepatic fibrosis | SGIB       | 30.9| 4.9 | 82  | 30  | 3.6 | U   | 1.2 |
| 11      | 13     | 44.1       | F      | W    | Cavernous transformation of the portal vein | SGIB and thrombosis | 28.4| 16.3| 286 | 29  | 2.3 | U   | 1.2 |
| 12      | 10     | 34.5       | M      | W    | Veno-occlusive disease/sinusoidal obstruction syndrome | PGIB (large gastric varices) | 33.2| 3.3 | 62  | 33  | 4.3 | U   | 1.3 |
| 13      | 18     | 52.6       | F      | U    | Hepatoportal sclerosis (congenital generalized lipodystrophy) | SGIB       | 31.1| 3.1 | 73  | 40  | 2.7 | 39  | 1.3 |
| 14      | 12     | 37.8       | F      | H    | Berardinelli-Seip syndrome | AGIB       | 26.6| 13.6| 109 | 97  | 2.1 | U   | 1.4 |
| 15      | 16     | 64.8       | M      | W    | Chronic rejection of liver transplant, fibrosis, and thrombus of the portal venous system | SGIB and thrombosis | 20.3| 17.2| 124 | 144 | 2.6 | U   | 1.2 |
| 16      | 5      | 22.7       | F      | W    | Cavernous transformation of the portal vein | SGIB       | 33.5| 4.6 | 136 | 53  | 3   | U   | 1.1 |
| 17      | 14     | 66         | M      | A    | Cavernous transformation of the portal vein | SGIB       | 40.3| 7.3 | 269 | U   | U   | U   | 1.1 |
| 18      | 6      | 23         | F      | AA   | Congenital hepatic fibrosis | SGIB       | 34.7| 10.1| 139 | 41  | 1.8 | 36  | 2.1 |
| 19      | 9      | 29         | F      | W    | Cavernous transformation of the portal vein | SGIB       | 40.9| 8.4 | 59  | 38  | U   | U   | 1.3 |
| 20      | 6      | 31         | F      | W    | Biliary atresia | AGIB       | 25.3| 15.3| 48  | 109 | 1.9 | 18  | 1.9 |
| 21      | 15     | 90.6       | F      | W    | Splanchnic thrombosis of the portal venous system | Thrombosis (TIPS placed to maintain flow after thrombolysis) | 42  | 8.4 | 1389| 31  | 2.8 | U   | 1.2 |
| 22      | 17     | 51.5       | F      | U    | Glycogen storage disease 1B, thrombosis of portal/splenic/mesenteric veins | Thrombosis and splenic sequestration (TIPS placed to maintain flow after thrombolysis) | 20.1| 3.4 | 36  | 6   | 2.9 | U   | 1.5 |
| 23      | 9      | 25.2       | F      | W    | Parenteral nutrition related liver disease, thrombosis of the portal vein | SGIB       | 32.8| 4.4 | 77  | 72  | 2   | 82  | 1.4 |
| 24      | 8      | 26.8       | F      | W    | Cavernous transformation of the portal vein | SGIB       | 25.3| 3.2 | 54  | 29  | 3.4 | U   | 1.2 |

(Continues)
with TIPS in children, the paradigm has shifted to greater application of endovascular shunting. The features favoring TIPS placement over surgical portosystemic shunt include durable patency of the covered shunts, the ease with which shunt dysfunction can be addressed, and much shorter recovery time in the hospital.

Portal hypertension was defined as a PSG of >5 mm Hg via direct measurement after vascular access by Interventional Radiology, and reported pressures are the difference between the portal confluence and the right atrium. PSG of >12 mm Hg was used to define portal hypertension with high risk for variceal bleeding and decompensation from cirrhosis as extrapolated from adult data and most influentially the Baveno Consensus statements.\(^2\) Attempts to measure the PSG or hepatic venous pressure gradient followed previously described specific guidelines to ensure accuracy as errors in measurements can lead to treatment changes.\(^29\) No shunts were intentionally occluded or reduced in our patients. TIPS diameter was calibrated at the time of placement for target gradient reduction with recognition that many stents passively auto-dilate over time.

After patient selection, the overall steps of TIPS creation followed standard techniques established in adults. Technical nuances pertinent to pediatric patients have been previously described.\(^16\) However, there are some technical nuances in our standard of care. Intravascular ultrasound has been used since 2015 for guidance to aid in limiting radiation exposure. Constrained TIPS and under dilation for passive dilation were both performed, and the decision between the two was based on operator preference. This has been mitigated to a degree with the introduction of covered stents with controlled expansion such as Viatorr CX\(^3\). In cases with cavernous transformation of the portal vein, the TIPS was placed across the obstructing vasculature ending in the main portal vein or further depending on the extent of vascular involvement. Technical success was defined as successful creation of a TIPS with a gradient reduction to <12 mm Hg or a reduction of 50% in PSG was already <12 mm Hg. Clinical success was defined as alleviation of the presenting portal hypertensive complications.

Following placement of shunt, patients were reassessed on a standard schedule with imaging and bloodwork within 1 week, 1 month, 3 months, and then every 6-12 months depending on severity of disease and clinical course. Imaging typically begins with a Doppler ultrasound of the shunt with follow-up venography if abnormalities, such as stenosis, increased velocities, or flow separation, are seen.

### 3 | RESULTS

Thirty-four consecutive patients undergoing TIPS for the treatment of portal hypertension between the years 2004 and 2018 at the Seattle Children’s Hospital were identified. Twenty-two (65%) were female, and age ranged from 1 to 19 years (median 12 years). There was no single etiology of portal hypertension that was present in the majority of our patients, but intrahepatic sinusoidal obstruction accounted for majority of cases. Etiologies included cavernous transformation of the portal vein (n = 6, 18%), congenital hepatic fibrosis

| Patient | Age, y | Weight, kg | Gender | Race | Underlying disease | Indication | Hct | WBC | Plt | ALT | Alb | NH3 | INR | Table 1 (Continued) |
|---------|--------|------------|--------|------|-------------------|------------|-----|-----|-----|-----|-----|-----|-----|------------------|
| 25      | 11     | 69.5       | F      | W    | Congenital hepatic fibrosis | Splenic sequestration | 35.2 | 7.8 | 25  | 69.5 | F   | 11  | 1   | 1.1          |
| 26      | 14     | 35.9       | F      | W    | Cystic fibrosis related Liver disease | Splenic sequestration | 45.4 | 9.6 | 3.8 | 37  | 4   | 4   | 1.2 | 1.1          |
| 27      | 19     | 63.3       | M      | W    | Congenital hepatic fibrosis | Cystic fibrosis related Liver disease | 34.7 | 4.3 | 7.4 | 4.1  | 3.1 | 2   | 1.3 | 1.1          |
| 28      | 12     | 40.1       | M      | W    | Cystic fibrosis related Liver disease | Cystic fibrosis related Liver disease | 41.4 | 6.4 | 8.8 | 3.4  | 4.3 | 2   | 1.3 | 1.1          |
| 29      | 17     | 46.6       | M      | W    | Autoimmune hepatitis | Cystic fibrosis related Liver disease | 29.4 | 3.1 | 37  | 4.1  | 3.1 | 2   | 1.3 | 1.1          |
| 30      | 1     | 11.81      | M      | U    | Bilary atresia | Cystic fibrosis related Liver disease | 35.9 | 6.5 | 56  | 3.2  | 2   | 1.3 | 1.1 | 1.4          |
| 31      | 14     | 43.5       | F      | W    | Hepatobiliary sclerosis and thrombosis of the portal vein | Cystic fibrosis related Liver disease | 31.4 | 4.7 | 184 | 2.4  | 1.3 | 2   | 1.3 | 1.1          |
| 32      | 10     | 36.9       | M      | W    | Bilary atresia | Cystic fibrosis related Liver disease | 37.8 | 4.7 | 184 | 2.4  | 1.3 | 2   | 1.3 | 1.1          |
| 33      | 14     | 45.7       | M      | AA   | Bilary atresia | Cystic fibrosis related Liver disease | 37.8 | 4.7 | 184 | 2.4  | 1.3 | 2   | 1.3 | 1.1          |
| 34      | 15     | 65.2       | M      | AA   | Primary sclerosing cholangitis | Cystic fibrosis related Liver disease | 37.8 | 4.7 | 184 | 2.4  | 1.3 | 2   | 1.3 | 1.1          |

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shown in Table 1. The most common indication for TIPS placement was secondary prevention of gastrointestinal bleeding (n = 23, 68%). Primary prevention of gastrointestinal bleeding as the sole indication for TIPS was undertaken in only two cases (6%) when there was a perceived high risk of variceal bleeding because of large gastric varices seen on endoscopy. We do not routinely endoscopically survey patients with portal hypertension endoscopically unless there is an intention to intervene or another indication. TIPS was placed in three cases to maintain portal flow; two cases had extensive splanchic thromboses associated with fibrotic liver disease, and the third, with cirrhosis secondary to autoimmune hepatitis, had a large splenic artery aneurysm embolized with coils. Acute TIPS placement for exsanguinating bleeding, from rupture esophageal varices that were uncontrollable endoscopically, occurred in two children. Refractory ascites (n = 2, 6%) and massive splenomegaly (n = 3, 9%) accounted for the remaining indications. There were two patients whose indications were splenomegaly and their outcomes are discussed below (Patients #25 and #26).

Technical success was seen in all patients, and clinical success was observed in all except Patients #20 and #25. A covered endoprosthesis (Viatorr; WL Gore, UK) was used in 32 patients (94%) and uncovered (Wallstent, Schneider, UK) was used in only two patients (6%). Covered endografts are generally preferred. One uncovered stent was placed in 2005 because a covered stent was unavailable at the time of the procedure (Patient #34). Since then, our practice has adapted to current literature and covered stents are almost exclusively used. The remaining uncovered stent was used for a palliative TIPS in a narrowed hepatic venous outflow tract where an uncovered stent was less likely to cause an acute outflow obstruction by walling off drainage from other hepatic veins (Patient #15). Co-axial stents were placed when necessary to extend the TIPS superiorly to the confluence of the hepatic vein. Further details including stent position, gradient changes, post-operative anticoagulation, and clinical success are shown on Table 2. Of note, six patients (Patient #3, 7, 11, 22, 24, 25) with PSG of less than 12 mm Hg had sequelae of portal hypertension including 3 with gastroesophageal bleeding. Gradients as low as 8 mm Hg (Patient #24) were noted in our population with significant gastrointestinal bleeding secondary to portal hypertension. All of these patients were noted to have clinical success following TIPS placement. Additionally, their ages ranged from 2 to 17 without clear age discrepancies. There were no reported difficulties specific any single etiology of PHTN.

One patient (3%) had a major complication of continued variceal bleeding and hemoperitoneum and went on to transplant 3 days later (Patient #20). Patient #25 was not willing to be excluded from all sports activities due to spleen size, and the TIPS was placed for palliation and quality of life. That patient did not have clinically significant improvement in splenomegaly following TIPS placement. An adolescent with cystic fibrosis-associated liver disease (Patient #26) had splenomegaly (28 cm maximum diameter) significant enough to interfere with pulmonary function and contributed to abdominal discomfort causing poor quality of life. She was not a transplant candidate due to multiple drug-resistant active infections and was at end-stage liver and lung disease. A multidisciplinary discussion was had, and the decision was made to place a TIPS for palliation recognizing that splenomegaly may not improve as an attempt to improve quality of life. There was significant reduction in spleen size to 22 cm and abdominal discomfort improved. However, due to infections and underlying cystic fibrosis, lung function continued to deteriorate.

There were minor complications in eight patients (24%) with the most common being hyperammonemia with encephalopathy (n = 5, 15%). These patients were treated with lactulose and/or rifaximin and had resolution of clinical symptoms. Patients #1, 3, 7, 20, 27, and 34 underwent liver transplantation due to progression of underlying

![FIGURE 1](image.png) Radiographic images of TIPS placement in Patient #13. 18-year-old female with hepatoportal sclerosis and portal hypertension complicated by gastroesophageal variceal bleeding. Portal venogram following transhepatic portal venous access (A) demonstrates patent but diminutive intrahepatic portal veins (open arrow) as well as markedly enlarged coronary vein (white arrow) supplying gastroesophageal varices. Portal venogram following placement of a 10 mm × 6 cm × 2 cm Viatorr endograft (WL Gore and Associates, Flagstaff, AZ, USA) (B) demonstrates brisk portal outflow through the TIPS and non-visualization of the previous collateral pathways.
| Patient | Endograft hardware material (mm × cm) | Stent position | Gradient (mm Hg) | Post-operative anti-coagulation? | Complications? | Outcome (time to transplant or death) |
|---------|--------------------------------------|----------------|-----------------|---------------------------------|----------------|-----------------------------------|
| 1       | V (size unknown)                     | RHV Portal     | 14              | No                             | HE             | Transplanted (U)                   |
| 2       | V 10 × 8                             | RHV Portal     | 9               | No                             | No             | Transplanted (2 mo)                |
| 3       | Two V 8 × 4                          | MHV SMV        | 13              | No                             | No             | Primary assisted patency           |
| 5       | V 8 × 6                              | CHV MPV        | 30              | No                             | No             | Primary patency                    |
| 6       | V 8 × 4                              | RHV MPV        | 20              | No                             | No             | Primary patency                    |
| 7       | V 10 × 6                             | CHV MPV        | 10              | Heparin                        | Melena with prophylactic aspirin | Transplanted (5 mo)                |
| 8       | V 10 × 6                             | CHV MPV        | 12              | No                             | HE             | Primary patency                    |
| 9       | V 10 × 6                             | CHV RPV        | 13              | Heparin                        | Small non-occlusive portal thrombus | Primary patency                   |
| 11      | V 10 × 8 and 10 × 6                  | CHV MPV        | 10              | Heparin                        | No             | Primary patency                    |
| 12      | V 10 × 6                             | CHV MPV        | 12              | No                             | No             | Primary patency                    |
| 13      | V 10 × 8                             | RHV RPV        | 13              | No                             | No             | Primary assisted patency           |
| 14      | V 10 × 8                             | RHV RPV        | 15              | No                             | No             | Primary patency                    |
| 15      | Two W 12 × 60                        | RHV MPV        | 20              | Heparin                        | No             | Death (17 mo)                      |
| 16      | V 10 × 8                             | CHV SV-SMV     | 18              | No                             | No             | Primary patency                    |
| 17      | V 10 × 8                             | IVC MPV        | 23              | No                             | No             | Secondary patency                  |
| 18      | V 10 × 8 constrained by E 6 × 27     | RHV MPV        | 13              | No                             | No             | Death (24 mo)                      |
| 19      | V 10 × 8 constrained by E 6 × 27     | RHV RPV        | 16              | Enoxaparin                     | No             | Primary patency                    |
| 20      | Two V 10 × 8 constrained by E 6 × 27 | MHV LPV        | 12              | No                             | Continued bleeding | Transplanted (3 d)                |
| 21      | Two V 10 × 8 constrained by E 6 × 27 | RHV RPV        | 15              | Alteplase/heparin              | No             | Occlusion                          |
| 22      | Two V 10 × 8                         | RHV RPV        | 10              | Heparin                        | HE             | Primary patency                    |
| 23      | Two V 8 × 6                          | RHV CPV        | 4               | No                             | HE             | Occlusion                          |
| 24      | V 8 × 6                              | RHV RPV        | 8               | Heparin                        | No             | Primary patency                    |
| 25      | V 8 × 8                              | RHV RPV        | 10              | No                             | HE             | Primary assisted patency           |

(Continues)
disease. The remaining patients did not require liver transplantation following TIPS placement. Patients #15, 18, and 26 eventually died due to complications of end-stage disease despite TIPS placement. Time to death was 17 months, 24 months, and 8 months following TIPS placement, respectively. None of the patients who died were considered to be transplant candidates. Patient #15 had chronic rejection from non-adherence and was not felt to be an appropriate candidate and declined evaluation at another center. Patient #18 had a multisystem genetic disorder (GLIS3 mutation) that precluded her from liver transplant. Patient #26 had pulmonary failure from cystic fibrosis that precluded liver transplantation during her decompensation. At the time of writing, patency has been maintained in 24 patients of the 25 patients who still have the shunt in situ with median follow-up of 24 months (range 4-69 months) following initial placement. Patency was maintained in 31/31 patients (100%) at 1 month and 29/29 patients (100%) at 6 months. At 12 months, 21/23 (91%) continued patency. At 24 months, there were 12/14 patients (86%), and beyond 24 months, there were 12/13 patients (92%) with preserved patency. Of the patients who survived without transplant, 18/25 (72%) had primary patency, 4/25 (16%) had primary assisted patency, and 1/25 (4%) had secondary patency at the time of their most recent follow-up. Two patients eventually occluded their TIPS, but achieved control of symptoms regardless. Patient #21 was found to be occluded after transition to an adult provider maintaining control of symptoms. Patient #23 occluded, but on follow-up imaging it was found that previously occluded distal splenorenal shunt had recanalization.

Standard biochemical and hematological parameters following placement of TIPS are shown on Figure 2. A significant increase in hematocrit was observed over the observational interval \((T = -2.13, P = 0.04)\), with weak trends observed for ALT, ammonia, and INR (ALT: \(T = -1.34, P = 0.19\), ammonia: \(T = -1.48, P = 0.15\), INR: \(T = -1.49, P = 0.14\)). No differences were observed between these paired measures for albumin, WBC count, or platelets (albumin: \(T = -0.6, P = 0.55\), WBC: \(T = 0.69, P = 0.49\), platelets: \(T = 0.41, P = 0.68\)). Evaluating those subjects with non-parenchymal liver disease (Patients #5, 13, 16, 17, 18, 21, 22, 23, 24, 31) did not demonstrate any differences among blood measures (data not shown), with the trend for hematocrit still present in the patients with parenchymal liver disease \((T = -1.65, P = 0.11)\).

### 4 | DISCUSSION

In pediatric portal hypertension, TIPS is becoming an established treatment option for select patients. Previously only reported in small single-center case series, there is increasing evidence that TIPS is feasible, safe, and effective when performed by experienced teams. With the introduction of covered stents, TIPS has been demonstrated to be durable shunt options that limit life-threatening complications of portal hypertension such as gastrointestinal bleeding. This is still accompanied by a risk of hyperammonemia and the need for dietary restriction/medication...
administration, shunt occlusion and the prospect of future interventions, and late term complications. It is not clear, however, whether surgical shunts, including selective shunts such as distal splenorenal shunts, carry fewer risks over time. With our study, we report our experience with pediatric TIPS placement and with a focus on indications, pressure measurements, laboratory changes over time, and outcomes.

In our case series, we reported our indications for TIPS placement. The Baveno V Consensus Workshop on Methodology of Diagnosis and Therapy in Portal Hypertension mainly discusses the use of TIPS in cases of medication and endoscopic treatment failure for gastrointestinal bleeding. Primary prevention of gastrointestinal bleeding was reserved for patients with large gastric varices that were not amenable to medical or endoscopic therapy or did not have ready access to adequate emergent pediatric care. Johansen et al had similar indications to our patient population including recurrent variceal bleeding (n = 35), refractory ascites (n = 4), and hypersplenism (n = 1) with similar underlying etiologies of portal hypertension. However, their group did not use TIPS in the setting of cavernous transformation of the portal vein.

Of note, 18% of patients (6/34) did not have a PSG ≥ 12 mm Hg (one patient’s gradient was as low as 8 mm Hg with gastrointestinal bleeding from varices). There was no unifying characteristic between these six patients such as continued use of beta-blockers or octreotide during the procedure; however, two patients had congenital hepatic fibrosis and another two had cavernous transformation of the portal vein. The Baveno V Consensus Workshop recommends using adult guidelines for the identification of high-risk portal hypertension in pediatrics while acknowledging that there needs to be further research into prognostic indicators of high-risk bleeding. In the adult literature, PSG greater than 10 mm Hg can be associated with varix formation while PSG above 12 mm Hg is predictive of

![FIGURE 2](image_url)

**FIGURE 2** Biochemical and hematological laboratory parameters following TIPS placement. Laboratory values plotted in 10 logarithmically spaced bins shown in boxplots at top (median, 25th, and 75th percentiles shown, + symbols outliers). Labels on x-axis reflect the upper bound of bin in days (e.g., 7 goes from 0 to 7, 12 from 7 to 12). Weak trends (P’s < 0.19) were observed for ALT, ammonia, and INR with hematocrit showing increases across the time interval (P < 0.04)
Many pediatric patients, especially those with extrahepatic portal vein obstruction, accommodate patient growth. Meanwhile, updated guidance for initial stent construct as well as revision techniques to placement of TIPS is substantially shorter than surgical shunt placement. Determining clinical superiority. Recovery time in the hospital following TIPS placement often times related to underlying thrombosis (Patients 15, 21, 22, 31); this did not appear to affect long-term patency. Many pediatric patients, especially those with extrahepatic portal vein obstruction (cavernous transformation of the portal vein), may never require liver transplantation. Therefore, long-term durability of TIPS is paramount and warrants reporting of long-term results as they become available. For TIPS placed in children with additional growth potential, long-term follow-up will provide additional guidance for initial stent construct as well as revision techniques to accommodate patient growth. Meanwhile, updated comparison of pediatric TIPS to surgical portosystemic shunts is required to determine clinical superiority. Recovery time in the hospital following placement of TIPS is substantially shorter than surgical shunt placement. Of the six patients (18%) who were bridged to transplantation, one patient had recurrence of bleeding episode and was subsequently transplanted. The remaining cases progressed to transplantation without significant complications. There were three deaths (9%) following TIPS placement, but these patients were not considered as candidates for transplant. Current adult guidelines do not recommend TIPS placement in patients with high-risk 30-day mortality such as MELD >15. However, MELD is not equivalent to PELD and all three patients who died had clinical resolution of their portal hypertensive sequelae. Their time from TIPS placement to death of 8, 17, and 24 months was significantly longer than 30 days.

Limitations to our study include the retrospective nature of our protocol, and some patient data sets were more than 10 years post-procedure with parts of data being unavailable to record into our database. As discussed above, there is no gold standard of indication and treatment to compare our case series to. There is a wide heterogeneity of our small patient population, and the age range is wide from young infants to young adults. The underlying liver diseases and comorbidities were variable with no single etiology reaching a majority of our cases which is also reflected on the wide range of indications for TIPS in our patient population. Lastly, our results may simply reflect our local situation (Interventional Radiology expertise available, patient pool) rather than a generalizable best practice.

Our experience with pediatric portal hypertension and TIPS is one of the largest currently available single institution case series in the published literature. TIPS creation is a safe and effective treatment of complications of pediatric portal hypertension and can be used as a bridge to transplantation. While further studies are needed to clarify the PSG that place children at high risk of variceal bleeding, our results suggest that extrapolating from adult literature sets a threshold not sufficiently sensitive and children may be susceptible to sequelae at lower PSG measurements. Laboratory values were found to be stabilized after TIPS placement with an increasing hematocrit over time. The TIPS procedure should be considered a safe alternative to surgical portosystemic shunts when technically feasible.

CONFLICTS OF INTEREST
The authors deny any conflicts of interest for this study.

AUTHOR’S CONTRIBUTIONS
VS, EM, SF, EH, and SH: Conceived and designed study; VS: Acquired the data; VS, EM, SF, EH, and SH: Analyzed and interpreted the data; VS, EM, EH, and SH: Drafted the manuscript; and VS, EM, SF, EH, and SH: Revised and approved the manuscript.

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