

Dear Editor and Reviewers,

Thank you very much for all your comment and suggestions. We have added and modified some parts according to your suggestions. Our responses to the reviewers' comments are as follows:

**Reviewer 1:** The authors investigated targeted puncture of left branch of intrahepatic portal vein in transjugular intrahepatic portosystemic shunt to reduce hepatic encephalopathy. The subject is interesting and the idea is novel. So, I suggest acceptance of the article.

**Response:** Thank you for your comment for acceptance of our article.

**Reviewer 2:** I read with great interest the manuscript entitled "Targeted puncture of left branch of intrahepatic portal vein in transjugular intrahepatic portosystemic shunt to reduce hepatic encephalopathy". The manuscript is well structured. The presented results have important clinical implication. But, I have several concerns regarding the manuscript:

1. Why autoimmune and metabolic etiology is not mentioned as etiology?

**Response:** The autoimmune and metabolic etiology was not cryptogenic hepatitis; therefore, we have changed the table below.

**Table 1. Baseline characteristics in the two groups**

Characteristics	Group A	Group B	<i>P</i>
Gender, M/F	398/539	166/141	0.308
Age (mean±SD) (yr)	44.48±18.23	40.80±17.76	0.381
Child-Pugh A/B/C	79/729/137	25/160/122	0.753
MELD score (mean±SD)	13.19±7.35	12.26±8.47	0.591
Viral hepatitis	585	194	0.947
Chronic ethanol consumption	210	61	0.651

Autoimmune hepatitis	53	23	0.463
Metabolic liver disease	89	29	0.527
Variceal hemorrhage	653	236	0.163
Refractory ascites	384	117	0.125
Laboratory tests			
Alanine transaminase (U/L)	69.13±12.21	56.24±11.17	0.615
Aspartate transaminase (U/L)	56.14±14.19	49.53±12.24	0.653
Alkaline phosphatase (U/L)	129.63±26.32	136.46±27.02	0.534
γ-glutamyl transpeptidase (U/L)	236.23±62.46	248.13±53.32	0.561
Total bilirubin (μmol/L)	24.32±5.63	26.46±6.37	0.482
Albumin (g/L)	29.14±7.22	31.23±6.52	0.237
Prothrombin time (s)	16.03±7.31	18.46±5.17	0.316
Clinical presentations			
Abdominal distention	627	193	0.164
Abdominal pain	48	17	0.237
Weakness	473	136	0.253
Poor appetite	729	275	0.428
Jaundice	15	6	0.107
Splenomegaly	482	174	0.316
Lower limbs edema	136	57	0.263
Endoscopic therapy	1736	625	0.421
Ascites paracentesis	1492	479	0.304

2. Taking into account that this is a retrospective study, how written informed consent was obtained?

**Response:** We have changed the sentence “The Institutional Review Board approved the study protocol and all of the patients provided written informed consent” to “The Institutional Review Board approved the study protocol”.

3. "The shunts were dilated to their full nominal diameter to reach a target portosystemic gradient (PSG) of  $< 12$  mmHg"- was HPVG measured during the procedure? According to the results it was, so, it should be adequately described in the methodology section . HPVG was measured during the procedure.

**Response:** TIPS was performed under standard local anesthesia as described previously<sup>[9]</sup>. The entire length of the intrahepatic tract was covered by the stent graft (BARD, Fluency, Voisins le Bretonneux, France; or Viatorr, W.L. Gore & Associates, Flagstaff, AZ, USA). Hepatic venous pressure gradient (HPVG) and portal vein pressure were measured during the procedure and the shunts were dilated to their full nominal diameter to reach a target portosystemic gradient (PSG) of  $< 12$  mmHg. Obvious gastroesophageal collateral vessels observed during the TIPS procedure were embolized with coils (Cook Inc., Bloomington, IL, USA; or Interlock Coil, Boston Scientific Corporation, Natick, MA, USA). Subsequent direct portography was performed to evaluate whether the portal venous system was completely patent. After the TIPS procedure, intravenous heparin (4000 U/d; Chase Sun Pharma Co. Ltd., Tianjin, China) was administered for 3 d and oral warfarin was given at 2.5 mg/d (Orion Pharma Co. Ltd., Orionintie, Finland) to achieve an international normalized ratio (INR)  $\leq 2.0$ , if prolonged INR, oral warfarin was not given.

4. "After the TIPS procedure, intravenous heparin (4000 U/d; Chase Sun Pharma Co. Ltd., Tianjin, China) was administered for 3 d and oral warfarin was given at 2.5 mg/d (Orion Pharma Co. Ltd., Orionintie, Finland) to achieve an international normalized ratio (INR)  $\leq 2.0$ ."-usually patients with liver cirrhosis have prolonged INR, and warfarin influence the INR in opposite way . If there is no thrombosis in the portal vein system, there is controversy about whether anticoagulation and antiplatelet after TIPS procedure currently. We generally give oral anticoagulants in the case of monitoring INR, if prolonged INR, oral warfarin was not given.

**Response:** TIPS was performed under standard local anesthesia as described previously<sup>[9]</sup>. The entire length of the intrahepatic tract was covered by the stent graft (BARD, Fluency, Voisins le Bretonneux, France; or Viatorr, W.L. Gore & Associates, Flagstaff, AZ, USA). The shunts were dilated to their full nominal diameter to reach a target portosystemic gradient (PSG) of < 12 mmHg. Obvious gastroesophageal collateral vessels observed during the TIPS procedure were embolized with coils (Cook Inc., Bloomington, IL, USA; or Interlock Coil, Boston Scientific Corporation, Natick, MA, USA). Subsequent direct portography was performed to evaluate whether the portal venous system was completely patent. After the TIPS procedure, intravenous heparin (4000 U/d; Chase Sun Pharma Co. Ltd., Tianjin, China) was administered for 3 d and oral warfarin was given at 2.5 mg/d (Orion Pharma Co. Ltd., Orionintie, Finland) to achieve an international normalized ratio (INR)  $\leq$  2.0, if prolonged INR, oral warfarin was not given.

5. “Among them, 221 patients died from hepatic tumor, 35 from hepatic failure, 116 from multiorgan failure, and 47 from other causes.” - define hepatic failure and multiorgan failure. Multiorgan failure is probably manifestation of ACLF.

**Response:** We have changed the sentence “Among them, 221 patients died from hepatic tumor, 35 from hepatic failure, 116 from multi-organ failure, and 47 from other causes.” to “Among them, 221 patients died from hepatic tumor, 151 from multiorgan failure, and 47 from other causes.”