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Predicting survival after TIPS: Child Pugh score is not inferior to MELD and FIPS score – back to basics?

To the Editor:

With great interest, we read the publication by Bettinger *et al.* who reported a newly developed prognostic score for patients after transjugular intrahepatic portosystemic shunt (TIPS) – the Freiburg index for post TIPS survival (FIPS).¹ In their multicenter cohort, the FIPS score showed a better survival prediction after TIPS implantation than widely known and used prognostic scores, namely the Child-Pugh and model for end-stage liver disease (MELD) score. When Kraglund *et al.* tried to validate the FIPS score in an independent patient cohort of 104 patients,² the Child-Pugh was not inferior for prognostication than the MELD and FIPS score. To assess this discrepancy, we retrospectively analyzed data on 104 patients who underwent TIPS implantation at our liver center between 2015 and 2020 (using the same in-/exclusion criteria as described in the original publication), and calculated c-indices for the MELD, Child-Pugh and FIPS score using the Harrell's c-index. Alcohol-related cirrhosis was the predominant etiology of chronic liver diseases (n = 60; 57.7%), followed by non-alcoholic fatty liver disease (NAFLD; n = 9; 8.7%), viral cirrhosis (n = 8; 7.7%) and others (25.9%). The median age of our patient cohort was 59.0 years (IQR 52.3–65.0) and 58.7% (n = 61) were male. Median MELD score was 14 (IQR 10.3–18.8), with 19 patients being classified as Child-Pugh A (18.3%), 66 patients Child-Pugh B (63.5%), and 19 patients Child-Pugh C (18.3%). Thus, our cohort is comparable to the original cohort described by Bettinger *et al.*, except for a higher percentage of patients with NAFLD in our center (8.7 vs. 2.5%). Survival at our center was 77.9% (23 deaths) after 3 months and 75.0% (26 deaths) after 6 months. In contrast to Kraglund *et al.*, our cohort had a relatively high number of patients with a FIPS score of ≥ 0.92 (14.4%); 11 of these patients died within the first 6 months (73.3%).

Analysis of our TIPS cohort revealed that the Child-Pugh score achieved the highest prognostic accuracy in comparison to the FIPS and MELD score for predicting the 3- and 6-month mortality. C-indices of the Child-Pugh score were 0.779 (95% CI 0.691–0.868) and 0.753 (0.664–0.843) for 3- and 6-month

survival. Our results closely resemble findings from Kraglund *et al.*, who reported c-indices of 0.75 (0.56–0.94) and 0.72 (0.54–0.90) for the Child-Pugh score. In line with the findings of Kraglund *et al.*, the c-indices of the Child-Pugh score, FIPS and MELD score were not significantly different (Table 1).

One of the biggest practical advantages of the Child-Pugh score is that it is easy to assess in a clinical setting. Another particularity of the Child-Pugh score is that it combines laboratory and clinical parameters, while the MELD and FIPS score solely include laboratory parameters and age. The good prognostic capacity of the Child-Pugh score (also for prognosis after TIPS implantation) was validated multiple times before in the literature, e.g. by an Austrian working group in 2003.³ In general, risk prediction models do not only require internal but also external validations. In external validations, these models often show a poorer performance and in these cases the models should consequently be modified to improve their performance.⁴ Regarding the FIPS score, 2 external validations (Aarhus and Berlin) could not confirm a better performance of FIPS compared to the Child-Pugh or MELD score. This could be related to the fact that the Child-Pugh score considers clinical parameters as well. Therefore, a multicenter approach should be conducted to develop an improved “FIPS 2.0” score, potentially by combining clinical parameters with prognostic laboratory parameters. The predictive power of an improved FIPS score should then be prospectively validated in a

Table 1. Statistical performance of FIPS, MELD and Child-Pugh scores to discriminate survivors vs. non-survivors in our cohort of 104 patients undergoing TIPS procedure at the Charité University Medical Center in Berlin.

	FIPS c index (95% CI)	MELD c index (95% CI)	Child-Pugh c index (95% CI)
3-month survival	0.705 (0.581–0.830)	0.706 (0.580–0.832)	0.779 (0.691–0.868)
p values vs. FIPS		0.990	0.199
6-month survival	0.692 (0.573–0.810)	0.692 (0.573–0.811)	0.753 (0.664–0.843)
p values vs. FIPS		1.000	0.267

FIPS, Freiburg index of post-TIPS survival; MELD, model for end-stage liver disease; TIPS, transjugular intrahepatic portosystemic shunt.

Keywords: Transjugular intrahepatic portosystemic shunt; Liver cirrhosis; External score validation; Survival.

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multicenter setting, in order to demonstrate that such an algorithm would be more useful than a “back to basics” approach using the Child-Pugh score.

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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

All authors contributed to the study and the final manuscript. JP collected the data, carried out the formal analyses and wrote the original draft.

Supplementary data

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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(6):1362–1372.
- [2] Kraglund F, Gantzel RH, Jepsen P, Aagaard NK. External validation of the freiburg index of post-TIPS survival. *J Hepatol* 2021.

- [3] Angermayr B, Cejna M, Karnel F, Gschwantler M, Koenig F, Pidlich J, et al. Child-Pugh versus MELD score in predicting survival in patients undergoing transjugular intrahepatic portosystemic shunt. *Gut* 2003;52(6):879–885.
- [4] Moons KG, Kengne AP, Grobbee DE, Royston P, Vergouwe Y, Altman DG, et al. Risk prediction models: II. External validation, model updating, and impact assessment. *Heart* 2012;98(9):691–698.

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SARS-CoV-2-specific immunity in immunosuppressed COVID-19 convalescents with autoimmune hepatitis

To the Editor:

We read with interest the article “SARS-CoV-2 infection in patients with autoimmune hepatitis” by Marjot, Buescher and Sebode *et al.*¹ recently published in the *Journal of hepatology*. While immunosuppressive therapy for autoimmune hepatitis (AIH) had no negative impact on the immediate outcome of COVID-19,^{1–3} the question remained, whether COVID-19 convalescents immunosuppressed for AIH (AIH-Con) have the same level of protection against SARS-CoV-2 reinfection as non-immunosuppressed convalescents (non-IS-Con).

To address this question, we prospectively quantified anti-SARS-CoV-2 antibodies against various SARS-CoV-2 antigens (Antigen Panel 1 IgG, IgM, IgA assays Millipore HC19SERM1-85K-04, HC19SERA1-85K-04, HC19SERG1-85K-04) and IFN- γ responses to anti-SARS-CoV-2 antigen pools, as previously described,⁴ in patients with AIH at their first appointment at our center following SARS-CoV-2 infection. We recruited 6 AIH-Con receiving ongoing immunosuppression (prednisolone

5–80 mg/day in 4/6 patients; mycophenolate 1,000 mg/day in 2/6 patients; azathioprine 50 and 75 mg in 2/6 patients). AIH-Con were compared to a matched cohort of 24 non-IS-Con (AIH-Con vs. non-IS-Con (Table S1): female sex: 50% vs. 46% (Fisher exact test: $p = 1.0$); age (median): 47 vs. 51 years (Mann-Whitney U test $p = 0.705$); time after COVID-19 (median): 48 vs. 52 days ($p = 0.631$); WHO COVID-19 severity: 100% mild-moderate vs. 91% mild-moderate; 9% severe-critical ($p = 1.0$). Two of the AIH-Con had concomitant primary sclerosing cholangitis, 3/6 had cirrhosis, 1/6 AIH-Con acquired COVID-19 during the diagnostic work-up of AIH and COVID-19 was diagnosed in 1 patient with AIH 4 days after the first mRNA vaccination.

Quantification of anti-SARS-CoV-2 antibodies was available in 4/6 AIH-Con and for 2 of these patients we had cryo-conserved pre-pandemic samples from our biorepository. Quantification of cellular immune response was available in 5/6 AIH-Con.

Apart from lower frequencies of IgA against spike S1 peptides and IgG against the nucleocapsid, the presence of all other anti-SARS-CoV-2 IgA, IgG and IgM specificities was comparable