affected by low/moderate engagement, as was observed in their project, with an engagement rate of below 50%. Nevertheless, they reported that half of those who tested positive were unaware of their viral status. On the other hand, considering that social and health characteristics may vary across different geographical areas, the opt-out screening approach is also a useful alternative that has been proven to be successful and cost-effective.[5] Thus, strategies such as healthcare-associated electronic alerts or even automatic referrals for positive cases are very likely to provide an adequate linkage to care.[6]

However, the usefulness of this new model in terms of improving healthcare access must be prospectively evaluated. In this regard, some items that must be clearly evaluated are both the acceptance and compliance of the pre-established follow-up schedule, as well as the degree of satisfaction. None of these relevant issues were reported in the work by Giacomelli *et al.*

Financial support
The authors received no financial support to produce this manuscript.

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

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

Authors' contributions
All authors contributed equally.

Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.04.043.

References
[1] Martinez I, Ryan P, Valencia J, Resino S. The challenging road to hepatitis C virus eradication. J Clin Med 2021;10.
[2] Buti M, Dominguez-Hernandez R, Casado MA. Impact of the COVID-19 pandemic on HCV elimination in Spain. J Hepatol 2021;74(5):1246–1248.
[3] Crespo J, Diaz-Gonzalez A, Iruzubieta P, Llerena S, Cabezas J. SARS-CoV-2 massive testing: a window of opportunity to catch up with HCV elimination. J Hepatol 2021;74(4):966–967.
[4] Giacomelli A, Pagani G, Conti F, Bassoli C, Galli M. Detecting HCV infection by means of mass population SARS-CoV-2 screening: a pilot experience in Northern Italy. J Hepatol 2021;75(2):484–486.
[5] Williams J, Vickerman P, Douthwaite S, Nebbia G, Hunter L, Wong T, et al. An economic evaluation of the cost-effectiveness of opt-out hepatitis B and hepatitis C testing in an emergency department setting in the United Kingdom. Value in health : the. J Int Soc Pharmacoeconomics Outcomes Res 2020;23:1003–1011.
[6] Crespo J, Tejerina Puente A, Cuadrado A, Llerena S, Cabezas J. Grupo de Trabajo para la Eliminacion de la Hepatitis C en Cantabria. Strategy for the Elimination of Hepatitis C in Cantabria. Rev Esp Enferm Dig 2020;112:565–570.

Javier Crespo[1,2,3]
Álvaro Díaz-González[1,2]
Joaquín Cabezas[1,2,*]
[1]*Gastroenterology and Hepatology Department. Marqués de Valdecilla University Hospital, Santander, Spain*
[2]*Research Institute Valdecilla (*IDIVAL*), Santander, Spain*
[3]*School of Medicine, University of Cantabria, Santander, Spain*
[*]Corresponding author. Address: Gastroenterology and Hepatology Department, Marques de Valdecilla University Hospital, Research Institute Valdecilla (IDIVAL), Avda. de Valdecilla s/n. Santander 39008. Cantabria. Spain; Tel.: +34 942 20 25 20, fax: +34 942 20 25 44.
E-mail address: joaquin.cabezas@scsalud.es (J. Cabezas)

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

To the Editor:

With great interest we read the excellent article by Bettinger and colleagues. In their well-designed study the authors proposed the newly developed Freiburg index of post-TIPS survival (FIPS) as a valuable tool for risk stratification before transjugular intrahepatic portosystemic shunt (TIPS) implantation.[1] The establishment of robust criteria for the selection of patients eligible for TIPS is crucial. Bettinger *et al.* collected a large, multicenter TIPS cohort and convincingly demonstrated the high prognostic capacity of the FIPS score for post-TIPS survival in various subgroups of patients including those with refractory ascites. However, a control group consisting of patients with refractory ascites, who were treated with paracentesis instead of TIPS, was not included. The FIPS score consists of age as well as bilirubin, creatinine and albumin, which are all well-known parameters associated with survival in patients with advanced liver disease. Thus, it remains unclear whether the FIPS score is specific for post-TIPS survival or rather predicts outcome in patients with decompensated cirrhosis in general. Moreover, because of the lack of a control group it is not possible to conclude whether TIPS insertion itself has any impact (beneficial or adverse) on survival in patients with high or low FIPS scores. As a result, it remains uncertain to what extent FIPS scores can help to select patients for TIPS.

We aimed to address these remaining questions by using 2 different patient cohorts from Hannover Medical School, the Hannover TIPS cohort and the Hannover Ascites cohort. The Hannover TIPS cohort currently consists of 256 patients with

Keywords: Transjugular intrahepatic portosystemic shunt; cirrhosis; portal hypertension; risk stratification; FIPS; Freiburg index of post-TIPS survival.
Received 15 February 2021; received in revised form 25 February 2021; accepted 28 February 2021; available online 12 March 2021
https://doi.org/10.1016/j.jhep.2021.02.031

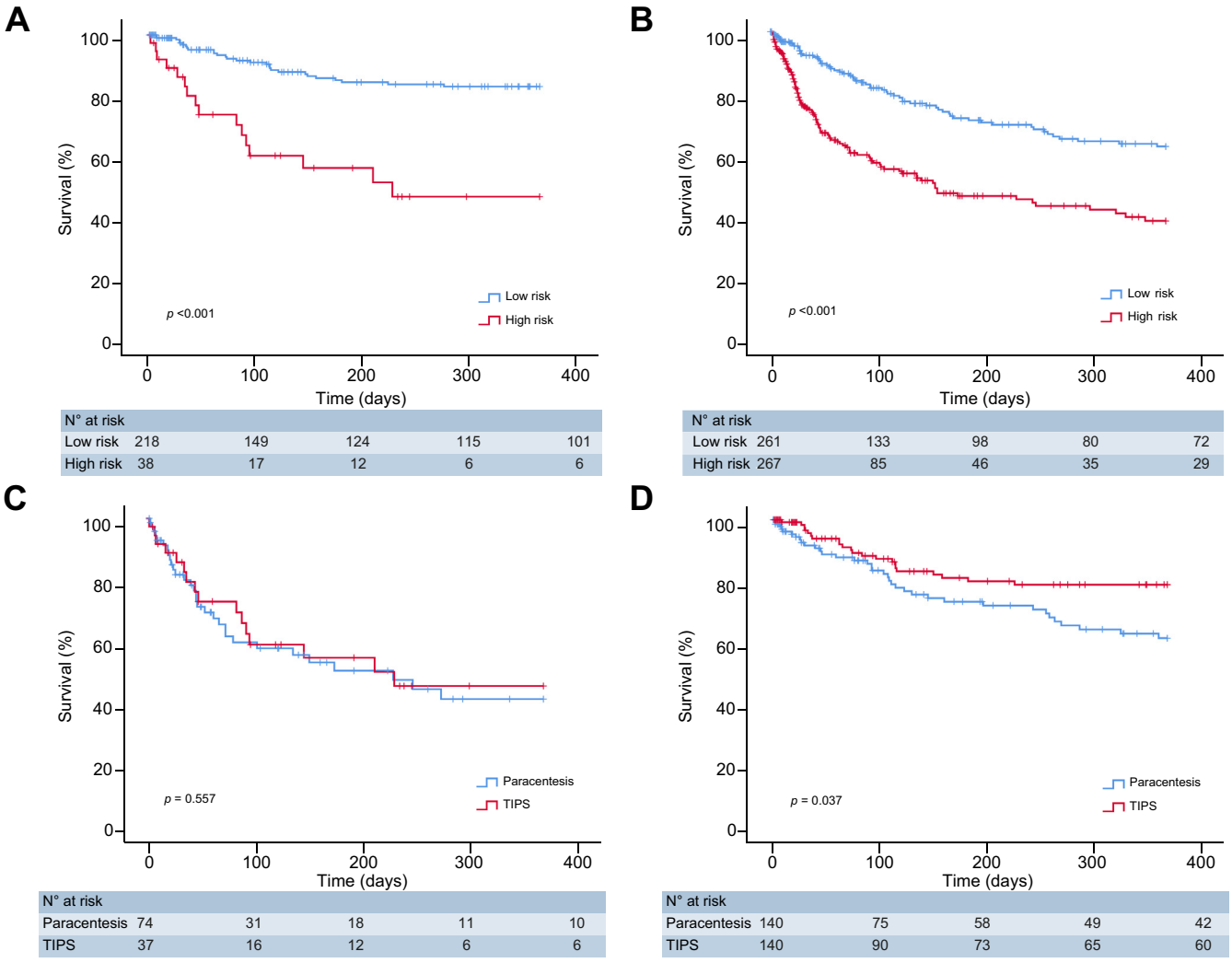

Fig. 1. Validation of the FIPS score in TIPS and paracentesis patients from Hannover Medical School (FIPS cut-off 0.64). (A,B) Survival of (A) patients receiving a TIPS, and (B) patients treated with paracentesis in dependence of the FIPS score. *p* values were obtained using the log-rank test. (C,D) Comparison of survival between matched cirrhotic patients treated with either TIPS or paracentesis. Shown are (C) FIPS high-risk patients and (D) FIPS low-risk patients. *p* values were obtained using a stratified log-rank test. Patients were censored if they underwent liver transplantation (10 patients [4%] in the TIPS cohort, 68 patients [13%] in the whole paracentesis cohort). FIPS, Freiburg index of post-TIPS survival; TIPS, transjugular intrahepatic portosystemic shunt. (This figure appears in color on the web.)

cirrhosis (baseline characteristics: Table S1).[2] The Hannover Ascites Cohort includes >600 patients with decompensated cirrhosis and ascites. 528 patients who did not receive a TIPS during follow-up were used as a control group (baseline characteristics: Table S2).[3]

First, we validated the prognostic value of the FIPS score for post-TIPS survival in the Hannover TIPS cohort. In fact, the FIPS score was confirmed as a valuable marker of post-TIPS survival when applying the proposed cut-off of 0.92 (p <0.001; Fig. S1A) or when using the 85th percentile of our own cohort as a cut-off, as done by Bettinger *et al.* (FIPS ≥0.64; p <0.001; Fig. 1A).

Next, we tested the prognostic value of the FIPS score in 528 non-TIPS patients with decompensated cirrhosis. Of note, the FIPS score was strongly associated with mortality in these patients when using the same 2 cut-offs (FIPS ≥0.64; p <0.001; Fig. 1B and FIPS ≥0.92; p <0.001; Fig. S1B).

Finally, we aimed to investigate whether the FIPS score identifies patients in whom TIPS has detrimental effects on survival and should therefore be considered as contraindicated. We performed propensity score matching to match patients with refractory/recurrent ascites treated with either TIPS or paracentesis.[2] Only patients without an established TIPS contraindication were considered for the matching.[4] The first matching included only high-risk patients (FIPS ≥0.64) and the second matching only low-risk patients (FIPS <0.64) from both cohorts. Matching covariates were model of end-stage liver disease (MELD) score, age, sex, FIPS score, platelet count and sodium (Table S3-6). Survival was analyzed using a stratified log-rank test. Importantly, there was no difference in survival between patients treated with TIPS or paracentesis in the FIPS high-risk group (p = 0.557; Fig. 1C). However, in the FIPS low-risk group, survival was significantly better among those treated with TIPS compared to those treated with paracentesis (p = 0.037; Fig. 1D). Of note, results were also confirmed when using the FIPS cut-off of 0.92 (Fig. S1C,D).

We were able to confirm the high accuracy and particular value of the FIPS score in predicting post-TIPS survival among patients with advanced liver disease. However, our data also demonstrate that the FIPS score might not be specific for TIPS

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.[5] 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.[1] Thus, we suggest that an individualized, multifactorial approach is warranted to make the decision for or against TIPS in these cases.

Financial support
LS, HS and TLT were supported by the 'KlinStrucMed' programme funded by the 'Else Kröner-Fresenius-Stiftung'.

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.

References
[1] Bettinger D, Sturm L, Pfaff L, Hahn F, Kloeckner R, Volkwein L, et al. Refining prediction of survival after TIPS with the novel Freiburg index of post-TIPS survival. J Hepatol 2021;74:1362–1372. https://doi.org/10.1016/j.jhep.2021.01.023.
[2] Stockhoff L, Schultalbers M, Tergast TL, Hinrichs JB, Gerbel S, Meine TC, et al. Safety and feasibility of transjugular intrahepatic portosystemic shunt in elderly patients with liver cirrhosis and refractory ascites. PloS one 2020;15(6):e0235199. https://doi.org/10.1371/journal.pone.0235199.
[3] Tergast TL, Wranke A, Laser H, Gerbel S, Manns MP, Cornberg M, et al. Dose-dependent impact of proton pump inhibitors on the clinical course of spontaneous bacterial peritonitis. Liver Int 2018;38(9):1602–1613. https://doi.org/10.1111/liv.13862.
[4] Angeli P, Bernardi M, Villanueva C, Francoz C, Mookerjee RP, Trebicka J, et al. EASL clinical practice guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018;69(2):406–460. https://doi.org/10.1016/j.jhep.2018.03.024.
[5] Piecha F, Radunski UK, Ozga A, Steins D, Drolz A, Horvatits T, et al. Ascites control by TIPS is more successful in patients with a lower paracentesis frequency and is associated with improved survival. JHEP Rep 2019;1(2):90–98. https://doi.org/10.1016/j.jhepr.2019.04.001.

Lena Stockhoff
Hannah Schneider
Tammo Lambert Tergast
Markus Cornberg
Benjamin Maasoumy*
Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Carl-Neuberg-Str.1, 30625 Hannover, Germany
*Corresponding author. Address: Carl-Neuberg-Str.1, 30625 Hannover, Germany; Tel.: 0049-5115326529, fax: 0049-5115324896.
E-mail address: maasoumy.benjamin@mh-hannover.de (B. Maasoumy)

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[1] 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.[2] 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.[2] 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.*[3] These stages

Received 20 April 2021; accepted 21 April 2021; available online 26 April 2021
https://doi.org/10.1016/j.jhep.2021.04.028