

patients, as it was equally associated with survival in non-TIPS patients with cirrhosis. By adding an adequate control group we demonstrated that the FIPS score failed to identify patients in whom TIPS impairs survival. Thus, in our opinion a high FIPS score should not be considered a strict contraindication for TIPS, as it may improve other aspects of cirrhosis, e.g. sarcopenia and/or paracenteses frequency. It is, however, of interest that there was a survival benefit among those with low FIPS scores. This emphasizes that TIPS should be considered earlier in the natural history of portal hypertension as suggested by other recent publications.<sup>5</sup> One might argue that liver transplantation remains the treatment of choice in patients with high FIPS scores (and a high risk of mortality). However, restricted organ supply often limits this option, especially in the Eurotransplant region. This was also confirmed in the study by Bettinger *et al.*, wherein <2% of patients were transplanted within 6 months.<sup>1</sup> Thus, we suggest that an individualized, multifactorial approach is warranted to make the decision for or against TIPS in these cases.

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### Conflict of interest

The authors declare that they do not have any relevant conflict of interest.

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

### Authors' contributions

LS: Study concept and design, data acquisition, analysis, interpretation of the data, drafting of the manuscript and critical revision thereof for important intellectual content. HS, TLT, and MC: Data acquisition, critical revision of the manuscript for important intellectual content. BM: Supervision, study concept and design, interpretation of the data, drafting the manuscript, critical revision of the manuscript for important intellectual content.

### Data availability statement

LS has access to all data and vouches for the integrity of the data analyses.

### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2021.02.031>.

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## Reply to: “Freiburg index of post-TIPS survival (FIPS) a valid prognostic score in patients with cirrhosis but also an advisor against TIPS?”

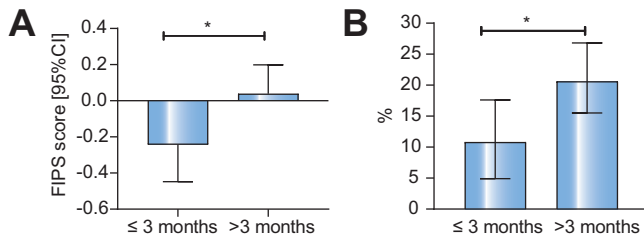
To the Editor:

We thank Dr. Stockhoff and her team for their interest in our study<sup>1</sup> and their analyses that confirmed the prognostic impact of the Freiburg index of post-TIPS survival (FIPS) score and even expanded it to patients with decompensated cirrhosis without transjugular intrahepatic portosystemic shunt (TIPS) implantation.<sup>2</sup> With great interest, we recognize their efforts in

addressing some important remaining questions from our study, especially with respect to the clinical application of the FIPS score for allocation to TIPS implantation. The authors point out several important issues which, however, require further attention.

First, they show that the FIPS score is also applicable to decompensated patients without TIPS implantation.<sup>2</sup> To address this hypothesis, we analyzed 612 patients with cirrhosis (baseline characteristics: [Table S1](#)) by stratifying according to decompensation stages defined by d’Amico *et al.*<sup>3</sup> These stages

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**Fig. 1. FIPS score in ascites patients with different duration of decompensation.** (A) Patients with decompensation >3 months showed a significantly higher FIPS score compared to patients with a shorter duration of decompensation. Differences were calculated using a Mann-Whitney *U* test. (B) Patients with decompensation >3 months were significantly more often allocated to the FIPS high-risk group (FIPS >0.92). Differences in the proportion of FIPS high-risk patients between the groups were calculated using a  $\chi^2$  test. Error bars indicate 95% CI; \**p* <0.05. FIPS, Freiburg index of post-TIPS survival; TIPS, transjugular intrahepatic portosystemic shunt.

are defined according to the kind and number of decompensating events (Table S2) and therefore reflect the severity of decompensation. Indeed, as shown in Fig. S1, the FIPS score significantly increased with progressing decompensation. Notably, only in the higher decompensation stages (stage 4 and 5) were patients allocated to the FIPS high-risk group, highlighting that this new risk score is especially useful for patients with decompensated cirrhosis and may also reflect the severity of decompensation.

Second, we highly appreciate that the authors added a control group without TIPS implantation. However, although patient numbers were small after sufficient propensity score matching, the authors showed that in the FIPS low-risk group, patients with TIPS implantation had significantly better overall survival compared to patients treated with paracenteses.<sup>2</sup> Indeed, as suggested by the authors, this observation may further underline the rationale that TIPS implantation should not be delayed in patients with ascites. To further address this interesting aspect, we analyzed 296 patients who received TIPS implantation for refractory ascites at the University Medical Center Freiburg (baseline characteristics: Table S3) and in whom the time between first ascitic decompensation and TIPS implantation was recorded. Patients were stratified according to the duration of decompensation (≤3 vs. >3 months). Patients with preexisting decompensation >3 months presented with higher FIPS score compared to patients with a shorter history of decompensation (-0.24±1.04 vs. 0.04±1.13; *p* = 0.016; Fig. 1A). The proportion of FIPS high-risk patients was significantly higher in patients with long-term decompensation (20.6% vs. 10.8%; *p* = 0.036, Fig. 1B) which underlines the need for early TIPS implantation in patients with ascites.

Third, Stockhoff *et al.* found no difference in overall survival in FIPS high-risk patients being treated with TIPS or paracentesis. Importantly, the comparability of these patient groups is limited due to different contraindications for TIPS in the paracentesis group. Further, the course of disease in FIPS high-risk patients with regard to development of acute-on-chronic liver failure, persistence of ascites and development of post-TIPS hepatic

encephalopathy has to be analyzed. These results are necessary to identify a subgroup of high-risk patients who still benefit from TIPS implantation.

Collectively, in TIPS patients, beside patient-specific parameters such as sarcopenia or hepatic encephalopathy, the new FIPS score is an objective component in decision-making and may be an important step towards personalized medicine.

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**Conflict of interest**

DB: Consultant: Bayer Healthcare, Boston Scientific, Shionogi. Lectures: Falk Foundation. RK: Consultant: Boston Scientific, Bristol-Myers Squibb, Guerbet, Roche, and SIRTEX. Lectures: BTG, Guerbet, Ipsen, SIRTEX, MSD Sharp & Dohme. MS: Consultant: Bayer Healthcare, L.W.Gore Lectures: Falk Foundation.

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

**Authors' contributions**

Design of the study: DB, MS. Acquisition of data: DB, TB, MS. Analysis of the data: DB. Statistical analyses and consulting: DB, RK. Interpretation of the data: DB, RK, TB, RT, MS. Drafting the manuscript: DB, MS. Revision for important intellectual content: RK, RT, TB.

**Supplementary data**

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2021.04.028>.

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