for measurement of HDL-C and apo-AI. In our study, we used a homogeneous assay for HDL-C and immunoturbidimetry for apo-AI, which we consider state-of-the-art assays for these biomarkers.[3,4] Unfortunately, the methods used in the Chinese cohort to measure HDL-C and apo-AI were not described in the letter by Wen *et al.*

It should be noted that HDL-C determination is generally problematic in disease states with very low HDL-C levels.[5] Nevertheless, the prognostic value of both HDL-C and apo-AI remained excellent in our ACLF subcohort. The use of an assay with optimal sensitivity and accuracy is of utmost importance given the low levels observed in chronic liver failure and especially in ACLF.

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Conflicts of interest
All authors declare that they have no conflicts of interest related to the study.

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Authors' contributions
RES, GM: data evaluation, manuscript writing; HS: lipid assay; all authors: final review.

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Achieving an effective pressure reduction after TIPS: The need for a new target

To the Editor:

We read with great interest the recent article by Jaume Bosch, proposing new insights into the hemodynamic target used to guide transjugular intrahepatic portosystemic shunt (TIPS).[1] The author also suggested small diameter TIPS, combined with other procedures or pharmacological therapy when necessary, might help avoid hepatic encephalopathy (HE). We would like to compare the outcomes of patients with portal pressure gradient (PPG) >12 mmHg and those with PPG ≤12 mmHg after TIPS creation.

Two hundred and sixteen cirrhotic patients who underwent *de novo* TIPS placement due to variceal bleeding between June 2015 and April 2019 in our department were retrospectively reviewed. Written informed consent was obtained from each patient, and the study protocol was approved by the ethics committee of our hospital. The TIPS procedure was performed under local anesthesia. The intrahepatic tract was dilated with an 8×60 mm angioplasty balloon, followed by the placement of an 8-mm Fluency ePTFE-covered stent (Bard, Murray Hill, USA). The stent lengths used were 6 cm (n = 163, 75.5%) and 8 cm (n = 53, 24.5%). Persistent visualized collaterals on post-TIPS portography were embolized. PPG was measured after the embolization. The haemodynamic success of TIPS (final PPG ≤12 mmHg) was not achieved in 37 patients (17.1%). The baseline characteristics of patients in group 1 (PPG >12 mmHg) and group 2 (PPG ≤12 mmHg) are

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Table 1. Demographics and clinical outcomes of patients in 2 groups.

Variables	Group 1 (n = 37)	Group 2 (n = 179)
Age, years	47.0 (42.0, 52.0)	49.0 (43.0, 59.0)
Sex, male/female	28/9	132/47
Cause of liver disease, n		
Chronic HBV infection	25 (67.6%)	117 (65.4%)
Alcohol	6 (16.2%)	28 (15.6%)
Others	6 (16.2%)	34 (19.0%)
Child-Pugh score	8 (7, 8)	7 (6, 8)
MELD score	9.8 (9.0, 12.6)	9.9 (8.6, 11.6)
Indication of TIPS, n (%)		
Acute variceal bleeding	4 (10.8%)	9 (5.0%)
Second prophylaxis of variceal bleeding	33 (89.2%)	170 (95.0%)
Variceal embolization, n (%)	36 (97.3%)	145 (81.0%)
PPG before TIPS, mmHg	27 (25, 30)	20 (17, 23)
PPG after TIPS, mmHg	15 (14, 19)	8 (6, 10)
Percentage of PPG reduction, %	44.0% (31.0%, 51.5%)	60.0% (51.2%, 68.5%)
Duration of follow-up, days	433 (252, 627)	419 (292, 643)
Outcomes		
Variceal rebleeding	6	23
TIPS dysfunction	9	44
Hepatic encephalopathy	11	54
Death	6	8

MELD, model for end-stage liver disease; PPG, portal pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.

summarized in Table 1. In group 1, the median PPG was reduced from 27 mmHg (IQR, 25-30 mmHg) to 15 mmHg (IQR, 14-19 mmHg). In group 2, the median PPG was reduced from 20 mmHg (IQR, 17-23 mmHg) to 8 mmHg (IQR, 6-10 mmHg). The median percentage reduction of PPG was 44% (IQR, 31%-51.5%) in group 1 and 60% (IQR, 51.2%-68.5%) in group 2.

There was no significant difference between group 1 and 2 in terms of 1-year probability of remaining free of variceal rebleeding (91.8% *vs.* 90.1%), 1-year probability of HE (29.1% *vs.* 29.5%), 1-year probability of shunt dysfunction (14.5% *vs.* 17%) and 1-year probability of survival (91.9% *vs.* 97.8%). In group 1, variceal rebleeding occurred in 6 patients. TIPS dysfunction was confirmed in each patient. Five patients received shunt revision, and 1 underwent endoscopic treatment. Still, 3/6 patients died of variceal rebleeding after discharge. During follow-up, another 3 patients died due to liver failure 56, 112 and 480 days after TIPS placement, respectively. None of them had an acute-on-chronic liver failure before TIPS.

Previous studies have demonstrated that variceal rebleeding rarely occurred in patients with a PPG of less than 12 mmHg.[2,3] Therefore, the final PPG ≤12 mmHg was generally considered the threshold of hemodynamic success of TIPS.[4] However, patients who had a reduction by 25-50% may still have a favorable outcome compared with a widely used threshold value of 12 mmHg after TIPS creation.[5] In our cohort, the cumulative rates of variceal rebleeding, HE and mortality were similar between the 2 groups and were consistent with patients who had a final PPG ≤12 mmHg in previous reports.[6] The relatively high TIPS dysfunction rate may be due to non-dedicated stent use because the dedicated stent was not available during that time in our institution.

In addition, the use of 8-mm stents may cause less reduction of PPG. Our previous study found that 8-mm TIPS in the Chinese population was sufficient to decompress the portal venous system, prevent variceal rebleeding and reduce HE incidence compared with 10-mm TIPS.[7] One randomized controlled trial also confirmed that 8-mm stents could reduce the risk of post-TIPS HE and liver function impairment.[8] More recently, Trebicka and his colleagues demonstrated that 8-mm stents were associated with prolonged survival compared with 10-mm stents.[9] In light of this, a smaller TIPS, despite a possible higher post-TIPS PPG may lead to a better outcome.

Spontaneous portosystemic shunt (SPSS) increased the risk of HE and a chronic course in patients with cirrhosis.[10] Whether or not SPSS should be embolised during TIPS placement remains controversial. The impact of TIPS in combination with embolization of SPSS on long-term outcomes in patients with cirrhosis requires further studies. Theoretically, PPG would be increased following embolization. PPG was also influenced by the diameter of the shunt, the timing of the measurement, the type of anesthesia and the patients' level of awareness *etc.* Therefore, the measurement of PPG needs to be standardized among different centers. The optimal final PPG after TIPS creation also requires validation using dedicated TIPS stents. Further studies are required to assess the efficacy of a small diameter TIPS which may lead to a PPG >12 mmHg, complemented by drugs, endoscopic or interventional procedures.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

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Authors' contributions

Concept and design: Xuefeng Luo and Li Yang. Data collection and interpretation: Xiaoze Wang and Xuefeng Luo. Manuscript drafting: Xiaoze Wang. Manuscript revising: Xuefeng Luo and Li Yang. All authors approved the final version of the article and the authorship list.

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Supplementary data

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Reply to: "Achieving an effective pressure reduction after TIPS: The need for a new target"

Effective portal pressure gradient reduction after small diameter TIPS

To the Editor:

I thank Drs Wang *et al.*[1] for their kind comments on my paper. As I emphasized, hemodynamic targets for TIPS are largely based on studies from the pre-covered stent era, when TIPS dysfunction was extremely common.[2] At that time, we showed that reducing the portal pressure gradient (PPG, the difference between portal vein and hepatic vein pressure) to values below 12 mmHg was necessary to prevent rebleeding or ascites, but that reductions below 10 mmHg were associated with an increased risk of encephalopathy.[3] Thus, it was difficult to achieve the correct balance between protecting against portal hypertension and not causing excessing shunting of portal blood away from the liver. The introduction of PFTE-covered stents (that are much less prone to dysfunction)[4] and more recently of controlled expansion stents (that do not progressively expand to their nominal diameter if under-dilated)[5,6] has opened new perspectives, since these allow for the insertion of smaller diameter TIPS tailored to the patients' needs. However, no prospective study has focused on how much the portal pressure should be reduced with these stents. Rather, most followed the traditional advice of going below 12 mmHg. Certainly, studies have shown that 8 mm stents appear preferable to 10 mm ones, with similar advantages and less encephalopathy and better survival.[7] However, to expand the safe use of TIPS it would be desirable to personalize the size of the TIPS to the minimal necessary for each patient rather than adopting a *one size fits all* strategy. It looks obvious that a 190 cm tall, 120 kg patient will likely need a greater shunt than a 160 cm, 55 kg patient, but we have no data to support it. On the other hand, it is likely that what could appear an insufficient reduction in PPG (to 14.5 mmHg, for instance) could be more than enough in a patient with a baseline PPG of 30 mmHg, or even if initial PPG was 21 mmHg, provided that the TIPS was complemented with a small dose of propranolol or with embolization of the collaterals (if TIPS was done to prevent rebleeding).[2]

The experience of Wang *et al.*[1] is in agreement with the above reasoning. They show equal results in terms of efficacy, adverse effects and survival between patients treated with covered 8 mm stents and collateral occlusion irrespective of achieving or not a final PPG below 12 mmHg (83% of the cohort) or not. The only clear difference they observed was a greater basal PPG in those not achieving the 12 mmHg target, since the mean decrease in PPG was equal in both groups. Unfortunately, other factors that could modulate the PPG response were not investigated: no patient received TIPS of a smaller diameter, only the short-term effects on PPG were assessed, and the response to graded dilation of the TIPS was not measured, so further studies are required to ascertain whether smaller

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