RESEARCH LETTERS

Evaluation of QuickStroop for Predicting Post-TIPS Hepatic Encephalopathy

Hepatic encephalopathy(HE) remains a frequent and relevant complication after insertion of a transjugular intrahepatic portosystemic shunt (TIPS).[1–3] Data on the value of minimal hepatic encephalopathy (MHE) tests for predicting post-TIPS HE are conflicting. The Stroop EncephalApp and its shortened form QuickStroop have not been studied in this context. This study aimed to analyze the predictive performance of cognitive tests for post-TIPS HE and mortality in patients undergoing TIPS insertion with a particular focus on Stroop. Additionally, we sought to investigate the trajectory of results in Stroop before and after TIPS.

This study enrolled patients from 2 prospective studies conducted at 2 tertiary care centers in Germany (Mainz [NCT05466669] and Hannover [NCT04801290]). Both studies included patients with liver cirrhosis aged ≥18 years with an indication for elective TIPS insertion because of ascites, as secondary prophylaxis after variceal bleeding, or a combination of portal vein thrombosis/ascites/hydrothorax (termed others). Patients with an indication for a rescue or preemptive TIPS were not approached. Further information can be found in the Supplementary Methods.

Before TIPS insertion, patients without HE ≥1 were tested with the Stroop EncephalApp (n = 95), QuickStroop (n = 95),[4,5] animal naming test (S-ANT1) (n = 91), and psychometric hepatic encephalopathy score (PHES) (n = 91). Results were evaluated according to German norms. Additional details are provided in the Supplementary Methods.

TIPS insertion was conducted according to the BAVENO recommendations.[6] Further details are given in the Supplementary Methods.

Patients were followed for the development of post-TIPS overt HE (HE ≥grade II according to the West-Haven-Criteria), liver transplantation, and/or death during scheduled outpatient visits at 1, 3, and 6 months after TIPS insertion. In patients from Mainz, PHES, S-ANT1, and the Stroop EncephalApp were repeated after 1 and 3 months.

Both studies were approved by the respective ethics committees (Hannover Medical School, Nr. 8498_BO_S_2019; Landesärztekammer Rheinland-Pfalz, Nr. 2021-16247_1). Written informed consent was obtained from all participants. The study was performed according to the principles of the Declaration of Helsinki.

Information on statistics are provided in the Supplementary Methods. In total, 95 patients were included (Mainz, n = 63; Hannover, n = 32). Baseline characteristics of the study cohort are displayed in Supplementary Table 1. Abnormal results in the MHE screening tests were present in 52% (Stroop), 41% (QuickStroop), 40% (PHES), and 60% (S-ANT1).

The cohort was followed for a median of 188 days (interquartile range, 71–362). During this period, 36 (37.9%) patients developed at least 1 post-TIPS overt hepatic encephalopathy (OHE) episode (grade 2, n = 22; grade 3, n = 12; grade 4, n = 2). In addition, 20 (21.1%) patients died or received a liver transplantation.

Patients with abnormal results in QuickStroop before TIPS insertion or MHE according to PHES had a significantly higher cumulative OHE incidence during follow-up (Figure 1*B* and *C*). In contrast, no significant difference was found in patients stratified by test results in Stroop or S-ANT1 (Figure 1*A* and *D*). In multivariable Fine and Gray regression analyses, only QuickStroop as a continuous variable was independently associated with a higher risk of post-TIPS OHE (subdistribution hazard ratio [sHR], 1.05; 95% confidence interval [CI], 1.00–1.10; $P = .035$), whereas Stroop, PHES, and S-ANT1 were not (Supplementary Table 2). Of note, QuickStroop remained independently associated with post-TIPS OHE (sHR, 1.05; 95% CI, 1.00–1.10; $P = .049$) in a multivariable model, which was additionally adjusted for sarcopenia (n = 82).

In the subgroup of patients with TIPS for refractory ascites, QuickStroop as a continuous variable (sHR, 1.06; 95% CI, 1.01–1.11; $P = .025$) and the complete EncephalApp (total time: sHR, 1.04; 95% CI, 1.00–1.08; $P = .042$) remained independently associated with a higher risk of post-TIPS OHE in multivariable Fine and Gray regression analyses (data not shown).

Given that all patients with a liver transplantation were transplanted because of organ failure, we treated

Abbreviations used in this paper: **ANT, animal naming test; CI, confidence interval; HE, hepatic encephalopathy; MHE, minimal hepatic encephalopathy; OHE, overt hepatic encephalopathy; PHES, psychometric hepatic encephalopathy score; sHR, subdistribution hazard ratio; TIPS, transjugular intrahepatic portosystemic shunt.**

Most current article

1542-3565
https://doi.org/10.1016/j.cgh.2025.07.016

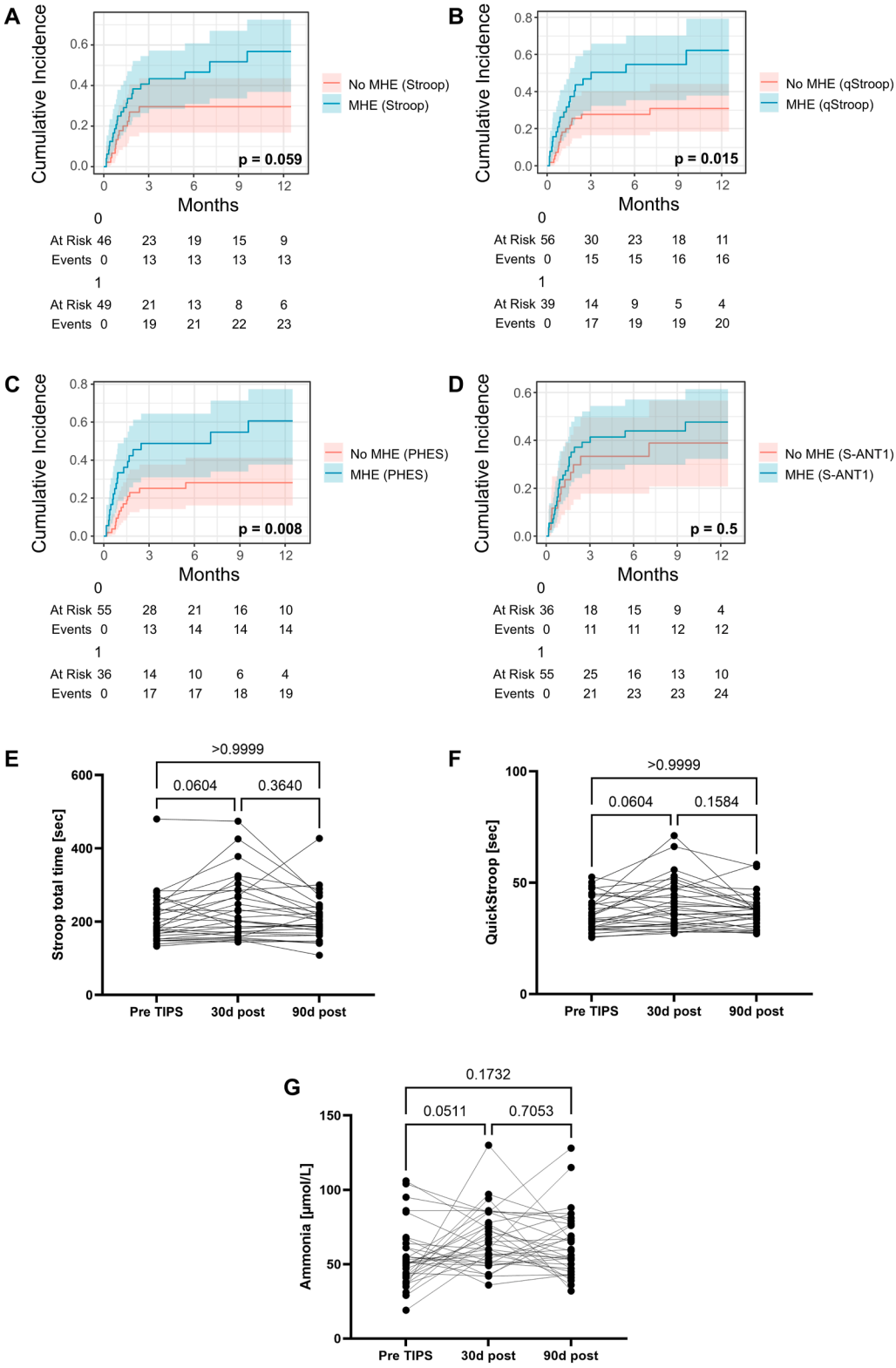

Figure 1. Cumulative OHE incidence stratified by the MHE screening test results and longitudinal changes of Stroop, QuickStroop, and ammonia after TIPS insertion. Cumulative OHE incidence in patients stratified by the Stroop-MHE (*A*), QuickStroop-MHE (*B*), PHES-MHE (*C*), or S-ANT1-MHE (*D*). (*E*-*G*) Display of the trajectory of Stroop total time, QuickStroop (time for off runs 1 + 2), and ammonia levels before and 30 and 90 days after TIPS insertion.

these patients as complete cases and decided to use the composite end point of death/liver transplantation. In multivariable Cox regression analyses after adjusting for model for end-stage liver disease, only S-ANT1 as a continuous variable was independently associated with death/liver transplantation during follow-up (HR, 0.91;

95% CI, 0.83–0.99; $P = .032$). Of note, PHES, Stroop, and QuickStroop were not associated with death/liver transplantation; however, Stroop (HR, 1.06; 95 CI, 1.00–1.11; $P = .050$) and QuickStroop (HR, 1.07; 95% CI, 1.00–1.15; $P = .060$) did closely not reach significance.

All patients from the Mainz cohort who attended the structured follow-up visits were longitudinally tested with the Stroop EncephalApp. During the observational period, performance in total time to complete the Stroop EncephalApp and QuickStroop (off runs 1 + 2) worsened at 1-month post-TIPS compared with baseline, whereas the performance returned to the baseline level after 3 months post-TIPS (Figure 1*E* and *F*). The changes in QuickStroop and the complete EncephalApp paralleled the trajectory of ammonia levels (Figure 1*G*).

In this study, we demonstrate that poorer performance in QuickStroop before TIPS insertion is associated with a higher risk of post-TIPS OHE, but not death or liver transplantation. Additionally, we found that QuickStroop is sensitive to changes in ammonia caused by TIPS insertion, validating its usefulness for the identification of patients with HE.

Data on the value of MHE and associated screening tests for predicting post-TIPS OHE have been conflicting. PHES and the critical flicker frequency are the most frequently studied tests.[7,8] A recent study of German patients found none of these tests, including ANT, to be associated with OHE. However, there was a numerical increase in the post-TIPS HE incidence with each additional abnormal test result.[8,9] Our study aligns with most of these studies by demonstrating that PHES-MHE and S-ANT1 alone are not reliable predictors to identify high-risk patients for post-TIPS OHE and expands the literature by demonstrating that QuickStroop has the potential to identify these high-risk patients. Of note, it is an interesting finding that QuickStroop is not inferior to the complete EncephalApp for predicting post-TIPS OHE. This means that testing cognitive flexibility and complex executive functions, which are tested with the complete EncephalApp among others, does not contribute to risk prediction regarding post-TIPS OHE. Therefore, testing of reaction time and psychomotor speed, which QuickStroop covers, seems to be sufficient. These findings are important for clinical practice, because QuickStroop can be easily used as a bedside test and seems implementable even in busy clinical practice to identify patients at higher risk of post-TIPS OHE.

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2025.07.016.

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Acknowledgments
The HaMa-TIPS-Study-Group includes Anja Tiede,[1] Julius F. M. Egge,[1] Heiner Wedemeyer,[1] Julia Weinmann-Menke,[2] Michael Bernhard Pitton,[3] and Peter Robert Galle[2,4]; from the [1]Department for Gastroenterology, Hepatology, Infectious Diseases, and Endocrinology, Hannover Medical School, Hannover, Germany; [2]Department of Internal Medicine I, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany; [3]Department of Radiology, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany; and [4]Cirrhosis Center Mainz, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany. This study contains parts of the thesis of Sina Liedtke. The authors thank Irina Wagner, Teresa Braun, Laura Schmidtke, Nathalie Eckel, Falko Zucker-Reimann, Dunja Amani, Annika Zietz, and Jennifer Witt for excellent technical assistance.

Conflicts of interest
These authors disclose the following: Simon J. Gairing received travel expenses from Ipsen and Gilead; and research grant from Schwiete Foundation. Eva Maria Schleicher received travel grants from Merz Therapeutics, AbbVie, and Advitos. Benjamin Maasoumy received lecture and consultant fees from AstraZeneca, AbbVie, Fujirebio, Falk Foundation e.V., Gilead, Luvos, MSD, Norgine, Roche, and W. L. Gore & Associates; and research grants from Altona, EWIMED, Fujirebio, and Roche. Christian Labenz received lecture and consultant fees from Merz Therapeutics, Norgine, Alfasigma, Intercept, Gilead Sciences, Falk Foundation e.V., CSL Behring, and Boehringer Ingelheim; and research grants from Merz Therapeutics, Norgine, and Schwiete Foundation. Peter Robert Galle received lecture fees and consulting from Merz Pharmaceuticals. The remaining authors disclose no conflicts.

Funding
This work was partly funded by the German Center for Infectious Research and partly supported by the Schwiete Stiftung (grant number: 2022-56), with a grant provided to Christian Labenz and Simon J. Gairing. Alena F. Ehrenbauer, Anja Tiede, and Julius F. M. Egge were supported by the KlinSMEtrucMed-Program of Hannover Medical School.