

Reply to: “Post-TIPS OHE: Are we really making a mountain out of a molehill?”

Can we really advise a patient undergoing TIPS that the onset of episodic hepatic encephalopathy will not influence his/her survival?

To the Editor:

We read with great interest the letter from Wang and colleagues¹ and we are grateful for their positive comments on our paper on the impact of episodic overt hepatic encephalopathy (OHE) on survival in patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt (TIPS).²

We completely agree that the occurrence of overt hepatic encephalopathy (OHE) after transjugular intrahepatic portosystemic shunt (TIPS) placement represents a relevant concern for hepatologists when proposing a TIPS to their patients. In fact, OHE is extremely frequent after a TIPS although persistent in a minority of patients. Post-TIPS OHE undoubtedly has a detrimental impact on patients' quality of life and represents a burden for caregivers and the healthcare system. Data reported in our recent study² indicate that the incidence of persistent post-TIPS OHE was higher in patients who died following TIPS, and our conclusions that post-TIPS OHE were not associated with higher mortality was based on patients with episodic OHE.

In their letter, based on the available literature, Wang and colleagues³⁻⁵ raise two relevant issues, (i) whether the timing and frequency of OHE episode(s) and (ii) the grade of OHE affect prognosis. Nonetheless, we re-analyzed our study database to address both points raised by Wang *et al.*¹ It should be noted that the relationship between the so-called early OHE (occurring within 3 months from TIPS) and survival³ was mainly related to the subgroup of patients with

recurrent OHE, in agreement with our observation on the negative prognostic impact of recurrent/persistent OHE.

In our patients, no significant differences in terms of survival were observed among those with early or late OHE and those with no episodes (Fig. 1A).

As far as the relationship between severe post-TIPS OHE (grade 3-4) and survival is concerned, it should be considered that the negative prognostic impact of severe OHE was based on the observation of very few patients, specifically 17 in the study of Stewart *et al.*⁴ and 11 in that of Bettinger *et al.*⁵ Our data clearly indicate that in the context of episodic OHE, its severity was not associated with any differences in survival (Fig. 1B).

Finally, the different population under investigation, considering that in our study a considerable fraction of patients received an undersized TIPS could have had an independent positive effect by preventing further potential detrimental effects of TIPS.

In conclusion, the original and the present analyses mitigate concerns regarding the prognostic impact of post-TIPS episodic OHE. Nevertheless, further studies are needed to dissect the factors associated with the development of this potentially deadly complication. In fact, the occurrence of persistent OHE is still largely unpredictable. The sample size of future studies must be considerably large given the lower incidence of persistent post-TIPS OHE afforded by the increasing use of undersized endoprotheses. At this time, while physicians should still be cautious in stating that the onset of post-TIPS OHE will not influence prognosis, the risks associated with the development of OHE must be balanced with the benefits related to the high efficacy in the control of portal hypertensive complications.

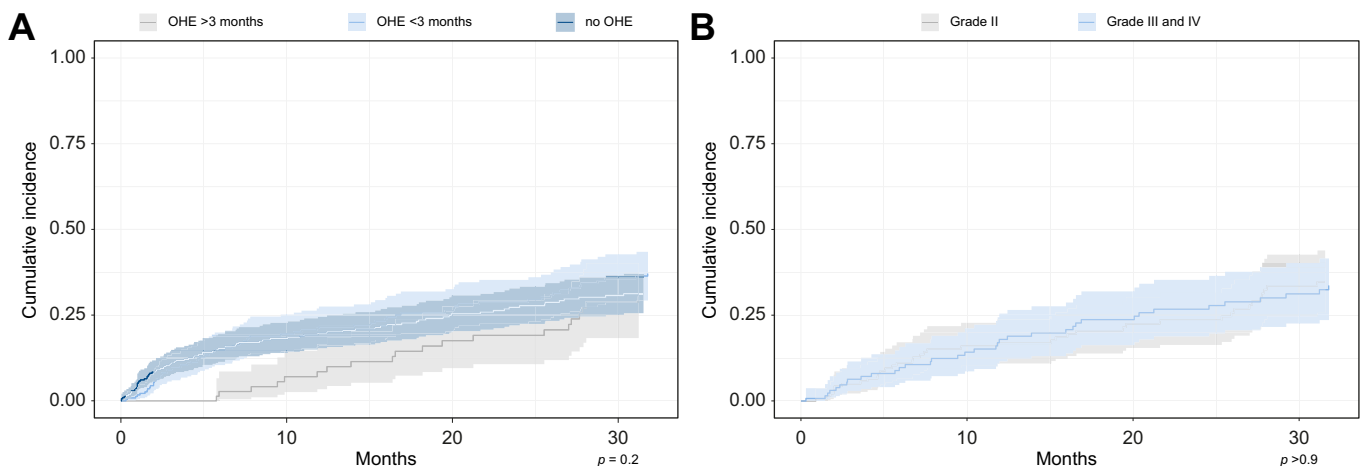


Fig. 1. The estimate of mortality post-TIPS, accounting for liver transplantation as a competing risk, by timing and severity of OHE. (A) The estimate of mortality post-TIPS, accounting for liver transplantation as a competing risk, among patients without OHE (n = 321) vs. patients with OHE within 3 months (n = 229) or patients with OHE after 3 months (n = 83). (B) The estimate of mortality post-TIPS, accounting for liver transplantation as a competing risk, among patients with OHE grade II (n = 178) vs. grade III-IV (n = 114). OHE, overt hepatic encephalopathy; TIPS, transjugular intrahepatic portosystemic shunt.

Silvia Nardelli^{1,*}
 Francesco Vizzutti^{2,3}
 Fabio Marra^{2,4}
 Filippo Schepis^{5,6}
 Oliviero Riggio¹

¹Department of Translational and Precision Medicine, Sapienza University of Rome, Italy

²Department of Experimental and Clinical Medicine, University of Florence, Italy

³Portal Hypertension Departmental Unit, Dipartimento Oncologico e di Chirurgia ad Indirizzo Robotico, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy

⁴Center for Research, High Education and Transfer DENOTe, University of Florence, Florence, Italy

⁵Division of Gastroenterology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy

⁶Severe Liver Diseases (M.E.C.) Departmental Unit, Department of Medical Specialties, Azienda Ospedaliero Universitaria of Modena, University of Modena and Reggio Emilia, Modena, Italy

*Corresponding author. Address: Sapienza University of Rome, Gastroenterology Viale dell'Università 37, 00161 Roma, Italy. E-mail address: nardelli.silvia@gmail.com (S. Nardelli)

Received 3 May 2024; Accepted 3 May 2024; Available online 9 May 2024

<https://doi.org/10.1016/j.jhep.2024.05.006>

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Financial support

The authors did not receive any financial support to produce this manuscript.

Conflict of interest

The authors declare that no conflict of interest exists concerning this paper. Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Conceptualization and writing: SN, FV, FM, FS and OR. All authors have reviewed and approved the final manuscript.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2024.05.006>.

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