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LETTER TO THE EDITOR

Hepatic encephalopathy: you should only comment on what you have actually measured

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To the Editor:

We read with interest, but with some concern, the manuscript by Thalheimer and colleagues [1] on their experience treating refractory ascites in patients with cirrhosis with 'limited diameter' TIPS. The authors devote a section of the *Results* and a significant part of their *Discussion* to the relationship between limited diameter TIPS insertion and hepatic encephalopathy, a condition that they measured in only a subgroup of patients, at irregular time points in relation to TIPS placement, and to no recognised or validated standards. In consequence, their conclusions with regards to the clinical and prognostic significance of this otherwise well-recognised complication of the TIPS procedure [2, 3] must be seriously questioned.

It is well accepted that even the most experienced of clinicians can miss the sometimes subtle neuropsychiatric changes that characterise hepatic encephalopathy [4, 5]. In consequence, it has been advised [5] that the assessment of neuropsychiatric status in this patient population should include a structured appraisal of mental status [6], psychometric performance [7, 8] and, if available, a neurophysiological variable such as the electroencephalogram (EEG) [9, 10]. TIPS insertion is associated with a high risk of precipitating or worsening of hepatic encephalopathy [2, 3, 11, 12]. Thus, rigorous assessment of patients' neuropsychiatric status pre-TIPS is essential, and in the non-emergency setting it should be mandatory.

Thalheimer and colleagues [1] did not provide details of their patients' past history of encephalopathy, and the assessments they undertook of their neuropsychiatric status before the TIPS procedure comprised 'an EEG if there was clinical suspicion of encephalopathy'. Overall, 30 (54%) of their 56 patients fulfilled this criterion; in 15 (50%) the EEG was said to be abnormal based on slowing of the mean cycle frequency (mcf) to <7 Hz. This degree of slowing is grossly abnormal; the diagnosis should be considered if the mcf is <8 Hz or if there are sporadic bursts of bi-temporal slowing in the presence of a mcf of ≥ 8 Hz [9, 10]. If the authors had trusted their clinical judgement, then 30 (56%) of their patients would have been diagnosed with hepatic encephalopathy pre-TIPS. However, if they based the diagnosis solely on the presence of an abnormal EEG, then 15 (26%) patients would have fulfilled their diagnostic criteria, although considering their use of an incorrect EEG threshold, it was probably higher. It is, therefore, impossible to deduce why they allege in their report that only six (11%) patients showed evidence of hepatic encephalopathy pre-procedure, as this clearly does not equate with the data they provided. Thus, the prevalence of pre-TIPS hepatic encephalopathy in this patient population, based on the information given, is unknown.

The assessment of the patients' neuropsychiatric status post-TIPS was entirely clinically based with no objective confirmation provided. During the first 3 months after

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TIPS insertion, 26 (46%) of the 56 patients died or had been lost to follow-up; by the end of the first year only 16 (29%) patients were alive and contactable. In all, 27 patients were said to have developed a 'new episode' of hepatic encephalopathy after a median of 18 (range 1–747) days, the majority of which were classified as grade I–II and responded to treatment. However, the attrition rate was extremely high, and the authors' assertion that it is likely that those lost to follow-up will behave similarly to those retained is not based on fact. Thus, the true prevalence of hepatic encephalopathy post-procedure, based on the data provided, is also unknown.

The authors undertook multivariate analysis to determine which variables predicted the development of post-TIPS encephalopathy. Greater age was the only predictor. Thus, in contrast to others [2, 3, 13, 14], they found that neither a history of previous episodes of hepatic encephalopathy (data not supplied), nor the presence of neuropsychiatric impairment at the time of the procedure (diagnostic method not specified) nor the presence of EEG signs correlated with the subsequent development of this complication of the procedure. However, given the methodological issues detailed above, these data must be treated with extreme caution. In contrast, the authors report that the presence of hepatic encephalopathy at the time of the TIPS insertion was associated with a significant risk of dying in the first month post-procedure (OR 3.10; CI 95% 1.29–7.44). However, according to the authors, only 6 (11%) of their 56 patients had encephalopathy at the time of the procedure, and 5 patients died within the first month. Once again, these data are most likely incorrectly ascribed and as such are difficult, if not impossible, to interpret.

Patients with refractory ascites should be very carefully assessed before they undergo a TIPS procedure as there is a real danger that if they develop significant hepatic encephalopathy they may be left with a complication that impinges even further on their quality of life. The assessments undertaken by Thalheimer and colleagues [1] of the neuropsychiatric status of the patients included in their study are inadequate. Use of a limited diameter TIPS may well be associated with a lower incidence of hepatic encephalopathy, but the methodological limitations of this study do not allow such a conclusion to be made.

Conflict of interest statement None to declare.

References

1. Thalheimer U, Leandro G, Samonakis DN, Triantos CK, Senzolo M, Fung K, et al. TIPS for refractory ascites: a single-centre experience. J Gastroenterol. 2009;44:1089–95.
2. Riggio O, Masini A, Efrati C, Nicolao F, Angeloni S, Salvatori FM, et al. Pharmacological prophylaxis of hepatic encephalopathy after transjugular intrahepatic portosystemic shunt: a randomized controlled study. J Hepatol. 2005;42:674–9.
3. Masson S, Mardini HA, Rose JD, Record CO. Hepatic encephalopathy after transjugular intrahepatic portosystemic shunt insertion: a decade of experience. QJM. 2008;101:493–501.
4. Amodio P, Montagnese S, Gatta A, Morgan MY. Characteristics of minimal hepatic encephalopathy. Metab Brain Dis. 2004;19:253–67.
5. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. Hepatic encephalopathy—definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. Hepatology. 2002;35:716–21.
6. Conn HO, Leevy CM, Vlahcevic ZR, Rodgers JB, Maddrey WC, Seeff L, et al. Comparison of lactulose and neomycin in the treatment of chronic portal-systemic encephalopathy. A double blind controlled trial. Gastroenterology. 1977;72:573–83.
7. Weissenborn K, Ennen JC, Schomerus H, Rückert N, Hecker H. Neuropsychological characterization of hepatic encephalopathy. J Hepatol. 2001;34:768–73.
8. Randolph C, Hilsabeck R, Kato A, Kharbanda P, Li YY, Mapelli D, et al. Neuropsychological assessment of hepatic encephalopathy: ISHEN practice guidelines. Liver Int. 2009;29:629–35.
9. Parsons-Smith BG, Summerskill WH, Dawson AM, Sherlock S. The electroencephalograph in liver disease. Lancet. 1957;273:867–71.
10. Amodio P, Marchetti P, Del Piccolo F, de Tourtchaninoff M, Varghese P, Zuliani C, et al. Spectral versus visual EEG analysis in mild hepatic encephalopathy. Clin Neurophysiol. 1999;110:1334–44.
11. Riggio O, Nicolao F, Angeloni S, Masini A, Salvatori F, Fanelli F, et al. Intractable hepatic encephalopathy after tips with polytetrafluoroethylene-covered stent-graft. Scand J Gastroenterol. 2003;38:570–2.
12. Deltenre P, Mathurin P, Dharancy S, Moreau R, Bulois P, Henrion J, et al. Transjugular intrahepatic portosystemic shunt in refractory ascites: a meta-analysis. Liver Int. 2005;25:349–56.
13. Jalan R, Elton RA, Redhead DN, Finlayson ND, Hayes PC. Analysis of prognostic variables in the prediction of mortality, shunt failure, variceal rebleeding and encephalopathy following the transjugular intrahepatic portosystemic stent-shunt for variceal haemorrhage. J Hepatol. 1995;23:123–8.
14. Tripathi D, Helmy A, Macbeth K, Balata S, Lui HF, Stanley AJ, et al. Ten years' follow-up of 472 patients following transjugular intrahepatic portosystemic stent-shunt insertion at a single centre. Eur J Gastroenterol Hepatol. 2004;16:9–18.