Short outcome comparison of elderly patients versus nonelderly patients treated with transjugular intrahepatic portosystemic stent shunt

A propensity score matched cohort study

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Abstract
A transjugular intrahepatic portosystemic stent shunt (TIPSS) has been widely used to treat portal hypertension and its complications. However, no established guidelines mentioned whether age was a risk factor for the treatment of TIPSS.

The aim is to determine whether age is a risk factor for poor outcomes following TIPSS.

The retrospective cohort study included 134 patients who received TIPSS treatment from 2003 to 2016. The adverse events after the TIPSS treatment were compared after propensity score matching to reduce the effect of selection bias. Multivariate logistic regression was conducted to confirm the potential confounders for rebleeding (RB) and ascites after TIPSS therapy.

After excluding 10 patients, 124 patients were analyzed. Among them, 37 patients were included in the elderly group. In the propensity score matched cohort (32 pairs), there was no significant difference between the elderly group and the nonelderly group in terms of the event after TIPSS therapy (All \( P > .05 \)). Multivariate logistic regression analysis revealed that hypertension (OR 13.246, 95% CI: [1.29, 136.073]; \( P = .03 \)) was an independent risk factor for RB. In addition, smoking (OR 4.48, 95% CI: [1.43, 14.033]; \( P = .01 \)) and preascites (OR 6.7, 95% CI: [2.04, 22.005]; \( P = .002 \)) were independent risk factors for ascites after TIPSS treatment.

Age is not an independent risk factor for poor outcomes following the treatment of TIPSS. Smoking and preascites are independent risk factors for patients’ asces, and hypertension is an independent risk factor for patients’ RB after TIPSS therapy.

Abbreviations: AAD = against advice discharge, ALT = glutamic-pyruvic transaminase, APTT = activated partial thromboplastin time, AST = aspartate transaminase, BRTO = balloon-occluded retrograde transvenous obliteration, BUN = blood urea nitrogen, CHD = coronary heart disease, CIs = confidence intervals, DBIL = direct bilirubin, HCC = hepatocellular carcinoma, HD = hospital deaths, HGB = hemoglobin, HM = hepatic myelopathy, HV = hepatic vein, IBIL = indirect bilirubin, IH = intraperitoneal hemorrhage, INR = international normalized ratio, LFI = liver function injury, ME = pleural effusion, PHS = postoperative hospital stay, PLT = platelet, Pre-HE = pre hepatic encephalopathy, PSE = partial splenic embolization, PT = prothrombin time, PTVE = percutaneous transhepatic variceal embolization, PVCT = portal vein cavernous transformation, PVTh = hepatic vein thrombosis, RB = re-bleeding, RH = right heart dysfunction, Scr = serum creatinine, SD = stent dysfunction, TBIL = total bilirubin, TIPSS = transjugular intrahepatic portosystemic stent shunt, TLS = total length of stay, TP = total protein, VOD = hepatic veno-occlusive disease.

Keywords: age TIPSS, propensity score matching

1. Introduction
Portal hypertension[1] is an increase in the porto-systemic pressure gradient in any portion of the portal venous system. Portal hypertension[2] results from a combination of both an increased resistance to and increased flow of portal blood that could be caused by prehepatic abnormalities (e.g., portal vein thrombosis), posthepatic abnormalities (e.g., Budd-Chiari syndrome), intrahepatic noncirrhotic causes (e.g., schistosomiasis), and cirrhosis. Many complications result from portal hypertension, such as refractory ascites, recurrent variceal bleeding, and portal vein thrombosis.

A transjugular intrahepatic portosystemic stent shunt (TIPSS) is a nonsurgical method of portal decompression that is currently used to treat major complications of portal hypertension[3] and has been proven to be an effective procedure for the treatment of portal hypertension and its complications during the last 25 years.[4,5] The aging process is deleterious for fitness[6] and is the main risk factor for prevalent diseases in developed countries, including cancer, cardiovascular disease, and neurodegeneration.

Propensity score matching studies regarding TIPSS have been published. Gaba et al[7] proved that a covered stent-graft TIPSS...
improved intermediate- to long-term survival without significantly increasing the short-term mortality of ascites patients. There were also propensity score matching studies concerning age and treatment efficiency. For example, Hu et al\(^9\) proved that age alone was not a parameter for the treatment of advanced hepatocellular carcinoma (HCC) patients.

However, no research has been published regarding the effect of age on TIPSS treatment with the analysis method of propensity score matching, and no established guidelines mentioned whether age was a risk factor for poor outcomes following TIPSS treatment. In our research, we thus studied whether age was a factor that influenced the efficacy of TIPSS.

2. Methods

2.1. Patients

This retrospective cohort study included 134 patients with TIPSS at Shandong Provincial Hospital, Shandong, China from 2003 to 2016. Patients who met any of the following criteria were excluded: patients who underwent transarterial chemoembolization (TACE) therapy within 1 month; patients who were treated with emergency TIPSS; the TIPSS operation was not successful; and patients who were lost to follow-up. Based on these criteria, a total of 10 patients were excluded from the study. Of these, 4 patients underwent TACE therapy within a month, 1 patient experienced emergency TIPSS treatment, the TIPSS operation of 1 patient failed, and 4 patients did not participate in the follow-up process. Finally, a total of 124 patients were included in our study. Among them, 37 were elderly patients (age ≥ 60 years), and 87 were nonelderly patients (age < 60 years).

To reduce the effects of selection bias and potential confounders in our study, we performed a rigorous adjustment for differences in baseline characteristics by using propensity score matching.\(^9\) We considered gender, hypertension, diabetes, coronary heart disease (CHD), smoking, drink, indication and etiology, prehepatic encephalopathy (pre-HE), preascites, splenectomy, Child–Pugh score, Child–Pugh classification, hemoglobin (HGB), platelet (PLT), total protein, albumin, glutamic-pyruvic transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), serum creatinine (Scr), blood urea nitrogen (BUN), prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), and treatment. Thirty-two patient pairs were selected (Fig. 1). The study protocol was conducted in accordance with the Declaration of Helsinki and current ethical guidelines. Our study was approved by the Medical Ethics Committee of Shandong Provincial Hospital, and informed consent was obtained from all subjects.

2.2. TIPSS

A standard, widely used TIPSS procedure was performed beginning with right jugular vein access through which a 10-F sheath was advanced into the right atrium.\(^10\) After pressure measurements were obtained, the 10-F sheath was advanced into the right or middle hepatic vein (HV). Next, a Roups-100 needle system was advanced into the HV over a guidewire, and the catheter-trocar apparatus was advanced toward the expected location of the right PV or the left PV if the middle HV was used. Next, a direct portal venogram and portal pressures were obtained. Then, the intraportal track was dilated with a balloon catheter, and the 10-F sheath system was advanced into the PV. A 7-mm/8-mm diameter Wallstent was inserted, and the stent was dilated with a balloon. Additional stents were inserted to produce a smooth track from the PV bifurcation to the right HV. The portosystemic gradient was measured, and if necessary, the shunt was dilated with a balloon until the gradient was < 10 mm Hg. If necessary, additional stents were placed. If varices were still opacified, variceal embolization was performed through the catheter in the PV.

2.3. Data collection and follow-up

The following demographic, laboratory and clinical information was collected from medical chart review: age, gender, hypertension, diabetes, CHD, smoking, drink, indication and etiology, pre-HE, preascites, splenectomy, Child–Pugh score, Child–Pugh classification, HGB, PLT, TP, albumin, ALT, AST, TBIL, DBIL, IBIL, Scr, BUN, PT, APTT, INT, and treatment.

The outcome was treatment-related adverse events within 1 year after TIPSS therapy. Adverse events included fever, vomit, bellyache, diarrhea, HE, ascites, pleural effusion (PE), liver function injury (LFI), hepatic myelopathy (HM), stent dysfunction (SD), intraperitoneal hemorrhage (IH), right heart dysfunction (RHD), and rebleeding (RB). We also calculated the total length of stay (TLS) of patients, the number of patients who were against discharge (AAD), and patients who experienced hospital deaths (HD). All patients were followed up for 1 year.

2.4. Propensity score analysis

The propensity scores were estimated regarding all categorical variables presented in the baseline characteristics with a parsimonious logistic regression model.\(^9\) We used a nearest-neighbor matching algorithm without replacement. One-to-one caliper matching was performed within 25% of the standard deviation of log-transformed propensity scores. The value of the caliper was 0.5. In the propensity-score-matched cohort, the 2 groups were compared in terms of their baseline characteristics.

![Figure 1. Flowchart of patient selection.](Image 394x578 to 463x603)
The balance of the matched cohort was evaluated using a standardized mean difference and a hypothetical test. Multinomial logistic regression was used to examine the potential confounders of RB and ascites after TIPSS treatment. Odds ratios with 95% confidence intervals (CIs) were calculated.

2.5. Statistical methods
In all study subjects, continuous variables were compared parametrically using Student t test or were compared nonparametrically using the Mann–Whitney U test. Categorical variables were compared using the χ² test or Fisher exact test as appropriate.

Statistical results are presented as the mean ± standard deviation and the number of patients (%). Two-sided test P values <.05 were defined as significant. Statistical analyses were conducted using the IBM SPSS statistical package 22.0 (IBM, Armonk, NY) with 3 plug-ins (SPSS R-plug-in, R and psmatching).

3. Results

3.1. Patient characteristics before propensity score matching
One hundred twenty-four patients treated with TIPSS were included in this study. Thirty-seven patients were older than the other 87 patients.

The baseline characteristics of the elderly group and the nonelderly group are summarized in Table 1. There were no significant differences between the groups with respect to gender, hypertension, diabetes, CHD, smoking, indication and etiology, pre-HE, preascites, splenectomy, Child–Pugh score, Child–Pugh classification, HGB, PLT, TP, albumin, ALT, AST, TBIL, DBIL, IBIL, Scr, BUN, PT, APTT, INT, or treatment. However, the number of patients who drank (P = .012) were significantly different between the elderly and nonelderly groups.

3.2. Patient characteristics after propensity score matching
In the propensity score matched cohort, there were no significant differences between the elderly group and the nonelderly group regarding gender, hypertension, diabetes, CHD, smoking, drink, indication and etiology, pre-HE, preascites, splenectomy, Child–Pugh score, Child–Pugh classification, HGB, PLT, TP, albumin, ALT, AST, TBIL, DBIL, IBIL, Scr, BUN, PT, APTT, INT, or treatment. The results are shown in Table 2.

3.3. Comparison of therapy-related events
In our research, we included the therapy-related events as follows: fever, vomit, bellyache, diarrhea, hepatic encephalopathy, ascites, PE, liver function injury (LFI), hepatic myelopathy (HM), stent dysfunction (SD), intraperitoneal hemorrhage (IH), right heart dysfunction (RHD), rebleeding (RB), TLS, PHS, AAD, and HD. There were no significant differences between the elderly group and the nonelderly group. The results are shown in Table 3.

3.4. Multivariate analysis for the association of confounding factors with RB
Multivariate logistic regression was performed to examine associations with patients’ RB after TIPSS (Table 4). The analysis

| Variables | Elderly group | Nonelderly group | P value |
|-----------|---------------|------------------|---------|
| Gender, male | 23 (62.6%) | 64 (73.6%) | .204 |
| Hypertension | 2 (5.4%) | 6 (6.9%) | .757 |
| Diabetes | 4 (10.8%) | 12 (13.8%) | .65 |
| CHD | 1 (2.7%) | 2 (2.3%) | .893 |
| Smoking | 12 (32.4%) | 30 (34.5%) | .825 |
| Drink | 7 (18.9%) | 37 (42.3%) | .012 |

Data are shown as the mean ± standard deviation or the number (%) of patients. PVT = hepatic vein thrombosis, PCTV = portal vein cavernous transformation, VOD = hepatic veno-occlusive disease, PTVE = percutaneous transhepatic veno-occlusive disease, PSE = percutaneous transhepatic veno-occlusive disease, BRTO = balloon-occluded retrograde transvenous obliteration.
Table 2
Comparison of baseline characteristics between the elderly (n=32) and nonelderly (n=32) groups after propensity score match.

| Variables         | Elderly group | Nonelderly group | P value |
|-------------------|---------------|------------------|---------|
| Gender, male      | 20 (62.5%)    | 19 (60.9%)       | .783    |
| Hypertension      | 2 (6.2%)      | 2 (6.2%)         | 1       |
| Diabetes          | 4 (12.5%)     | 4 (12.5%)        | 1       |
| CHD               | 0             | 0                |         |
| Smoking           | 11 (34.4%)    | 8 (29.3%)        | .412    |
| Drink             | 7 (21.9%)     | 9 (28.1%)        | .567    |
| Indication and etiology | 0.564 | – |
| Recurrent hemorrhage | 18 (56.2%) | 19 (59.4%) | – |
| Refractory ascites | 3 (9.4%)    | 4 (12.5%)        | –       |
| Budd-Chiari       | 1 (3.1%)      | 2 (6.2%)         | –       |
| Rebled after surgery | 1 (3.1%) | – |
| PVT               | 9 (28.1%)     | 4 (12.5%)        | –       |
| PVTCT             | 0             | 2 (6.2%)         | –       |
| VOD               | 0             | 1 (3.1%)         | –       |
| HE                | 0             | 0                | 1       |
| Ascites           | 22 (68.8%)    | 25 (78.1%)       | .396    |
| PE                | 6 (18.8%)     | 6 (18.8%)        | .601    |
| Splenectomy       | 11 (34.4%)    | 9 (28.1%)        | .542    |
| Child-Pugh score  | 6.34 ± 1.23   | 6.56 ± 1.16      | .468    |
| Child-Pugh classfication | – | – |
| A                 | 20 (62.5%)    | 17 (53.1%)       | –       |
| B                 | 12 (37.5%)    | 15 (46.9%)       | –       |
| C                 | 0             | 0                | –       |
| HGB               | 5.46 ± 3.59   | 5.07 ± 5.80      | .807    |
| PLT               | 4.78 ± 3.59   | 4.78 ± 3.59      | .529    |
| Normal            | 11 (34.4%)    | 8 (25%)          | –       |
| > 300 × 10^9/mm^3 | 1 (3.1%)      | 5 (15.6%)        | –       |
| > 50 × 10^9/mm^3  | 16 (50%)      | 15 (46.9%)       | –       |
| 30–50 × 10^9/mm^3 | 2 (6.2%)      | 2 (6.2%)         | –       |
| < 30 × 10^9/mm^3  | 2 (6.2%)      | 2 (6.2%)         | –       |
| TP                | 50.73 ± 9.62  | 61.27 ± 9.67     | .467    |
| Albumin           | 30.96 ± 5.72  | 32.52 ± 3.64     | .187    |
| ALT               | 26.19 ± 12.94 | 24.06 ± 17.35    | .974    |
| AST               | 38.88 ± 18.65 | 37.78 ± 20.52    | .824    |
| TBL               | 27.19 ± 19.34 | 27.94 ± 18.40    | .862    |
| IBIL              | 7.78 ± 7.79   | 7.16 ± 5.35      | .712    |
| ILB               | 19.31 ± 12.08 | 20.76 ± 13.50    | .652    |
| SCR               | 31 (96.9%)    | 30 (93.8%)       | –       |
| Normal            | 31 (96.9%)    | 30 (93.8%)       | –       |
| <= 178 μmol/L     | 1 (3.1%)      | 1 (3.1%)         | –       |
| 178–445 μmol/L    | 0             | 1 (3.1%)         | –       |
| > 445 μmol/L      | 0             | 0                | –       |
| BUN               | 6.25 ± 3.21   | 6.72 ± 3.49      | .58     |
| PT                | 14.60 ± 2.00  | 15.04 ± 1.83     | .368    |
| APTT              | 35.42 ± 7.45  | 33.71 ± 9.27     | .42     |
| INR               | 1.23 ± 0.17   | 1.27 ± 0.17      | .308    |
| Treatment         | 3.57          | –                | –       |
| Tips              | 9 (28.1%)     | 9 (28.1%)        | –       |
| Tips+PTVE         | 23 (71.9%)    | 19 (59.4%)       | –       |
| Tips+PSE          | 0             | 1 (3.1%)         | –       |
| Tips+PTVE+PSE     | 0             | 0                | –       |
| Tips+thrombolysis | 0             | 2 (6.2%)         | –       |
| Tips+PTVE+thrombolysis | 0 | 1 (3.1%) |
| Tips+PTVE+BRTD    | 0             | 0                | –       |

Data are shown as the mean ± standard deviation or the number (%) of patients.

PVT = hepatic vein thrombosis, PVTCT = portal vein cavernous transformation, VOD = hepatic veno-occlusive disease, PTVE = percutaneous transhepatic variceal embolization, PSE = partial splenic embolization, BRTD = balloon-occluded retrograde transvenous obliteration.

Table 3
Comparison of therapy-related events between the elderly and nonelderly groups.

| Events                        | Elderly group (N=32) | Nonelderly group (N=32) | P value |
|-------------------------------|----------------------|-------------------------|---------|
| Fever                         | 11 (34.4%)           | 7 (21.9%)               | .266    |
| Vomit                         | 5 (15.6%)            | 7 (21.9%)               | .443    |
| Bellalanche                   | 8 (25%)              | 6 (18.8%)               | .59     |
| Diarrhea                      | 2 (6.2%)             | 0                       | 0.151   |
| HE                            | 4 (12.5%)            | 6 (18.8%)               | .491    |
| Ascites                       | 15 (46.9%)           | 17 (53.1%)              | .393    |
| PE                            | 5 (15.6%)            | 3 (9.4%)                | .701    |
| RHD                           | 6 (18.8%)            | 3 (9.4%)                | .542    |
| RB                            | 7 (21.9%)            | 3 (9.4%)                | .27     |
| TLS                           | 17 ± 7.7             | 16.78 ± 9.0             | .905    |
| PHS                           | 9.28 ± 5.1           | 8.63 ± 5.6              | .625    |
| AAD                           | 1 (3.1%)             | 2 (6.2%)                | .554    |
| HD                            | 1 (3.1%)             | 1 (3.1%)                | 1       |

AAD = against advice discharge, HD = hospital death, HE = hepatic encephalopathy, HM = hepatic myopathy, IBIL = indirect bilirubin, IH = intraperitoneal hemorrhage, LFI = liver function injury, PE = pleural effusion, PHS = postoperative hospital stay, RB = re-bleeding, RHD = right heart dysfunction, SD = stent dysfunction, TLS = total length of stay.

Multivariate logistic regression was performed to examine the associations with patients’ ascites after TIPSS (Table 3). The analysis revealed that smoking (OR 4.48, 95% CI: [1.43, 14.033]; P= .01) and preascites (OR 6.7, 95% CI: [2.04, 22.005]; P=.002) were independent risk factors for ascites after TIPSS treatment.

4. Discussion

TIPSS has been widely used for the treatment of portal hypertension and its complications. Many studies have confirmed the role of TIPSS for portal hypertension. For example, Bissonnette et al. thought that TIPSS was an excellent option to treat severe complications of idiopathic noncirrhotic portal hypertension. Gastroesophageal variceal bleeding is a severe complication of portal hypertension. RB is associated with significant morbidity and mortality, thus, preventing varical RB may be a substitute outcome of survival. However, the studies about the effect of age on the treatment of TIPSS were limited. And, different researchers had different conclusions about the role of age in the treatment of TIPSS. Garcia-Pagan et al. proved age was a risk factor for Budd-
Chiari syndrome patients with TIPSS. Syed et al\(^{[17]}\) thought TIPSS was an effective procedure to control refractory complications of portal hypertension in elderly patients. We found no significant differences between elderly patients and nonelderly patients receiving TIPSS treatment (all \( P > .05 \)). Age should thus not be the limitation for the choice of patients for TIPSS treatment.

Unlike us, the patients in Garcia-Pagan study were included from 1997 to 2006 years, which were almost 10 years earlier than our patients. Syed et al only studied 23 patients, and there were not control group in their study. In our study, our valid 124 patients were included from 2003 to 2016 years. In recent 10 years, all aspects of technology and the operation level of doctors have developed rapidly. And we used propensity score matching to narrow the gap between elderly group and nonelderly group to make our conclusions more believable.

TACE has emerged as an effective treatment strategy for patients with HCC. Although TACE was an effective treatment strategy for HCC with TIPSS, Miura et al\(^{[18]}\) proved that TACE might be associated with higher complication rates for patients who are treated with TIPSS. Thus, we excluded the patients treated with TACE.

There are limitations to the present study because of its retrospective design. More patients are needed to match more pairs and increase the credibility of the results.

We set 60 years old as the boundary between the elderly group and the nonelderly group because of the number of patients. There were only 5 patients over 70 years old in the original data, and the nonelderly group because of the number of patients. Therefore we excluded the patients over 70 years old.

In conclusion, our propensity matching score study suggests there is no significant difference in TIPSS between elderly and nonelderly patients. Age is not a risk factor for poor outcomes following TIPSS therapy. Hypertension can significantly affect patients’ RB after TIPSS therapy and is an independent risk factor for patients’ RB after TIPSS therapy. Additionally, smoking and ascites before TIPSS can significantly affect patients’ ascites after TIPSS therapy; therefore, they both are independent risk factors for patients’ ascites after TIPSS.

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**Table 4**

Multivariate analysis for the association of confounding factors with RB.

| Factors | B    | SE  | \( \chi^2 \) | \( P \) value | ORs  | 95% CI  |
|---------|------|-----|-------------|--------------|------|--------|
| Age     | -0.619 | 0.648 | 0.913 | .339 | 0.539 | 0.151 | 1.917 |
| Gender  | 0.086  | 0.818 | 0.011 | .916 | 1.09  | 0.219 | 5.417 |
| Hypertension | 2.584 | 1.188 | 4.727 | .03 | 13.249 | 0.582 | 115.158 |
| Smoking | -0.026 | 0.788 | 0.01 | .973 | 0.974 | 0.208 | 4.56 |
| Preascites | 1.681 | 1.067 | 2.479 | .115 | 5.37  | 0.663 | 43.511 |
| After-fever | 0.947 | 0.689 | 1.888 | .169 | 2.578 | 0.668 | 9.953 |
| After-diarrhea | 2.103 | 1.349 | 2.43 | .119 | 8.187 | 0.582 | 115.158 |
| After-ascites | 1.578 | 0.895 | 3.112 | .078 | 4.847 | 0.839 | 27.99 |
| After-HE | -1.658 | 1.252 | 1.755 | .185 | 0.19  | 0.016 | 2.214 |

CI = confidence intervals, HE = hepatic encephalopathy.

**Table 5**

Multivariate analysis for the association of confounding factors with after-ascites.

| Factors | B    | SE  | \( \chi^2 \) | \( P \) value | ORs  | 95% CI  |
|---------|------|-----|-------------|--------------|------|--------|
| Age     | -0.385 | 0.505 | 0.579 | .447 | 0.681 | 0.253 | 1.833 |
| Gender  | -0.707 | 0.609 | 1.348 | .246 | 0.493 | 0.15  | 1.626 |
| Hypertension | -0.015 | 0.919 | 0 | .987 | 0.985 | 0.163 | 5.961 |
| Smoking | 1.5  | 0.583 | 6.626 | .01 | 4.48  | 1.43  | 14.033 |
| Preascites | 1.902 | 0.607 | 9.828 | .002 | 6.7  | 2.04  | 22.005 |
| After-fever | 0.067 | 0.553 | 0.015 | .904 | 1.069 | 0.362 | 3.158 |
| After-diarrhea | 1.212 | 1.304 | 0.864 | .353 | 3.362 | 0.261 | 43.332 |
| After-HE | -0.256 | 0.672 | 0.145 | .703 | 1.292 | 0.346 | 4.818 |

CI = confidence intervals, HE = hepatic encephalopathy.
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