# Association Between Institutional Factors and Long-Term Survival Following Transjugular Intrahepatic Portosystemic Shunt

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**Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure designed to treat portal hypertension. Hospital teaching status is an institutional factor found to be predictive of outcomes following several complex procedures; however, its impact on outcomes following TIPS is unknown. The aim of this study was to determine the association between hospital teaching status and long-term survival in patients with cirrhosis receiving TIPS. We performed a retrospective population-based cohort study using linked administrative health data from Ontario, Canada. Adult patients with cirrhosis who received TIPS between January 1, 1998, and December 31, 2016, with follow-up until December 31, 2017, were included. Hospital teaching status was defined based on hospital participation in the instruction of medical students and/or resident physicians. Liver transplant-free (LTF) survival was evaluated using Kaplan-Meier analysis, and overall survival was assessed using competing risks regression analysis, which accounted for hospital clustering. A total of 857 unique patients were included (mean age 57.1 years; 69.1% male). The TIPS procedures were performed in teaching hospitals (84.3%) as well as nonteaching hospitals (15.7%). Median LTF survival was more than twice as long for procedures performed in teaching hospitals compared to nonteaching hospitals (2.2 years versus 0.9 year, respectively; *P* < 0.001). After adjusting for confounders and clustering, hospital teaching status was not independently associated with mortality (nonteaching subdistribution hazard ratio [sHR], 1.32; 95% confidence interval [CI], 0.97-1.81; *P* = 0.08); however, annual hospital procedure volume was (per unit increase sHR, 0.96; 95% CI, 0.93-0.99; *P* = 0.003). *Conclusion:* Hospital procedure volume is associated with long-term survival following TIPS. These results further support the centralization of TIPS to high-volume hospitals to improve long-term outcomes in this population. (*Hepatology Communications* 2019;3:838-846).**

Cirrhosis is the tenth most common cause of mortality in the United States,(1) and the burden of disease is growing, with increases demonstrated in both the incidence and prevalence of cirrhosis over the past 2 decades.(2) Portal hypertension and liver synthetic dysfunction are the two major mechanisms of morbidity and mortality in patients with cirrhosis.(3) Portal hypertension is responsible for the development of gastroesophageal varices, ascites, hepatic hydrothorax, and hepatorenal syndrome. Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure designed to treat portal hypertension

*Abbreviations: CI, confidence interval; GI, gastroenterology; IQR, interquartile range; LTF, liver transplant-free; MELD, Model for End-Stage Liver Disease; OHIP, Ontario Health Insurance Program; sHR, subdistribution hazard ratio; TIPS, transjugular intrahepatic portosystemic shunt; VA, Veterans Affairs.*

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and its sequelae by inserting a stent between the portal vein and the hepatic vein under fluoroscopic guidance. Meta-analyses of randomized controlled trials have established that the use of TIPS results in decreased rebleeding rates compared to endoscopic therapy in patients with recurrent variceal bleeding[4] as well as improved control of ascites and transplant-free survival compared to therapeutic paracenteses in patients with refractory ascites.[5] More recently, early TIPS has been found to be associated with improved survival in selected patients with variceal hemorrhage[6] and hepatorenal syndrome.[7]

It has been suggested that TIPS performed in high-volume hospitals is associated with improved, short-term, in-hospital survival. Specifically, an analysis of the National Readmission Database in the United States established that in-hospital mortality was decreased in hospitals that performed more than 20 TIPS per year compared to lower volume centers.[8] This study was unable to establish if this association persisted following discharge, and therefore the impact of TIPS procedure volume on long-term survival remains unknown. Nevertheless, these results have prompted a discussion regarding whether the centralization of TIPS to high-volume centers of excellence should occur.[9]

In addition to procedure volume, hospital teaching status has been implicated as an important factor when considering centralization of specialized care. For several complex procedures, including radical cystectomy,[10] radical prostatectomy,[11] and hepatopancreaticobiliary surgery,[12] outcomes have been shown to be superior in teaching hospitals, irrespective of procedure volume. This association is hypothesized to be secondary to the subspecialized expertise and multidisciplinary approach that typically exists in a teaching environment.[13] This is particularly important in the management of patients with decompensated cirrhosis as these individuals are usually cared for by a team of specialized physicians and allied health professionals. To date, the impact of hospital teaching status on long-term outcomes following TIPS has not been evaluated.

The primary objective of this study was to explore the extent to which hospital teaching status is associated with long-term survival following TIPS in the general population of patients with cirrhosis. The secondary objectives were to evaluate the association between hospital procedure volume and long-term survival, describe trends in TIPS usage over the past 2 decades, and identify other patient or system factors associated with long-term survival following TIPS.

# Participants and Methods

## STUDY DESIGN

We conducted a retrospective cohort study using routinely collected administrative health care data from the province of Ontario, Canada. Ontario provides



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universal health care coverage for its population of approximately 13.5 million through the Ontario Health Insurance Program (OHIP). The population of Ontario is ethnically diverse, with 25% belonging to a visible minority and 2.4% being of indigenous descent. The main databases used in this analysis were the Registered Persons Database (RPDB), which includes demographic and vital status information for individuals covered under OHIP; the Canadian Institute for Health Information Discharge Abstract Database, which captures diagnostic and procedural information from inpatient hospital admissions; the National Ambulatory Care Reporting System, which captures diagnostic and procedural information from ambulatory care visits; and the OHIP Physician Claims Database, which includes all claims made by physicians for universally insured services. These databases were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences. This study was approved by the Health Sciences Research Ethics Board at Queen's University (DMED 1651-13).

## STUDY POPULATION AND HOSPITAL TEACHING STATUS

All patients with cirrhosis ≥18 years old without prior liver transplantation who received TIPS between January 1, 1998, and December 31, 2016, with follow-up until December 31, 2017, were included. Patients were identified as having cirrhosis using a validated administrative coding algorithm that requires one inpatient or outpatient code for cirrhosis or nonbleeding esophageal varices.[14] The date of the TIPS insertion was identified using OHIP billing code J057. For patients with more than one TIPS billing code during the study period, the date of the first procedure was used as subsequent procedures were assumed to represent a TIPS revision. The primary exposure was hospital teaching status defined according to the Ministry of Health and Long-Term Care in Ontario.[15] In order to be designated a teaching hospital, the hospital must either provide facilities for the instruction of medical students or be approved by the Royal College of Physicians and Surgeons of Canada to provide postgraduate education leading to certification or fellowship in one or more specialties recognized by the college.

## COVARIATES AND OUTCOME MEASURES

Baseline patient characteristics at the time of TIPS, including sex, age, income quintile, comorbidity, and indication for TIPS, were recorded. Income quintiles are determined using Statistics Canada census data by first calculating the average income per single-person equivalent for each dissemination area (small relatively stable geographic unit with an average population of 400 to 700 persons). Next, population quintiles by neighborhood income were constructed for each census metropolitan area or census agglomeration within Ontario. As such, these income quintiles capture the prosperity of a neighborhood relative to the region.[16] Comorbidity was evaluated by calculating the Charlson–Deyo Comorbidity Index during the year prior to TIPS.[17] Indication for TIPS was determined using a stepwise algorithm that categorized patients into four groups: (1) refractory ascites and/or hepatic hydrothorax; (2) variceal hemorrhage; (3) both; or (4) unknown (Supporting Fig. S1). In the algorithm, procedure codes were used first to categorize patients because they have been found to be the most accurate for use in administrative data.[18] If the indication remained unclear, then diagnostic codes were considered. System-related factors evaluated included urgency of admission (urgent/emergent versus elective) and annual hospital procedure volume. Procedure volume was determined by calculating the mean number of TIPS performed per year at each institution during the study period. Procedure volume was evaluated as both a categorical variable for descriptive purposes (low, <5 per year; medium, 5-10 per year; high, >10 per year) and as a continuous variable in survival analyses. Colinearity between hospital teaching status and procedure volume was assessed using Cramér's V statistic.

The primary outcome of this study was liver transplant-free (LTF) survival as defined from the date of TIPS to either (1) the date of death from the RPDB or (2) the date of liver transplantation based on OHIP billing code S294. Secondary outcomes consisted of early clinical endpoints, including length of hospital stay, in-hospital mortality, in-hospital gastroenterology (GI) consultation, and 30-day outpatient GI follow-up.

## STATISTICAL ANALYSIS

Means and SDs were used to describe normally distributed variables and medians, and interquartile ranges (IQRs) were used for variables with a nonnormal distribution. Poisson regression was used to evaluate secular trends in the number of TIPS being performed annually between 2000 and 2016. Years 1998 and 1999 were excluded because of the relatively small number of cases performed during those years (14 and 29, respectively), likely explained by the fact that the publication of randomized trials supporting the use of TIPS did not occur until the late 1990s. Median, 30-day, 1-year, and 5-year LTF survival rates were described by hospital teaching status using the Kaplan-Meier method and compared using the log-rank test. Univariate and multivariate competing risks regression was performed to evaluate the association between hospital teaching status and overall survival, with liver transplant and death treated as competing events. The competing risks analysis considers that patients are at risk not only for death but also liver transplantation and produces a subdistribution hazard ratio (sHR), which represents the hazard of death in the presence of liver transplant as a competing event. Potential confounders were included in the multivariate model using a backward selection method with an alpha value of <0.1. The robust sandwich estimator for the covariance matrix was used in the regression model to account for the clustering effect at the hospital level.[19] The significance level was set at 0.05. All statistical analyses were performed using SAS version 9.4.

# Results

A total of 857 unique individuals met the eligibility criteria and were included in the study cohort. The median follow-up time was 355 days (IQR, 55-1,203); 565 (65.9%) patients died, and 109 (12.7%) received liver transplantation during follow-up.

## BASELINE CHARACTERISTICS

The baseline characteristics of the study population are shown in Table 1. Patients were predominantly male adults (69.1%) with a mean age of 57.1 years (±10.8 years). The majority of TIPS were performed in one of 11 teaching hospitals (84.3%) compared to 14 nonteaching hospitals (15.7%). Review of the 11 hospitals classified as "teaching" confirmed that all were tertiary care teaching institutions, two of which had liver transplantation programs. Of the teaching hospitals, eight were considered low volume, two were medium volume, and one was high volume. Of the nonteaching hospitals, one was medium volume and 13 were low volume. Two thirds of TIPS were performed during an urgent/emergent admission, and the most common indication for TIPS was refractory ascites/hepatic hydrothorax (52.6%), followed by variceal hemorrhage (34.5%).

## SECULAR TRENDS

Between 2000 and 2016, the number of TIPS performed per year in Ontario remained constant (median, 49; IQR, 45-51; $P = 0.08$). Similarly, annual TIPS volume at teaching and nonteaching hospitals did not change significantly during that time period (median, 40; IQR, 38-43; $P = 0.30$; and median, 8; IQR, 5-10; $P = 0.06$, respectively).

## EARLY OUTCOMES AFTER TIPS

Early outcomes following TIPS are shown in Table 2. During the hospitalization following TIPS, patients in teaching hospitals had a longer length of stay than those in nonteaching hospitals (median, 4 days; IQR, 2-10; versus median, 2 days; IQR, 1-10; $P < 0.001$). In-hospital mortality was similar in teaching hospitals compared to nonteaching hospitals (16.2% versus 18.7%; $P = 0.48$). GI subspecialists were more involved in the care of these patients in teaching hospitals compared to nonteaching hospitals, both during hospitalization (inpatient GI consult 80.6% versus 36.6%, respectively; $P < 0.001$) and at 30 days following discharge (45.6% versus 19.4%, respectively; $P < 0.001$). Liver transplantation was more frequently performed in patients whose TIPS were done in teaching hospitals (13.8%) compared to nonteaching hospitals (6.0%).

## LONG-TERM SURVIVAL

Of the patients, 7 died on the same day as TIPS, and therefore 850 patients had follow-up time for survival analyses. The overall median LTF survival

### TABLE 1. BASELINE CHARACTERISTICS OF PATIENTS WITH CIRRHOSIS RECEIVING TIPS

| | | Hospital Type | | |
|---|---|---|---|---|
| | All Patients (N = 857) | Teaching (n = 723) | Nonteaching (n = 134) | *P* Value* |
| Patient related | | | | |
| Age, mean years (SD) | 57.1 (10.8) | 56.7 (10.6) | 59.3 (11.7) | 0.01 |
| Sex, n (%) | | | | |
| Male | 592 (69.1) | 492 (68) | 100 (74.6) | 0.13 |
| Female | 265 (30.9) | 231 (32) | 34 (25.4) | |
| Income quintile, n (%) | | | | 0.31 |
| 1 (lowest) | 204 (23.8) | 172 (23.8) | 32 (23.9) | |
| 2 | 189 (22.1) | 154 (21.3) | 35 (26.1) | |
| 3 | 159 (18.6) | 142 (19.6) | 17 (12.7) | |
| 4 | 147 (17.2) | 121 (16.7) | 26 (19.4) | |
| 5 (highest) | 150 (17.5) | 128 (17.7) | 22 (16.4) | |
| Missing | 8 (0.9) | 6 (0.8) | 2 (1.5) | |
| Charlson–Deyo Comorbidity Index, n (%) | | | | 0.88 |
| <4 | 682 (79.6) | 576 (79.7) | 106 (79.1) | |
| ≥4 | 175 (20.4) | 147 (20.3) | 28 (20.9) | |
| Indication, n (%) | | | | 0.10 |
| Refractory ascites/hepatic hydrothorax | 445 (51.9) | 364 (50.3) | 81 (60.4) | |
| Variceal hemorrhage | 298 (34.8) | 264 (36.5) | 34 (25.4) | |
| Both | 30 (3.5) | 25 (3.5) | 5 (3.7) | |
| Other | 84 (9.8) | 70 (9.7) | 14 (10.4) | |
| System related | | | | |
| Urgency of admission, n (%) | | | | 0.07 |
| Urgent/emergent | 273 (31.9) | 219 (30.3) | 54 (40.3) | |
| Elective | 583 (68) | 503 (69.6) | 80 (59.7) | |
| Missing | 1 (0.1) | 1 (0.1) | 0 (0) | |
| Hospital procedure volume, n (%) | | | | <0.001 |
| Low, <5/year | 284 (33.1) | 249 (34.4) | 35 (26.1) | |
| Medium, 5-10/year | 335 (39.1) | 236 (32.6) | 99 (73.9) | |
| High, >10/year | 238 (27.8) | 238 (32.9) | 0 (0) | |

**P* values comparing teaching versus nonteaching hospitals are from chi-square tests, with the exception of age, which was determined by *t* test.

### TABLE 2. EARLY OUTCOMES IN PATIENTS WITH CIRRHOSIS RECEIVING TIPS

| | | Hospital Type | | |
|---|---|---|---|---|
| | All Patients (N = 857) | Teaching (n = 723) | Nonteaching (n = 134) | *P* Value* |
| LOS, median days (IQR) | 4 (1-10) | 4 (2-10) | 2 (1-10) | 0.001 |
| In-hospital mortality, n (%) | 142 (16.6) | 117 (16.2) | 25 (18.7) | 0.48 |
| In-hospital GI consultation, n (%) | 634 (74) | 585 (80.9) | 49 (36.6) | <0.001 |
| 30-day outpatient GI follow-up, n (%) | 356 (41.5) | 330 (45.6) | 26 (19.4) | <0.001 |
| Liver transplant, n (%) | 108 (12.6) | 100 (13.8) | 8 (6.0) | 0.01 |

**P* values comparing teaching versus nonteaching hospitals are from chi-square tests, with the exception of LOS, which was determined by the Mann-Whitney U test.
Abbreviation: LOS, length of stay.

of the cohort was 1.8 years (IQR, 0.2-7.5). Using Kaplan-Meier analysis, median LTF survival after TIPS was more than twice as long in patients whose procedure was performed at a teaching hospital compared to a nonteaching hospital (median, 2.2 years; IQR, 0.2-8.0; versus median, 0.9 years; IQR, 0.1-4.3; $P < 0.001$) (Fig. 1 and Table 3). Both 1-year and 5-year LTF survival were approximately 10% higher for TIPS performed in teaching hospitals compared to nonteaching hospitals (Table 3).

The results of the competing risks regression analysis evaluating predictors of overall survival with liver transplant as a competing event are shown in Table 4. In the univariate model, hospital teaching status, hospital procedure volume, age, comorbidity, and urgency of admission were all associated with overall survival. The Cramér's V statistic between hospital teaching status and procedure volume was 0.33, which indicates a moderate correlation but does not meet the 0.4 threshold for collinearity. Therefore, both variables were included in the multivariate model. After adjusting for potential confounders and hospital clustering, hospital teaching status was not associated with death (nonteaching sHR, 1.32; 95% confidence interval [CI], 0.97-1.81; $P = 0.08$); however, the association with procedure volume remained (per unit increase sHR, 0.96; 95% CI, 0.93-0.99; $P = 0.003$). Other factors independently associated with mortality included age (sHR, 1.03 per year increase; 95% CI, 1.02-1.04; $P < 0.001$), Charlson–Deyo Comorbidity Index ≥4 (sHR, 1.26; 95% CI, 1.05-1.51; $P = 0.01$), and urgent/emergent admission (sHR, 1.33; 95%, CI 1.20-1.49; $P < 0.001$).

# Discussion

In this population-based study, we evaluated the association between hospital teaching status and procedure volume as well as long-term survival following TIPS in the general population of patients with cirrhosis. Although patients whose TIPS were performed in teaching hospitals lived twice as long as those in nonteaching hospitals, our results showed that after controlling for confounders and clustering between hospitals, teaching status was no longer associated with long-term overall survival. Importantly, however, our results show that annual hospital procedure volume is independently associated with survival even after hospital discharge, with a 4% decreased hazard of death for each additional TIPS procedure performed.

To date, three population-based studies have described outcomes following TIPS[8,20,21]; however, none have evaluated the impact of hospital teaching status or procedure volume on long-term survival. In comparing our study cohort with previous work studying short-term outcomes following TIPS,[8,20] we found similar age and sex distributions as well as similar rates of emergent TIPS and in-hospital mortality. Further, our median LTF survival of 1.84 years was comparable to the study using the

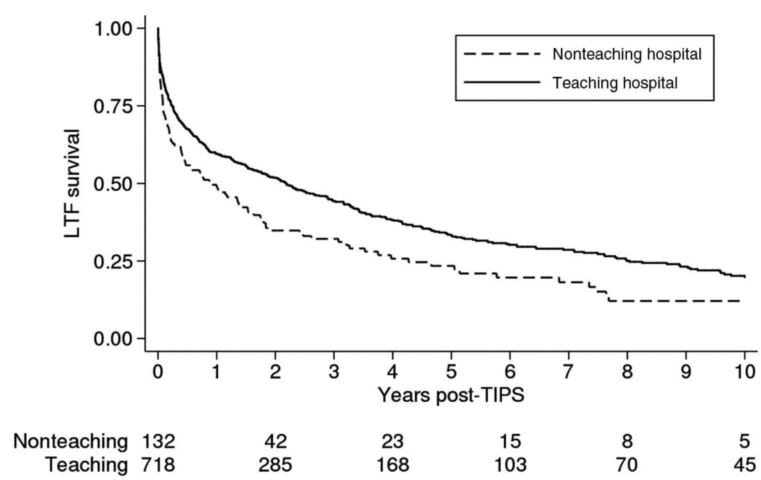


**FIG. 1.** LTF survival in patients with cirrhosis who received TIPS in Ontario between 1998 and 2016 (n = 850).

**TABLE 3. LTF SURVIVAL IN PATIENTS WITH CIRRHOSIS RECEIVING TIPS**

| | All Patients (N = 850) | Teaching (n = 718) | Nonteaching (n = 132) |
|---|---|---|---|
| Median LTF survival, years (IQR) | 1.84 (0.19-7.50) | 2.16 (0.22-7.99) | 0.88 (0.08-4.27) |
| 30-day LTF survival, % (SEM) | 82.2 (0.01) | 83.7 (0.01) | 73.9 (0.04) |
| 1-year LTF survival, % (SEM) | 57.4 (1.7) | 59.1 (1.9) | 48.0 (4.3) |
| 5-year LTF survival, % (SEM) | 31.5 (1.8) | 32.9 (2.0) | 23.1 (4.0) |

**TABLE 4. FACTORS ASSOCIATED WITH DEATH FOLLOWING TIPS**

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | sHR | 95% CI | *P* Value | sHR | 95% CI | *P* Value |
| Hospital teaching status | | | | | | |
| Nonteaching | 1.55 | 1.07-2.24 | 0.02 | 1.32 | 0.97-1.81 | 0.08 |
| Teaching | Ref | – | – | Ref | – | – |
| Patient related | | | | | | |
| Age (per year increase) | 1.04 | 1.02-1.05 | <0.001 | 1.03 | 1.02-1.04 | <0.001 |
| Sex | | | | | | |
| Male | 0.97 | 0.82-1.15 | 0.76 | | | |
| Female | Ref | – | – | | | |
| Income quintile | | | | | | |
| 1 (lowest) | 1.18 | 0.77-1.81 | 0.44 | | | |
| 2 | 1.03 | 0.70-1.52 | 0.88 | | | |
| 3 | 1.31 | 0.76-2.26 | 0.32 | | | |
| 4 | 1.09 | 0.61-1.95 | 0.76 | | | |
| 5 (highest) | Ref | – | – | | | |
| Charlson–Deyo Comorbidity | | | | | | |
| ≥4 | 1.37 | 1.20-1.55 | <0.001 | 1.26 | 1.05-1.51 | 0.01 |
| <4 | Ref | – | – | Ref | – | – |
| Indication for TIPS | | | | | | |
| Variceal hemorrhage | 1.29 | .97-1.71 | 0.08 | | | |
| Both | 1.66 | 1.09-2.52 | 0.02 | | | |
| Other | 1.04 | 0.76-1.44 | 0.79 | | | |
| Refractory ascites/hepatic hydrothorax | Ref | – | – | | | |
| System related | | | | | | |
| Urgency of admission | | | | | | |
| Urgent/emergent | 1.39 | 1.17-1.66 | <0.001 | 1.33 | 1.20-1.49 | <0.001 |
| Elective | Ref | – | – | Ref | – | – |
| Hospital procedure volume (per unit increase) | 0.94 | 0.91-0.98 | 0.002 | 0.96 | 0.93-0.99 | 0.003 |

–, not applicable.
Abbreviation: Ref, reference group.

Veterans Affairs (VA) population where the median survival was 1.74 years.[21] Of note, however, the rate of liver transplantation following TIPS was higher in our population compared to the VA (12.7% versus 5%, respectively), which may be explained by the VA population having a higher degree of comorbid illness compared to the general population that may have precluded transplantation as an option. Overall, our cohort is consistent with previous work examining patients with TIPS.

Our study is the first to evaluate the association of teaching status on post-TIPS outcomes. For several other procedures, it has been suggested that hospital teaching status is predictive of survival independent of procedure volume.[10-12] Of these three studies, two did not account for clustering between hospitals[11,12] and the third did not evaluate for collinearity between hospital volume and teaching status.[10] In an initial regression analysis not accounting for clustering, we did find an association between hospital teaching status and long-term survival (nonteaching sHR for death, 1.32; 95% CI, 1.06-1.65; $P = 0.01$). However, after accounting for clustering, this relationship was attenuated with widening of the CI, suggesting that the difference in survival between teaching and nonteaching hospitals initially observed was likely secondary to differences in processes of care between intuitions unrelated to teaching status.

Previous research surrounding the impact of institutional factors on post-TIPS outcomes has focused on hospital procedure volume as opposed to teaching status. The most influential study to date found that TIPS performed in high-volume (>20 TIPS/year) hospitals were associated with improved in-hospital mortality. The authors suggested that this association was based on the "practice makes perfect" phenomenon of specialized procedures.[8] Consistent with this study, we also found an association between higher annual procedure volume and improved overall survival. Furthermore, we revealed that this association persists beyond the in-hospital period after TIPS.

Our findings support a growing body of literature suggesting that centralization of TIPS may improve patient outcomes. The centralization of complex procedures in acute complicated patients is not a new phenomenon as referral of care to select centers already occurs for several other procedures. In Ontario, percutaneous coronary intervention for acute coronary syndromes is only performed in eight centers of excellence across the province.[22] Compared to the United States, where care has not been designated to certain cardiac catheterization laboratories, Ontario has lower rates of adverse outcomes, suggesting that centralization improves care.[22] Furthermore, lobectomy for lung cancer was regionalized in Ontario in the early 2000s.[23] Secular analysis of length of stay and in-hospital mortality has demonstrated improvements in both outcomes after regionalization. The successes observed with both percutaneous coronary intervention and lobectomy indicate that this approach may be feasible for TIPS. We recognize, however, that performing TIPS exclusively in high-volume centers might not be practical for all cases. This would be especially true in the instance of acute refractory variceal hemorrhage where it may not be safe or practical to transfer patients to another facility. Nevertheless, future research focusing on centralization of TIPS to high-volume centers is still necessary.

The strength of our study stems from the inclusivity of our patient cohort. Because we used linked data sets from a province that provides universal health care, we were able to include essentially all patients with cirrhosis in a large demographically diverse population over a long time period, with reliable follow-up. As such, our results have strong external validity.

The results of this study must also be considered in the context of methodologic limitations. First, we were unable to quantify the degree of liver dysfunction at the time of TIPS or describe the development of worsening liver failure following the procedure. Liver decompensation is most commonly evaluated using the Model for End-stage Liver Disease (MELD) and Child-Turcotte-Pugh scores, both of which require laboratory values to calculate. Given the administrative nature of these data, we were unable to calculate these values in our cohort. However, previous work has suggested that adjusting for the Charlson–Deyo Comorbidity Index has a comparable effect to adjusting for MELD in patients receiving TIPS,[21] and therefore the inclusion of MELD at the time of TIPS would likely have had minimal effect on our results. Second, we are unable to completely account for "selective referral bias," which occurs when patients who are more likely to have better outcomes are referred to specific institutions. To minimize this, we adjusted for TIPS indication, urgency of admission, and comorbid illness and accounted for hospital clustering in our regression models. Finally, we could not identify which TIPS were performed using covered stents. Covered stents were approved by Health Canada in 2008 and have been shown to improve outcomes post-TIPS compared to uncovered stents.[24] In an exploratory analysis, we found no association between TIPS performed before and after 2008 and overall survival; however, this remains a limitation.

In conclusion, our results show that TIPS performed in high-volume hospitals are associated with a significant improvement in long-term survival compared to lower volume hospitals. Our results support future research focusing on the centralization of TIPS to high-volume centers of excellence to improve long-term outcomes in this population.

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# Supporting Information

Additional Supporting Information may be found at onlinelibrary.wiley.com/doi/10.1002/hep4.1345/suppinfo.