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Propensity-matched comparison of transjugular intrahepatic portosystemic shunt placement techniques: Intracardiac echocardiography (ICE) versus fluoroscopic guidance

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ABSTRACT

Purpose: To compare procedure characteristics and outcomes when TIPS is performed under intracardiac echocardiography guidance (iTIPS) compared to conventional fluoroscopic guidance (cTIPS).

Materials and methods: A retrospective propensity-matched study of 30 iTIPS and 30 cTIPS procedures from January 2014 to March 2017 at a single US high volume academic medical center was performed. iTIPS and cTIPS cases were propensity score matched using predictive variables: age, race, gender, etiology of liver disease, indication for TIPS, MELD score, and portal vein patency. Procedure characteristics and post- procedure outcomes were compared between propensity-matched groups including: total procedure time, technical success, radiation dose, contrast volume, complication rate, 30- day mortality, and revision rate within 3 months.

Results: Radiation dose (875.3 vs 457.4 mGY, p = 0.039) and contrast volume (141 vs 103 mL, p = 0.005) were significantly decreased in the iTIPS versus the cTIPS group. There was no significant difference in procedure time (81.5 cTIPS vs 84 min iTIPS) or rate of TIPS revisions within 3 months. Average operator experience in the iTIPs group was 4.2 years and cTIPS group 11.0 years (p = 0.0004). All procedures were technically successful with no mortalities within 30 days.

Conclusion: iTIPS resulted in significantly reduced radiation dose and contrast volume. However, there was no difference in total procedure time or overall outcomes despite greater operator experience in the cTIPS group.

1. Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) placement has become an important treatment option to reduce the portosystemic gradient in portal hypertension patients.

since its initial description in 1969 by Rösch et al. [1] followed by multiple studies demonstrating safety and efficacy [2]. Despite becoming a common procedure, it can still be technically challenging. Technically, the most challenging step in TIPS creation is obtaining access into the portal vein.

Conventional TIPS (cTIPS) placement technique relies upon fluoroscopically guided needle passes through the hepatic parenchyma from a hepatic vein to a portal vein. One of the challenges of portal vein cannulation is the two dimensional nature of venography, which makes precise localization of the portal vein difficult. Initial guidance is typically obtained by wedge carbon dioxide portography in multiple projections. Intracardiac echocardiography (ICE) provides direct visualization of the portal vein, which allows for operators to directly visualize the path of the needle used to access the portal vein. However, the use of ICE carries a steep learning curve that requires understanding anatomic relationships from a longitudinal side-firing probe.

Initial reports utilizing ICE for portosystemic shunt creation describe utility of the tool for direct intrahepatic portosystemic shunt placement [3] and TIPS placement [4,5]. Later retrospective case series compared outcomes between cTIPS and ICE-guided TIPS (iTIPS), demonstrating decreased fluoroscopy time, procedure time and radiation dose [6,7] as well as a decreased number of needle passes [8]. However, given the lack of case matched controls, potential confounders include a

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disparate distribution of case complexity and ever-increasing technical expertise with the more recent cases of iTIPS.

Given the limitations of previous studies including inherent selection bias that results from heterogeneous, non-randomized cohorts comparing these TIPS placement methods is warranted. The purpose of this study is to compare procedure characteristics and outcomes when TIPS is performed under intravascular ultrasound guidance (iTIPS) compared to conventional fluoroscopic guidance (cTIPS) after propensity matching to control for relevant demographic and anatomic characteristics.

2. Materials and methods

A retrospective review of consecutive patients undergoing TIPS procedures performed between January 2014 and March 2017 was conducted at a single academic institution, after approval by the institutional review board. Demographic and anatomic characteristics of all TIPS cases performed over this period were obtained.

2.1. Technique

Initial access was gained through the right internal jugular vein and placement of a 10 French vascular sheath (Cook Medical, Bloomington, IN) was obtained for both TIPS procedures. All iTIPS procedures used a side-firing variable 5–10 MHz intravascular ultrasound or intracardiac echocardiography catheter (ACUSON, AcuNav; Siemens Medical Solutions, Mountain View, California) connected to a GE Vivid ultrasound machine (GE, Boston, MA) for guidance (Fig. 1) placed through a 10 French vascular sheath from the right common femoral vein. Selection of an appropriate hepatic vein was performed with a 5 French catheter using fluoroscopic guidance only or in combination with ICE guidance for iTIPS. For cTIPS, wedged CO_2 venography was performed to identify the portal vasculature, followed by puncture of the portal vein under fluoroscopic guidance using a Colapinto needle and catheter combination (Cook Medical, Bloomington, IN). For iTIPS, the ICE catheter was positioned within the retrohepatic IVC to visualize the relationship between the hepatic and portal veins. Continous ICE guidance was used to map and monitor the course of the Colapinto needle through the hepatic parenchyma and portal vein puncture. After wire and catheter access of the portal vein, simultaneous portal and hepatic contrast venography was performed for both TIPS procedures. Both right atrial and direct portal pressures were obtained to result in a pre-TIPS portosystemic gradient. The hepatic parenchyma tract was dilated with an 8 mm balloon and an appropriate length 8 mm or 10 mm Viatorr TIPS Endoprosthesis stentgraft (W. L. Gore & Associates, Inc., Flagstaff, AZ), depending on the portosystemic gradient, and clinical indication. In the case of iTIPS, ICE was used to ensure that the uncovered portion of the Viatorr stentgraft was properly positioned at the portal puncture site before full deployment. The deployed Viatorr stentgraft was then dilated with an appropriately sized (8 mm or 10 mm) high pressure balloon (Conquest, Bard, Murray Hill, NJ). Post-TIPS deployment portosystemic gradient and venography were performed (Fig. 2).

2.2. Propensity matching

Propensity matching was performed due to the inherent selection bias that results from heterogeneous, non-randomized cohorts. Propensity matching is the most aggressive statistical method to control for patient background variables in a cohort study, ensuring that explanatory variables each group were similarly distributed. This method has been shown in multiple studies to observationally mimic randomized control trials [9]. Propensity score matching was used to create iTIPS and cTIPs groups with similar baseline characteristics. Study investigators were blinded to procedure characteristics and outcomes during the creation of propensity-matched groups. The propensity score

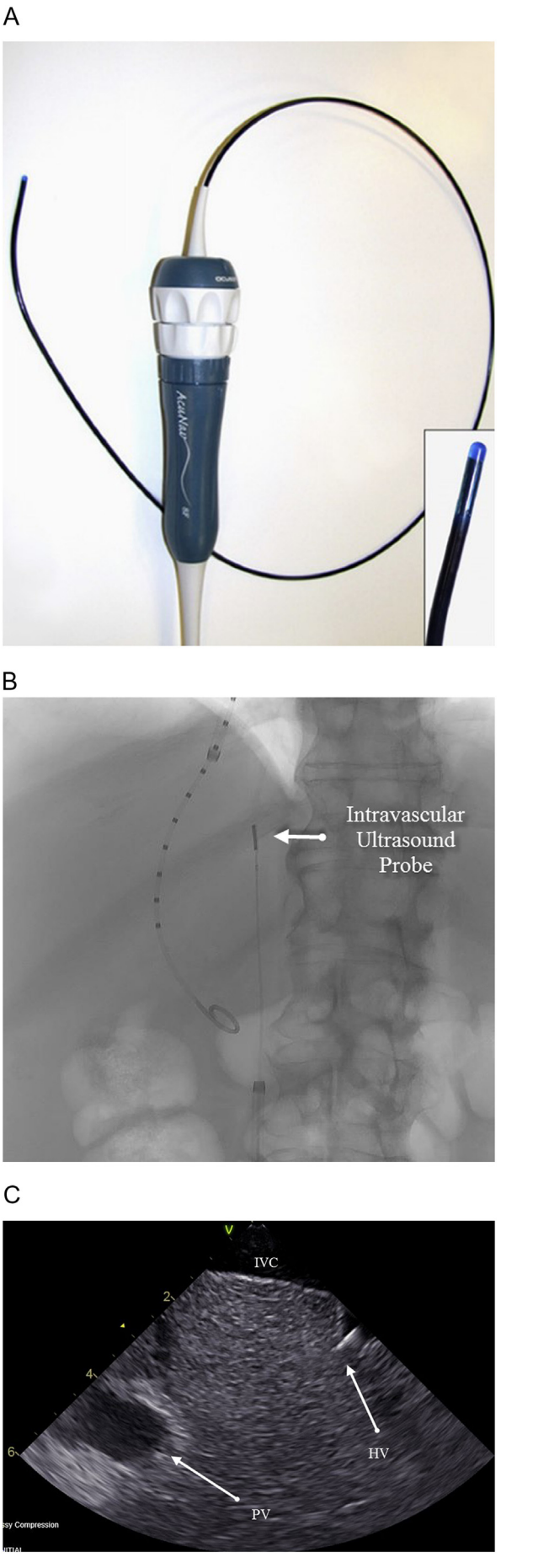

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Fig. 1. ICE catheter apparatus. A) Image of the ICE catheter apparatus. The catheter tip (inset consists of a longitudinal side-firing variable 5 to 10-MHZ prove (ACUSON AcuNav; Siemens Medical Solutions, Mountain View, California). B) Fluoroscopic image obtained during iTIPS placement demonstrates the position of the ICE probe tip within the retrohepatic IVC in relation to the catheter in the middle heptic vein. C) ICE images during portal vein puncture demonstrates the relationship between the IVC (where the ultrasound probe is situated), hepatic vein (HV), and portal vein (PV).

was estimated using a logistic regression model with the group as the dependent variable and the following variables as potential confounders: sex, race (Caucasian/African American), age, BMI, insurance type, presence of ascites, portal vein patency, etiology of liver disease, indication for TIPS placement, original MELD score, bilirubin, INR, creatinine, sodium, albumin and platelet level. The matching process used a 1:1 nearest neighbor method within specified caliper widths (caliper = 0.20*standard deviation [logit of the propensity score]) without replacement [10]. After matching, the balance of covariates was evaluated. The absolute standardized differences of the covariates for the unmatched and matched cohorts were compared between the iTIPS and matched cTIPS patients. Standardized differences greater than 0.1 have been shown to indicate some covariate imbalance between matched groups [11].

Once matched groups were created, outcome data was collected for all iTIPS and cTIPS procedures, which were successfully matched. Evaluated outcomes included: contrast volume, radiation dose, total procedure time, time from internal jugular vein (IJV) puncture to portal vein access, technical success, complications, extracapsular punctures, 30 day mortality, and 3 month TIPS revision rate. Comparisons between the matched groups for dichotomous outcomes were performed using McNemar's test and continuous variables were compared using a paired *t*-test.

3. Results

Over a thirty-eight month period, 40 iTIPS procedures were performed. Out of these cases, 30 iTIPS cases were successfully propensity score matched to 30 of out 200 cTIPS cases. Overall, 12/30 (40%) of each group were male and 28/30 (93.3%) were Caucasian. The average age in the cTIPS group was 56.3 years and the average age in the iTIPS group was 56.7 years. Additional demographic information for all matched subjects is presented in Table 1.

The most common etiologies for liver disease were non-alcoholic steatohepatitis (NASH) and alcoholic cirrhosis in both groups with the most common indication for TIPS placement being refractory ascites or hepatic hydrothorax. The average Model for End- Stage Liver Disease (MELD) score in the cTIPS group was 13.1 and the average MELD score in the iTIPS group was 12.8. 26/30 (86.7%) of portal veins were patent in the cTIPS group compared to 28/30 (93.3%) in the iTIPS group. Additional pre-procedure characteristics are presented in Table 2.

The average total procedure time in the cTIPS group was 81.5 ± 47.0 min compared to 84.0 ± 33.6 min in the iTIPS group. All

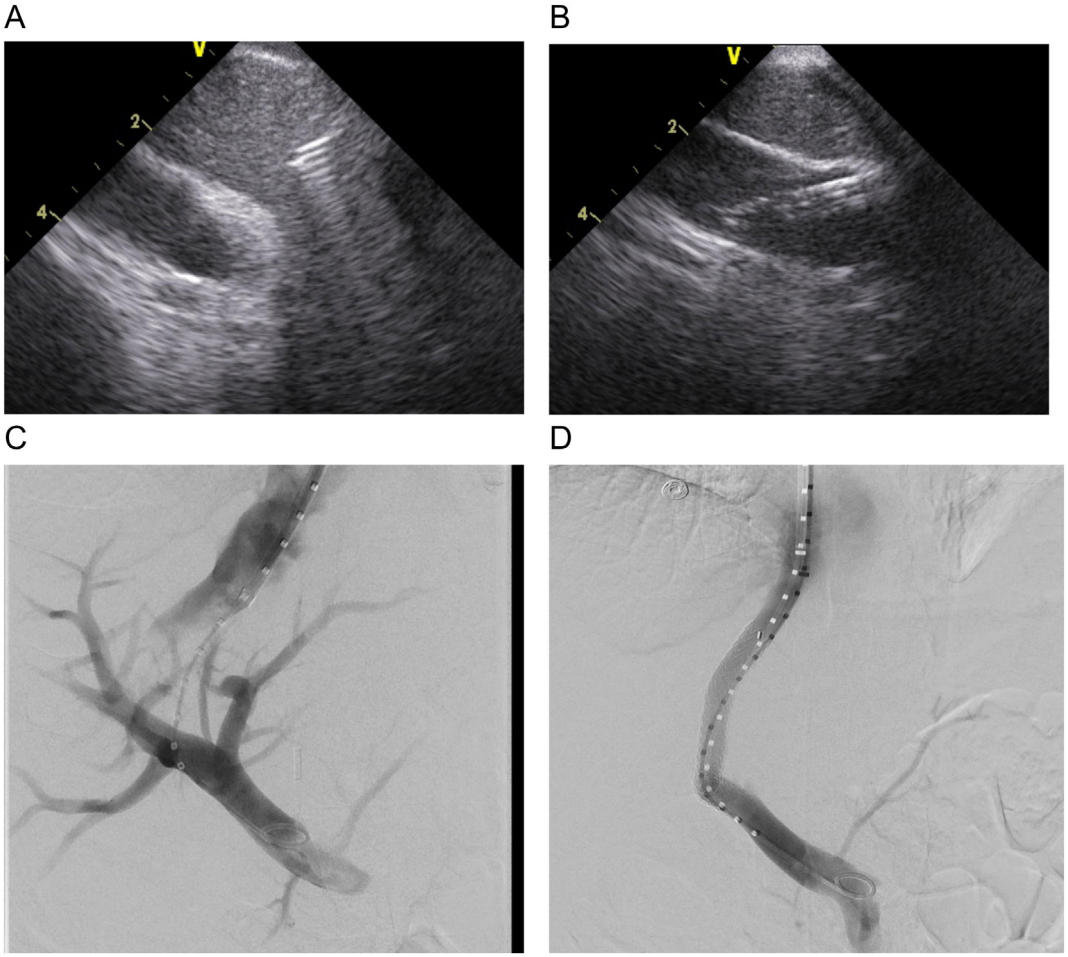

Fig. 2. iTIPS Procedure. 53 year old male with portal hypertension with a refractory ascites and esophageal varices. A side firing ICE catheter was used obtain images of the portal vein relationship to the hepatic veins in a sagittal plane. A single pass was made from the middle hepatic vein into the right portal vein (A, B) with clear visualization of the needle traversing the hepatic parenchyma. Venogram following entry into the portal vein (C) demonstrates access into the portal vein. Following TIPS placement (D) a venogram was obtained which showed appropriate stent placement.

Table 1
Demographic information used for propensity score matching.

		cTIPS (n = 30)	iTIPS (n = 30)	Standardized differences (unmatched)	Standardized differences (matched)
Age, mean (SD)	–	56.3 (9.8)	56.7 (11.9)	0.13162	0.04274
BMI, mean (SD)	–	32.9 (7.8)	30.5 (7.9)	0.12515	0.31032
Sex, n (%n)	Male	12 (40%)	12 (40%)	0.35839	0.00000
	Female	18 (60%)	18 (60%)		
Race, n (%n)	Caucasian	28 (93.3%)	28 (93.3%)	0.06845	0.00000
	African American	2 (6.7%)	2 (6.7%)		

cases were technically successful. There was no statistically significant difference in total procedure time, internal jugular vein puncture to portal vein access time, technical success rate, complication rate, 30 day mortality rate or TIPS revision rate between the propensity-matched cTIPS and iTIPS groups (Table 3).

Radiation dose and contrast volume were significantly lower in the iTIPS group. The reference point air kerma in the cTIPS group was 875.277 ± 838.826 compared to.

457.414 ± 554.022 in the iTIPS group ($p = 0.0390$). The contrast volume in the cTIPS group was significantly higher at 141.167 mL ± 59.650 compared to 102.667 mL ± 47.192 in the iTIPS group ($p = 0.0054$). The average operator experience in the iTIPS group was 4.2 years and the average operator experience in the cTIPS group was 11.0 years ($p = 0.0004$).

4. Discussion

TIPS placement is equally safe and successful whether it is performed using the cTIPS technique or the iTIPS technique. After propensity-matching for several key factors including etiology of liver disease, indication for TIPS placement, MELD scores and anatomic considerations, the total procedure time, complication rates, and revision rates are comparable between the iTIPS and cTIPS groups despite significantly greater operator experience in the cTIPS group.

Table 2
Pre-procedural characteristics used for propensity score matching.

		cTIPS (n = 30)	iTIPS (n = 30)	Standardized differences (unmatched)	Standardized differences (matched)
Etiology of liver disease, n (%n)	Alcohol	6 (20.0%)	8 (26.7%)	0.10120	0.15811
	Alcohol + Viral	1 (3.3%)	1 (3.3%)	0.00000	0.00000
	Viral	3 (10.0%)	4 (13.3%)	0.21909	0.10398
	NASH	11 (36.7%)	10 (33.3%)	0.17108	0.06993
	PBC/PSC	2 (6.7%)	0 (0%)	0.02351	0.37796
	Other	7 (23.3%)	7 (23.3%)	0.09920	0.00000
Indication for TIPS placement, n (n %)	Hydrothorax/refractory ascites	26 (86.7%)	23 (76.7%)	0.00000	0.26062
	Secondary variceal bleeding	3 (10.0%)	6 (20.0%)	0.17101	0.28284
	Thrombosis	1 (3.3%)	1 (3.3%)	0.03372	0.00000
Presence of ascites, n (n%)	Present	26 (86.7%)	24 (80.0%)	0.19861	0.17961
	Not present	4 (13.3%)	6 (20.0%)		
Portal vein patency, n (%n)	Patent	26 (86.7%)	28 (93.3%)	0.13523	0.22361
	Non-occlusive thrombus	3 (10.0%)	1 (3.3%)	0.31270	0.26968
	Occlusive thrombus	1 (3.3%)	1 (3.3%)	0.08467	0.00000
Original MELD score, mean (SD)	–	13.1 (4.1)	12.8 (3.5)	0.03186	0.08790
Bilirubin, mean (SD)	–	1.4 (1.6)	1.3 (0.8)	0.07924	0.06665
INR, mean (SD)	–	1.3 (0.21)	1.3 (0.22)	0.05479	0.07730
Creatinine, mean (SD)	–	1.3 (0.64)	1.3 (0.61)	0.04261	0.03354
Sodium, mean (SD)	–	136 (4.9)	137 (4.4)	0.01409	0.14983
Albumin, mean (SD)	–	3.2 (0.59)	3.2 (0.63)	0.11860	0.07091
Platelets, mean (SD)	–	137 (90.1)	126 (79.5)	0.16266	0.14199

Table 3
TIPS outcomes.

		cTIPS	iTIPS	p-Value
Total procedure time (minutes), mean (SD)	–	81.5 (47.0)	84 (33.6)	0.8281
Internal jugular vein puncture to portal vein access time (minutes)	–	62.7 (49.5)	53.5 (30.9)	0.4237
Technical success, n (%n)	–	30 (100.0%)	30 (100.0%)	*
Complications, n (%n)	Hemoperitoneum	0 (0.0%)	1 (3.33%)	*
	Extracapsular puncture	6 (20.00%)	5 (16.67%)	0.7055
Mortality within 30 days, n (%n)	–	0 (0.0%)	0 (0.0%)	*
Revision within 3 months, n (%n)	–	2 (6.67%)	3 (10.00%)	0.6547
Contrast Volume (mL), mean (SD)	–	141.17 (59.7)	102.67 (47.2)	**0.0054**
Reference Point Air Kerma (mGy), mean (SD)	–	875.28 (838.83)	457.41 (554.02)	**0.0390**

The asterisk indicates that a p-value was not able to be calculated based on the collected data.
Bold indicates a statistically significant difference between the two groups.

The most clinically significant advantage of iTIPS is the measurable radiation dose savings to the patient. It can also be extrapolated that radiation dose exposure to the operator, nursing staff, and technologist are decreased. As the hepatic and portal veins are directly visualized, iTIPS obviates the need for wedged carbon dioxide portograms, which are radiation intensive. It also avoids the risks of portograms including the potential for parenchymal laceration and subcapsular hematomas [12,13].

iTIPS also offers the advantages of significantly decreased contrast volume, which is in accordance with previous studies [6–8]. However, it is difficult to definitively ascertain whether the absolute amount of contrast saved leads to a decrease in contrast-induced nephropathy. These advantages may prove worthwhile despite the potential need for a second venous puncture site and a second pair of skilled hands, familiar with iTIPS.

Additionally, it is worthwhile to note that while the total procedure times for iTIPS and cTIPS cases were comparable, the time is spent on different tasks. In particular, in the iTIPS group, additional time is required to obtain secondary venous access, identify the portal and hepatic veins, and plan an adequate path between the two. In the cTIPS group, this additional time is spent performing the portogram and ultimately taking passes through the hepatic parenchyma, which can add potential risk.

Criticisms of the use of intravascular ultrasound are the steep learning curve, potential need for a second operator, and cost. Regardless of the procedure, a learning curve is always present when using new technologies. In the current study all cases were performed with a second access in the right common femoral vein with a separate operator driving the ultrasound. It is possible to remove the need for a second operator if side-by-side access is obtained via the right IJV. The cost of an individual ICE probe is roughly $1000 per use with many hospitals currently owning compatible ultrasound machines.

There are several limitations to this study. There is a retrospective study and after propensity-matching there was a limited sample size in each cohort which makes comparing outcomes challenging. The choice of TIPS placement method was not randomized or standardized amongst operators. As expertise with the ICE catheter increased, procedure times decreased and there probably was a bias that developed against using fluoroscopy. There is the potential of limited applicability to other centers due to the inherent cost of obtaining an intracardiac echocardiography probe and compatible ultrasound.

The results of this study validate some of the findings of prior retrospective case series examining results between iTIPS and cTIPS patients including decreased radiation dose and contrast usage [6–8]. However, in the current study after propensity matching, overall procedure time was not significantly lower in the iTIPS group compared to the cTIPS group. Potential reasons for this disparity include the presence of several experienced TIPS operators (greater than 10 years of experience) at our institution leading to an overall optimized cTIPS technique, leaving little room for improvement in efficiency, compared to a more junior group of operators (less than 5 years of experience) utilizing the iTIPS technique. As a result, future studies are warranted to evaluate the effect controlling for operator experience on a propensity-matched analysis of iTIPS compared to cTIPS cases.

5. Conclusion

The introduction of intravascular US guidance for TIPS creation has changed our institutional practice. Most TIPS cases at our institution are now performed with ICE guidance which has led to significant reductions in radiation exposure to the patient and staff. Total procedural time did not change between the two methods of TIPS placement owing to the experience of operators that perform conventional TIPS. ICE is particularly useful for operators that have limited experience in TIPS placement. Prospective studies comparing TIPS placement methods are warranted for future investigation.

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