Supplementary data

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References

[1] Bosch J. Small diameter shunts should lead to safe expansion of the use of TIPS. J Hepatol 2021;74:230–234.
[2] Bosch J, Garcia-Pagan JC. Prevention of variceal rebleeding. Lancet 2003;361:952–954.
[3] Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. Hepatology 1985;5:419–424.
[4] Krajina A, Hulek P, Fejfar T, Valek V. Quality improvement guidelines for Transjugular Intrahepatic Portosystemic Shunt (TIPS). Cardiovasc Interv Radiol 2012;35:1295–1300.
[5] Thalheimer U, Leandro G, Samonakis DN, Triantos CK, Senzolo M, Fung K, et al. TIPS for refractory ascites: a single-centre experience. J Gastroenterol 2009;44:1089–1095.
[6] Weber CN, Nadolski GJ, White SB, Clark TW, Mondschein JI, Stavropoulos SW, et al. Long-term patency and clinical analysis of expanded polytetrafluoroethylene-covered transjugular intrahepatic portosystemic shunt stent grafts. J Vasc Interv Radiol 2015;26:1257–1265. quiz 1265.
[7] Luo X, Wang X, Zhu Y, Xi X, Zhao Y, Yang J, et al. Clinical efficacy of transjugular intrahepatic portosystemic shunt created with expanded polytetrafluoroethylene-covered stent-grafts: 8-mm versus 10-mm. Cardiovasc Interv Radiol 2019;42:737–743.
[8] Wang Q, Lv Y, Bai M, Wang Z, Liu H, He C, et al. Eight millimetre covered TIPS does not compromise shunt function but reduces hepatic encephalopathy in preventing variceal rebleeding. J Hepatol 2017;67:508–516.
[9] Trebicka J, Bastgen D, Byrtus J, Praktiknjo M, Terstiegen S, Meyer C, et al. Smaller-diameter covered transjugular intrahepatic portosystemic shunt stents are associated with increased survival. Clin Gastroenterol Hepatol 2019;17:2793–2799. e2791.
[10] Simón-Talero M, Roccarina D, Martínez J, Lampichler K, Baiges A, Low G, et al. Association between portosystemic shunts and increased complications and mortality in patients with cirrhosis. Gastroenterology 2018;154:1694–1705. e1694.

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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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diameter TIPS can be used to safely expand its indications for the treatment of portal hypertension and its complications.

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Conflict of interest
Jaume Bosch is consultant for the following companies: Actelion, BMS, BioVie, Gilead, Lipocine, Surrozen, Zydus.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data
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References
[1] Wang X, Luo X, Yang L. Achieving an effective pressure reduction after TIPS: the need for new target. J Hepatol 2021;75:246–248.
[2] Bosch J. Small diameter shunts should lead to safe expansion of the use of TIPS. J Hepatol 2021 Jan;74(1):230–234.
[3] Casado M, Bosch J, García-Pagán JC, Bru C, Bañares R, Bandi JC, et al. Clinical events after transjugular intrahepatic portosystemic shunt: correlation with hemodynamic findings. Gastroenterology 1998 Jun;114(6):1296–1303.
[4] Bureau C, Garcia-Pagan JC, Otal P, Pomier-Layrargues G, Chabbert V, Cortez C, et al. Improved clinical outcome using polytetrafluoroethylene-coated stents for TIPS: results of a randomized study. Gastroenterology 2004 Feb;126(2):469–475.
[5] Miraglia R, Maruzzelli L, Di Piazza A, Mamone G, Caruso S, Gentile G, et al. Transjugular intrahepatic portosystemic shunt using the new gore viatorr controlled expansion endoprosthesis: prospective, single-center, preliminary experience. Cardiovasc Interv Radiol 2019;42:78–86.
[6] Pieper CC, Jansen C, Meyer C, Nadal J, Lehmann J, Schild HH, et al. Prospective evaluation of passive expansion of partially dilated transjugular intrahepatic portosystemic shunt stent grafts-A three-dimensional sonography study. J Vasc Interv Radiol 2017 Jan;28(1):117–125.
[7] Trebicka J, Bastgen D, Byrtus J, Praktiknjo M, Terstiegen S, Meyer C, et al. Smaller-diameter covered transjugular intrahepatic portosystemic shunt stents are associated with increased survival. Clin Gastroenterol Hepatol 2019;17:2793–2799. e2791.

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A step forward to predict the risk of post-hepatectomy portal hypertension

To the Editor:

We read with great interest the article by Golse *et al.*[1] In the study, a mathematical (0D) model of hepatic circulation in combination with the entire cardiovascular system was constructed, which could be used in the simulation of hepatectomy and prediction of post hepatectomy liver failure (PHLF).[1] A cohort of 47 patients undergoing major hepatectomy were included and assessed using the mathematical model with hepatic flows being determined by preoperative flow MRI, intraoperative flowmetry, or estimation based on cardiac output. The cut-off values of portal vein pressure >17.5 mmHg and portocaval gradient (PCG) >13.5 mmHg were proposed to accurately predict the occurrence of PHLF.[1] We commend the authors for this excellent work providing a mathematical model on portal hemodynamic changes. However, additional limitations in this study should be pointed out.

The lumped parameter model has been proved to be a competent mathematical tool for simulating blood flow,[2,3] and has been widely used to address hemodynamic problems related to the hepatic circulation[4] and the surgical treatment of liver diseases.[5] The model-predicted post-hepatectomy portal pressures showed a good correlation with the *in vivo* measurements in a large cohort, while the present mathematical model would be more accurate if the effects of liver fibrosis or cirrhosis could be precisely considered. Portal hypertension before hepatectomy was considered a high-risk factor for serious postoperative complications in cirrhosis,[6] just as 1 out of 3 cirrhotic patients (33.3%) had PHLF-related deaths in the cohort, while in 38 non-cirrhotic patients, the ratio was only 7.9%. Accordingly, modeling the effects of liver fibrosis or cirrhosis is necessary, which might be improved by correlating the coefficient (*i.e.*, the one in the expression calculating pressure-dependent resistance of the intrahepatic portal venous system) with the level of fibrosis stratification instead of the bisection scheme (*i.e.*, rigid or elastic) used in the present model.

The primary objective of the study was to predict the post-operative PCG with a precision of ± 3 mmHg. However, we believe that this quality control (the accuracy of ±3 mmHg) of the PCG simulation may be poor since the valid measurement of hepatic venous pressure gradient (HVPG) requires 2 consecutive determinations that differ by less than 1 mmHg.[7]

It is noted that anesthesia may also affect the results of PCG measurement.[8,9] Reverter *et al.*[8] demonstrated that PCG measured under deep sedation showed higher respiratory oscillations and has a clear tendency to underestimate the results under waking. The study by Silva-junior *et al.*[9] further confirmed that the underestimation of PCG under general anesthesia is more serious than under deep sedation. To better understand the effects of anesthesia, a portal vein catheter

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