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No Increased Mortality After TIPS Compared with Serial Large Volume Paracenteses in Patients with Higher Model for End-Stage Liver Disease Score and Refractory Ascites

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Abstract
Purpose To compare survival after transjugular intrahepatic portosystemic shunt (TIPS) creation versus serial large volume paracenteses (LVP) in patients with refractory ascites and higher Model for End-Stage Liver Disease (MELD) scores.
Materials and Methods In this retrospective study, from 1/1/2013 to 10/1/2018, 478 patients (294 male; mean age 58, range 23–89) underwent serial LVP (n = 386) or TIPS (n = 92) for ascites. Propensity-matched cohorts were constructed based on age, MELD, Charlson comorbidity index, varices, and hepatic encephalopathy. Survival was analyzed using a Cox proportional hazards model in which MELD score and TIPS were treated as time-dependent covariates. An interaction term was used to assess the impact of TIPS versus serial LVP on survival as a function of increasing MELD.
Results In the overall patient sample, higher MELD score predicted worse survival after either serial LVP or TIPS [hazard ratio (HR) = 1.13; $p < 0.001$], but there was no significant interaction between TIPS and higher MELD score conferring worse survival (HR = 1.01; $p = 0.55$). In 92 propensity-matched serial LVP and 92 TIPS patients, higher MELD score predicted worse survival after either serial LVP or TIPS (HR = 1.19; $p < 0.001$), but there was no significant survival interaction between TIPS and higher MELD (HR = 0.97; $p = 0.22$). In 30 propensity-matched serial LVP patients and 30 TIPS patients with baseline MELD greater than 18, TIPS did not predict worse survival (HR = 0.97; $p = 0.94$).
Conclusion Higher MELD predicts poorer survival after either serial LVP or TIPS, but TIPS creation is not associated with worse survival compared to serial LVP in patients with higher MELD scores
Level of Evidence Level 4, case series.

Keywords Transjugular intrahepatic portosystemic shunt · Paracentesis · Model for End-Stage Liver Disease · Survival

Introduction

A higher Model for End-Stage Liver Disease (MELD) score is a strong predictor of poor survival after transjugular intrahepatic portosystemic shunt (TIPS) creation [1, 2]. The correlation between higher MELD and poor survival after TIPS has led many authors to suggest that TIPS should be avoided as treatment for refractory ascites in patients with higher MELD scores [3–6], based on the assumption that a TIPS may accelerate liver failure and shorten survival in these patients [7]. However, the correlation between a higher MELD score and poor survival after TIPS does not immediately imply that TIPS worsens survival in higher MELD patients [8]. A higher MELD score also predicts poor survival in cirrhotic patients

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without TIPS as well [9]. Furthermore, patients with a higher MELD and an indication for TIPS such as refractory ascites may have higher mortality than patients with equivalent MELD but no ascites [10]. Unfortunately, definitive studies randomizing higher MELD patients with refractory ascites to TIPS creation versus serial large volume paracenteses (LVP) are lacking.

In patients with lower MELD scores and refractory ascites, a recent randomized trial has shown a survival benefit for TIPS constructed with covered stents compared with serial LVP [11]. The observation that TIPS may improve survival [11–14], or at least not worsen it [15], compared to serial LVP in lower MELD patients in combination with the assumption that TIPS worsens survival in higher MELD patients implies an *interaction* between TIPS and the MELD score [16]. The presence of such an interaction, and the assumption that TIPS worsens survival in higher MELD patients, has recently been called into question [8, 16].

The purpose of this study was to compare survival after TIPS creation versus serial LVP in patients with refractory ascites and higher MELD scores by directly testing for an interaction between TIPS versus serial LVP and increasing MELD score.

Methods

Patient Population

This single-institution retrospective Health Insurance Portability and Accountability Act compliant study was approved by our Institutional Review Board. A waiver for informed written consent was obtained. The institutional electronic medical record was searched using an established query platform [17] to identify adult patients age 18 or older with cirrhosis who underwent TIPS or serial LVP, defined as at least 1 LVP per month, for management of medically refractory ascites from 1/1/2013 to 10/1/2018. Medically refractory ascites was defined as ascites which could not be mobilized despite dietary sodium restriction and maximal diuretic therapy. Patients with non-cirrhotic causes of ascites were excluded. TIPS procedures were performed for either first-line treatment of medically refractory ascites or following initial management by serial LVP after multidisciplinary consensus between hepatologists and interventional radiologists. The study population included 478 patients, 92 of whom underwent TIPS and 386 of whom underwent serial LVP (Fig. 1). Two hundred sixty-seven patients died and 77 patients underwent liver transplant. Demographics, laboratory values, complications of cirrhosis, and components of the updated Charlson comorbidity index [18], an internationally validated metric based on the summation of weighted scores for heart failure, dementia, chronic pulmonary disease, rheumatologic disease, liver disease, diabetes, hemi- or paraplegia, renal disease, localized malignancy or metastatic solid tumor, and human immunodeficiency virus/acquired immunodeficiency syndrome were extracted from the electronic medical record.

TIPS Procedures

All TIPS procedures were performed using conventional techniques [19] under the supervision of a subspecialty board-certified interventional radiologist with 2–27-years experience. Briefly, after obtaining portal vein access, portal venography was performed and the portal vein to hepatic vein pressure gradient was measured. In all cases, a GORE® VIATORR® TIPS Endoprosthesis covered stent graft (W. L. Gore, Flagstaff, AZ) was deployed and dilated to 8–10 mm at the discretion of the interventional radiologist performing the procedure. A completion portal venogram was performed, and a completion portal to hepatic vein pressure gradient was then measured. Hemodynamic success was defined as a post-TIPS gradient < 12 mm Hg [20].

Statistical Analyses

All statistical analyses were performed using R version 3.5.1 [21]. Continuous variables were compared using t tests. Categorical variables were compared using Chi-squared or Fisher's exact tests. Survival was estimated from the time of first documented LVP or TIPS, whichever occurred first, to the time of death, liver transplant, or loss to follow-up. A cause-specific Cox proportional hazards model with time-dependent covariates [22] with death as the endpoint of interest was utilized. MELD score and TIPS were treated as time-dependent covariates to model patients whose ascites was treated first with serial LVP and then later by TIPS. In addition to TIPS and MELD score, age, gender, and any variables with p values less than 0.10 in univariate analyses were included in multivariate analyses. An interaction term between TIPS versus LVP and MELD score was included to assess for a differential effect on survival of TIPS versus LVP at the same MELD score [16]; this interaction term was only utilized in multivariate models. A propensity score based on age, gender, baseline MELD, the updated Charlson comorbidity index, history of varices, and history of hepatic encephalopathy was formed, and matched cohorts were identified using a nearest neighbor approach [23]. Univariate and multivariate Cox proportional hazards models were applied to the matched cohorts in the same manner as the overall cohorts. p values less than 0.05 were considered statistically significant.

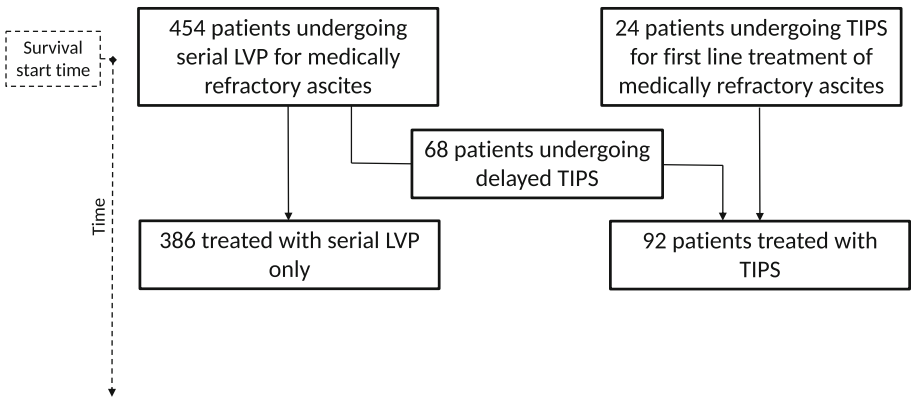

Fig. 1 Flowchart showing study population

Results

There were 386 patients with medically refractory ascites who underwent serial LVP with a frequency of at least 1 per month (mean 1.9 LVP per month, range 1.0–9.9). Among the 92 patients who underwent TIPS creation, 24 patients underwent TIPS as initial treatment for refractory ascites after failure of medical management, whereas 68 underwent serial LVP for a median of 67 days prior to TIPS (range 3–1720). TIPS creation was hemodynamically successful in all but 2 patients, and the mean post-TIPS portosystemic gradient was 5.5 mm Hg. The mean number of paracenteses per month prior to TIPS was 0.87 (range 0.1–6) and following TIPS was 0.25 (range 0–4), a statistically significant reduction ($p = 0.002$). Despite elevated post-TIPS portosystemic gradients of 18 and 12 mmHg, the two patients with hemodynamically unsuccessful TIPS required 1 and 0 LVP in 104- and 1811-days follow-up after TIPS, respectively. The mean MELD score was significantly higher (22 vs. 16; $p < 0.001$), and the mean Charlson comorbidity score was non-significantly increased (5.7 vs. 5.3; $p = 0.13$) among patients undergoing serial LVP compared with TIPS (Table 1). Median survival in the overall cohort was 76 days (range 1–1928).

In a multivariate cause-specific Cox proportional hazards model treating TIPS and MELD score as time-dependent covariates (Table 2), higher MELD score [hazard ratio (HR) = 1.13; 95% confidence interval (CI) = 1.11–1.14; $p < 0.001$], as well as older age (HR = 1.03; CI 1.02–1.04; $p < 0.001$) and higher Charlson comorbidity index (HR = 1.08; CI 1.01–1.14; $p = 0.01$), were significant predictors of shorter survival. Despite the increased risk of death in patients with higher MELD score, there was no significant interaction between TIPS creation and a higher MELD on survival (HR = 1.01; CI 0.97–1.05; $p = 0.55$), indicating equivalent risk of death with either TIPS or serial LVP at each level of MELD.

To reduce imbalances between groups, propensity score-matched cohorts of patients undergoing either serial LVP or TIPS were constructed using age, gender, Charlson comorbidity index, MELD score, presence of varices, and history of hepatic encephalopathy. After matching, there were no significant differences between the TIPS and LVP cohorts (Table 3; Fig. 2). Median survival in the matched cohort was 452 days (range 1–1928), longer than in the overall cohort as a result of exclusion of serial LVP patients with significantly higher MELD scores and Charlson comorbidity indices. In multivariate analysis, although a higher MELD score was a significant predictor of worse survival (HR = 1.19; CI 1.15–1.23; $p < 0.001$), there was no significant interaction between TIPS creation and higher MELD on survival in the matched cohorts (HR = 0.97, CI 0.92–1.02; $p = 0.22$) (Table 4).

In a subanalysis of 30 propensity score-matched serial LVP patients and 30 propensity score-matched TIPS patients with baseline MELD score greater than or equal to 18, median survival was 162 days (range 1–1928). TIPS creation was not associated with worse survival compared to serial LVP on univariate analysis (HR = 0.97; CI 0.41–2.28; $p = 0.94$) (Table 5). In multivariate analysis, neither TIPS creation (HR = 2.09; CI 0.13–34.0; $p = 0.60$) nor the interaction between TIPS and MELD (HR = 0.97; CI 0.87–1.07; $p = 0.52$) was a significant predictor of worse survival.

Discussion

In this study, there was no evidence of an interaction between TIPS creation and MELD score to indicate that TIPS creation confers worse survival in patients with higher MELD scores compared with serial LVP. A higher MELD score predicted poor survival, but survival was equally poor among patients whose refractory ascites was treated with serial LVP as opposed to TIPS. The results of this study should not be misconstrued to suggest that patients with higher MELD scores have lengthy survival

Table 1 Baseline demographics of the overall cohorts

Characteristic	TIPS cohort (n = 92)	Serial LVP cohort (n = 386)	p value
Male gender	60%	62%	0.80
Mean age (range)	56 (23–76)	59 (23–89)	0.10
Cirrhosis etiology[a]			
Alcohol	35%	36%	0.92
Hepatitis C	21%	23%	0.76
Nonalcoholic steatohepatitis	30%	24%	0.22
Hepatitis B[b]	1%	3%	0.48
Primary biliary cirrhosis[b]	5%	5%	0.79
Hepatitis A[b]	0%	1%	1.0
Hemochromatosis[b]	1%	2%	1.0
Autoimmune[b]	2%	3%	1.0
Wilson's[b]	1%	0%	0.19
Alpha-1-antitrypsin[b]	1%	2%	1.0
Cryptogenic	23%	30%	0.24
Mean MELD (range)	16 (7–33)	22 (6–45)	< 0.001
Mean Charlson comorbidity index (range)	5.3 (4–12)	5.7 (4–15)	0.13
History of varices	42%	35%	0.22
History of hepatic encephalopathy	25%	35%	0.10

[a]Multiple etiologies in some patients

[b]Fisher's exact test

Table 2 Cox proportional hazards model in overall cohorts

Feature	Univariate HR (95% CI) p value	Multivariate HR (95% CI) p value
Age	1.02 (1.01–1.03)	1.03 (1.02–1.04)
	< 0.001	< 0.001
Male gender	1.24 (0.97–1.59)	1.12 (0.87–1.45)
	0.09	0.38
MELD score	1.13 (1.11–1.14)	1.13 (1.11–1.14)
	< 0.001	< 0.001
Charlson comorbidity index	1.11 (1.05–1.18)	1.08 (1.01–1.14)
	< 0.001	0.01
Varices	1.01 (0.79–1.30)	
	0.94	
Hepatic encephalopathy	1.50 (1.17–1.93)	1.22 (0.95–1.58)
	0.001	0.12
TIPS	0.41 (0.28–0.61)	0.39 (0.14–1.07)
	< 0.001	0.07
TIPS × MELD interaction		1.01 (0.97–1.05)
		0.55

after TIPS. Instead, these results call into question the idea that a higher MELD score is a contraindication to TIPS.

The results reported here replicate a recent study by Spengler et al. [16] demonstrating similar findings. In that study which compared 106 patients with TIPS to 79 patients with refractory ascites without TIPS, there was no significant interaction between TIPS and the MELD score, with the reported confidence intervals overlapping those of this study. There are several important differences between this study and that of Spengler et al. First, the serial LVP cohort in this study was on average a decade older than the serial LVP cohort in Spengler et al. In that study serial LVP

Table 3 Baseline demographics of the matched cohorts

Characteristic	TIPS cohort (n = 92)	Serial LVP cohort (n = 92)	p value
Male gender	60%	60%	1.0
Mean age (range)	56 (23–76)	57 (29–88)	0.55
Cirrhosis etiology[a]			
Alcohol	35%	42%	0.36
Hepatitis C	21%	23%	0.85
Nonalcoholic steatohepatitis	30%	20%	0.13
Hepatitis B[b]	1%	5%	0.21
Primary biliary cirrhosis[b]	5%	2%	0.44
Hepatitis A[b]	0%	0%	1.0
Hemochromatosis[b]	1%	1%	1.0
Autoimmune[b]	2%	3%	1.0
Wilson's[b]	1%	0%	1.0
Alpha-1-antitrypsin[b]	1%	1%	1.0
Cryptogenic	23%	30%	0.32
Mean MELD (range)	16 (7–33)	16 (6–33)	0.77
Mean Charlson comorbidity index (range)	5.3 (4–12)	5.0 (4–13)	0.39
History of varices	42%	36%	0.45
History of hepatic encephalopathy	25%	23%	0.86

[a]Multiple etiologies in some patients

[b]Fisher's exact test

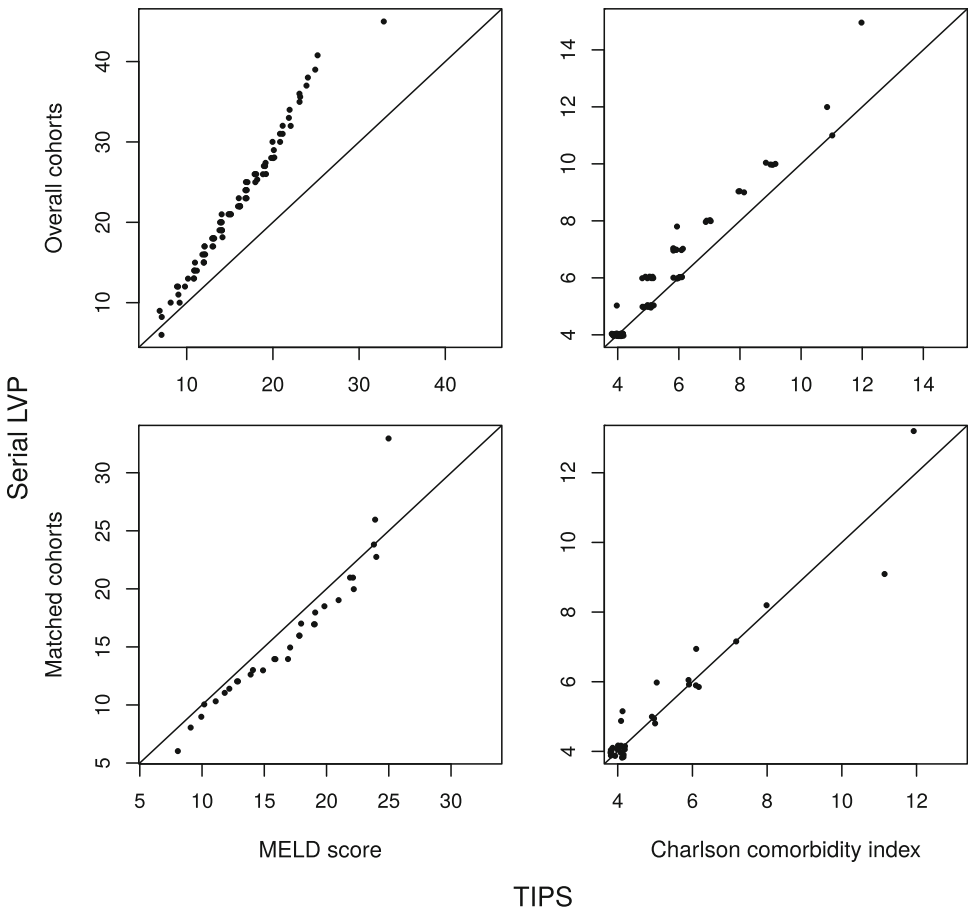

Fig. 2 Quantile–quantile plots showing the distribution of MELD scores and Charlson comorbidity indices in the overall and propensity score-matched TIPS and serial LVP cohorts

Table 4 Cox proportional hazards model in matched cohorts

Feature	Univariate HR (95% CI) *p* value	Multivariate HR (95% CI) *p* value
Age	1.01 (0.99–1.03)	1.02 (0.99–1.04)
	0.23	0.14
Male gender	1.01 (0.72–1.69)	1.29 (0.83–2.00)
	0.66	0.25
MELD score	1.17 (1.14–1.20)	1.19 (1.15–1.23)
	< 0.001	< 0.001
Charlson comorbidity index	1.11 (1.00–1.25)	1.05 (0.94–1.17)
	0.06	0.38
Varices	1.18 (0.77–1.80)	
	0.46	
Hepatic encephalopathy	1.45 (0.92–2.30)	
	0.11	
TIPS	0.82 (0.50–1.33)	1.39 (0.38–5.10)
	0.42	0.62
TIPS × MELD interaction		0.97 (0.92–1.02)
		0.22

Table 5 Cox proportional hazards model in matched cohorts with baseline MELD greater than or equal to 18

Feature	Univariate HR (95% CI) *p* value	Multivariate HR (95% CI) *p* value
Age	1.01 (0.97–1.06)	1.04 (0.98–1.08)
	0.50	0.17
Male gender	1.93 (0.89–4.19)	2.09 (0.91–4.80)
	0.10	0.08
MELD score	1.16 (1.11–1.22)	1.18 (1.09–1.27)
	< 0.001	< 0.001
Charlson comorbidity index	1.09 (0.93–1.27)	
	0.29	
Varices	1.22 (0.59–2.53)	
	0.60	
Hepatic encephalopathy	1.95 (0.93–4.08)	1.60 (0.74–3.46)
	0.08	0.24
TIPS	0.97 (0.41–2.28)	2.09 (0.13–34.0)
	0.94	0.60
TIPS × MELD interaction		0.97 (0.87–1.07)
		0.52

patients were significantly younger than TIPS patients, whereas in this study serial LVP patients showed a non-significant trend toward older age than TIPS patients. This difference likely reflects differences in institutional practices in patients selected to undergo TIPS. Second, in Spengler et al., 62% of all patients had cirrhosis due to alcoholic liver disease compared to only 36% in this study. Third, Spengler et al. did not determine the survival impact of comorbidities unrelated to cirrhosis. This study utilized the internationally validated, updated Charlson comorbidity index [18] to characterize overall health status in the serial LVP and TIPS cohorts. As might be expected serial LVP patients tended to have more comorbidities than TIPS patients, and a higher comorbidity score was a significant predictor of worse survival. Fourth, to address confounding this study utilized both multivariate analysis as well as propensity score matching, whereas Spengler et al. did not attempt to adjust for differences, such as history of variceal bleeding, between TIPS and LVP patients. However, despite the differences in patient demographics and statistical methodology, the results of these two studies are concordant and add to the generalizability of the

conclusion that TIPS does not worsen survival in higher MELD patients. However, given the entrenched view that a higher MELD score is a contraindication to TIPS for ascites [3–7], further replication, in populations with other demographic characteristics, at institutions with differing practices for managing refractory ascites, and to achieve a more robust sample size for meta-analysis, will be required to shift clinical practice.

The study by Spengler et al. [16] and this study illustrate an approach for dealing with several challenges encountered in retrospective comparison of survival between patients managed with TIPS versus serial LVP. First, in this study many patients undergoing TIPS initially underwent serial LVP prior to TIPS. Taking the start time in a serial LVP cohort as the time of first LVP and the start time in a TIPS cohort as the time of TIPS creation will introduce a survival lead time bias against TIPS. To avoid this bias, TIPS creation was treated as a time-dependent covariate to allow all patients' start times to be their first LVP [16]. Second, due to concerns that TIPS may worsen survival in patients with higher MELD scores [3–7], most single-institution studies contain few patients with higher MELD scores in whom TIPS were created for refractory ascites. To deal with this, an interaction between TIPS and MELD score was evaluated [16]. This statistical approach takes advantage of the continuous distribution of MELD scores and extracts information on the effect of TIPS creation as a function of increasing MELD utilizing the complete patient sample with scores across the entire spectrum. Although evaluation of an interaction allows the complete distribution of MELD scores to be analyzed, we also performed a subanalysis on only those patients with baseline MELD scores greater than or equal to 18, a previously used threshold [16]. However, MELD thresholds at which TIPS for ascites is reportedly contraindicated range from 15 to 25 [3, 5, 6], and setting such a threshold ignores the continuous nature of the MELD score. The continuous nature of the MELD score, combined with the absence of any survival interaction between TIPS and increasing MELD, suggests that defining a threshold that constitutes a high MELD score may be unnecessary. Third, there is selection bias in patients undergoing TIPS versus serial LVP as evidenced by the lower MELD scores and Charlson comorbidity scores in the TIPS cohort at baseline. In this study, selection bias was reduced through multivariate analysis and through propensity score matching [23] to exclude serial LVP patients who were unlike TIPS patients.

Although MELD score predicts survival after TIPS, this study suggests it does not accurately distinguish patients who benefit from TIPS creation versus those who are harmed by it. Thus, the MELD score appears to represent a prognostic but not predictive biomarker. Other physiologic biomarkers, such as nutritional status [24], sarcopenia [25], or prior encephalopathy [26], may be needed to predict patients who benefit from or are harmed by TIPS. Furthermore, the accuracy of the MELD score is limited in other settings that are of clinical relevance in cirrhotic patients, such as in those with hepatocellular carcinoma [2].

This study has a number of limitations. First, as in any retrospective study, selection bias may be present and may not be fully resolved by statistical techniques such as propensity score matching or multivariate analysis. Second, the relatively small sample size does not allow analysis of competing causes of death and also precludes subanalyses to discern if TIPS confers better survival in certain higher MELD patients such as those with hepatorenal syndrome or confers worse survival in certain higher MELD patients such as those with hepatic encephalopathy [27]. Third, lack of identification of a statistically significant survival interaction between TIPS creation and MELD score does not definitively prove the absence of such an interaction, although it does suggest that any such hypothetical interaction is either small or nonexistent. Perhaps most importantly, this study focused exclusively on overall survival and did not analyze other equally important outcomes such as complications or quality of life. Some patients in this study continued to require intermittent LVP after TIPS, albeit at a lower rate, a finding consistent with previous data suggesting that as many as 65% of patients may still require LVP within 3 months after TIPS and a year may be required for TIPS to be of maximum benefit [28]. This study is unable to assess whether survival after TIPS in higher MELD score patients is sufficient to reach a point where ascites control leads to improved quality of life.

Conclusion

In conclusion, this study found no evidence of an interaction between TIPS creation and MELD score to suggest that TIPS confers worse survival than serial LVP in patients with higher MELD scores and refractory ascites. These results suggest that patients should not be denied a TIPS on the basis of a higher MELD score if a TIPS would otherwise be the most appropriate means of palliating medically refractory ascites.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964

Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. This article does not contain any studies with animals performed by any of the authors.

References

1. Gaba RC, Couture PM, Bui JT, Knuttinen MG, Walzer NM, Kallwitz ER, et al. Prognostic capability of different liver disease scoring systems for prediction of early mortality after transjugular intrahepatic portosystemic shunt creation. J Vasc Interv Radiol JVIR. 2013;24(3):411–20. https://doi.org/10.1016/j.jvir.2012.10.026 **20.e1-4; quiz 21**.
2. Ronald J, Wang Q, Choi SS, Suhocki PV, Hall MD, Smith TP, et al. Albumin-bilirubin grade versus MELD score for predicting survival after transjugular intrahepatic portosystemic shunt (TIPS) creation. Diagn Interv Imaging. 2018;99(3):163–8. https://doi.org/10.1016/j.diii.2017.10.008.
3. Ferral H, Gamboa P, Postoak DW, Albernaz VS, Young CR, Speeg KV, et al. Survival after elective transjugular intrahepatic portosystemic shunt creation: prediction with model for end-stage liver disease score. Radiology. 2004;231(1):231–6. https://doi.org/10.1148/radiol.2311030967.
4. Ferral H, Patel NH. Selection criteria for patients undergoing transjugular intrahepatic portosystemic shunt procedures: current status. J Vasc Interv Radiol JVIR. 2005;16(4):449–55. https://doi.org/10.1097/01.rvi.0000149508.64029.02.
5. Pan JJ, Chen C, Caridi JG, Geller B, Firpi R, Machicao VI, et al. Factors predicting survival after transjugular intrahepatic portosystemic shunt creation: 15 years' experience from a single tertiary medical center. J Vasc Interv Radiol JVIR. 2008;19(11):1576–81. https://doi.org/10.1016/j.jvir.2008.07.021.
6. Montgomery A, Ferral H, Vasan R, Postoak DW. MELD score as a predictor of early death in patients undergoing elective transjugular intrahepatic portosystemic shunt (TIPS) procedures. Cardiovasc Interv Radiol. 2005;28(3):307–12. https://doi.org/10.1007/s00270-004-0145-y.
7. Dariushnia SR, Haskal ZJ, Midia M, Martin LG, Walker TG, Kalva SP, et al. Quality improvement guidelines for transjugular intrahepatic portosystemic shunts. J Vasc Interv Radiol. 2016;27(1):1–7. https://doi.org/10.1016/j.jvir.2015.09.018.
8. Choe WH. Do cirrhotic patients with a high MELD score benefit from TIPS? Clin Mol Hepatol. 2014;20(1):15–7. https://doi.org/10.3350/cmh.2014.20.1.15.
9. Kamath PS, Kim WR. The model for end-stage liver disease (MELD). Hepatology. 2007;45(3):797–805. https://doi.org/10.1002/hep.21563.
10. Somsouk M, Kornfield R, Vittinghoff E, Inadomi JM, Biggins SW. Moderate ascites identifies patients with low model for end-stage liver disease scores awaiting liver transplantation who have a high mortality risk. Liver Transplant. 2011;17(2):129–36. https://doi.org/10.1002/lt.22218.
11. Bureau C, Thabut D, Oberti F, Dharancy S, Carbonell N, Bouvier A, et al. Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. Gastroenterology. 2017;152(1):157–63. https://doi.org/10.1053/j.gastro.2016.09.016.
12. Bai M, Qi XS, Yang ZP, Yang M, Fan DM, Han GH. TIPS improves liver transplantation-free survival in cirrhotic patients with refractory ascites: an updated meta-analysis. World J Gastroenterol. 2014;20(10):2704–14. https://doi.org/10.3748/wjg.v20.i10.2704.
13. Narahara Y, Kanazawa H, Fukuda T, Matsushita Y, Harimoto H, Kidokoro H, et al. Transjugular intrahepatic portosystemic shunt versus paracentesis plus albumin in patients with refractory ascites who have good hepatic and renal function: a prospective randomized trial. J Gastroenterol. 2011;46(1):78–85. https://doi.org/10.1007/s00535-010-0282-9.
14. Qi X, Guo X, Fan D. A trend toward the improvement of survival after TIPS by the use of covered stents: a meta-analysis of two randomized controlled trials. Cardiovasc Interv Radiol. 2015;38(5):1363–4. https://doi.org/10.1007/s00270-014-0996-9.
15. Saab S, Nieto JM, Lewis SK, Runyon BA. TIPS versus paracentesis for cirrhotic patients with refractory ascites. Cochrane Database Syst Rev. 2006;4:Cd004889. https://doi.org/10.1002/14651858.cd004889.pub2.
16. Spengler EK, Hunsicker LG, Zarei S, Zimmerman MB, Voigt MD. Transjugular intrahepatic portosystemic shunt does not independently increase risk of death in high model for end stage liver disease patients. Hepatol Commun. 2017;1(5):460–8. https://doi.org/10.1002/hep4.1053.
17. Horvath MM, Rusincovitch SA, Brinson S, Shang HC, Evans S, Ferranti JM. Modular design, application architecture, and usage of a self-service model for enterprise data delivery: the Duke Enterprise Data Unified Content Explorer (DEDUCE). J Biomed Inform. 2014;52:231–42. https://doi.org/10.1016/j.jbi.2014.07.006.
18. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011;173(6):676–82. https://doi.org/10.1093/aje/kwq433.
19. Loffroy R, Favelier S, Pottecher P, Estivalet L, Genson PY, Gehin S, et al. Transjugular intrahepatic portosystemic shunt for acute variceal gastrointestinal bleeding: Indications, techniques and outcomes. Diagn Interv Imaging. 2015;96(7–8):745–55. https://doi.org/10.1016/j.diii.2015.05.005.
20. Parvinian A, Bui JT, Knuttinen MG, Minocha J, Gaba RC. Transjugular intrahepatic portosystemic shunt for the treatment of medically refractory ascites. Diagn Interv Radiol. 2014;20(1):58–64. https://doi.org/10.5152/dir.2013.13131.
21. R Development Core Team. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2010.
22. Poguntke I, Schumacher M, Beyersmann J, Wolkewitz M. Simulation shows undesirable results for competing risks analysis with time-dependent covariates for clinical outcomes. BMC Med Res Methodol. 2018;18(1):79. https://doi.org/10.1186/s12874-018-0535-5.
23. Ho D, Imai K, King G, Stuart EA. MatchIt: nonparametric preprocessing for parametric causal inference. J Stat Softw. 2011;42(8):28. https://doi.org/10.18637/jss.v042.i08.
24. Rowley MW, Choi M, Chen S, Hirsch K, Seetharam AB. Refractory hepatic encephalopathy after elective transjugular intrahepatic portosystemic shunt: risk factors and outcomes with revision. Cardiovasc Interv Radiol. 2018. https://doi.org/10.1007/s00270-018-1992-2.
25. Trebicka J. Does transjugular intrahepatic portosystemic shunt stent differentially improve survival in a subset of cirrhotic patients? Semin Liver Dis. 2018;38(1):87–96. https://doi.org/10.1055/s-0038-1627457.
26. Pereira K, Carrion AF, Salsamendi J, Doshi M, Baker R, Kably I. Endovascular management of refractory hepatic encephalopathy complication of transjugular intrahepatic portosystemic shunt (TIPS): comprehensive review and clinical practice algorithm. Cardiovasc Interv Radiol. 2016;39(2):170–82. https://doi.org/10.1007/s00270-015-1197-x.

27. Rossle M, Gerbes AL. TIPS for the treatment of refractory ascites, hepatorenal syndrome and hepatic hydrothorax: a critical update. Gut. 2010;59(7):988–1000. https://doi.org/10.1136/gut.2009.193227.

28. Gaba RC, Parvinian A. How quickly does ascites respond to TIPS? Clinical follow-up of a cohort of eighty patients. Diagn Interv Radiol. 2014;20(4):364. https://doi.org/10.5152/dir.2014.13479.