We read with interest the paper by Fagan et al in which authors aimed to assess the role of albumin infusion on Minimal Hepatic Encephalopathy (MHE) and Quality Of Life (QOL) in patients with previous Hepatic Encephalopathy (HE) [1]. In this double-blind, placebo-controlled randomized clinical trial it has been demonstrated that albumin infusions were associated with improved cognitive function and psychosocial quality of life likely through amelioration of endothelial dysfunction. Authors interestingly enrolled patients at risk for bouts of HE: subjects with previous HE and cognitive impairment detected at psychometric tests and considered the resolution/amelioration of MHE/psychometric performance as a robust surrogate marker able both to identify patients with a worst outcome as well as subjects in which the positive effects of any
given treatment could be evaluated. Transjugular Intrahepatic Portosystemic Shunt (TIPS) is widely used to treat some complications of portal hypertension such as recurrent variceal bleeding or refractory ascites, by shunting blood flow bypassing the liver and consequently reducing portal pressure, with the aim to reduce mortality and bridge patients to liver transplant. TIPS often represents a life-saving procedure, but is characterized, due to the blood diversion directly into systemic circulation, by development of HE, particularly in the immediately first period after the procedure [2]. To date, the role of drug therapy in prophylaxis of HE after TIPS is not yet clear and supported by strong scientific evidence [3]. Given this premise, also TIPS carriers could be considered as subjects at high risk of HE. This condition may have also worsened by the presence of cognitive impairment before TIPS placement. Here we retrieved and analyzed some data from our databases on cirrhotic patients submitted to TIPS placement, treated with human albumin infusion for the first month after TIPS and prospectively followed by our unit, in which a comprehensive assessment of liver disease as well as of mental status has been performed [3, 4]. MHE was assessed at baseline and during the follow up by using the Psychometric Hepatic Encephalopathy Score (PHES) [3]. Patients were treated with albumin infusion as follows 1g/kg at day 1 and 2, 0.5 g/kg at day 4 and 0.5g/kg weekly for the following three weeks after TIPS. Psychometric performance was reassessed 4 weeks after TIPS placement as well as presence and severity of overt HE episodes were recorded.

23 cirrhotic patients submitted to TIPS (M/F: 17/6; virus/alchol/other aetiology: 9/8/6), age 57.7.5±9.8 years were followed up for one month. Indication to TIPS were (refractory bleeding/ascites 13/10). Severity of cirrhosis was evaluated by Child Pugh Class (A/B/C: 7/14/2) and MELD score (11.6±3.2). MHE was present in 12/23 patients (52%) before TIPS placement. All patients experienced none previous bout of HE and were not taking any prophylactic therapy. TIPS was successfully implanted in all 23 patients and portosystemic pressure gradient fell from 18.6±5 to 5.4±3.6 mmHg. PHES score was not improved after TIPS placement (-3.15±3.7 vs post -3.7±4.1 p ns), as well as the prevalence of MHE (52% vs 43%, p ns), whereas 8 patients developed at least one episode of overt HE during the first 4 weeks. This evidence does not clearly demonstrate the efficacy of human albumin administration in patients undergoing TIPS placement in improving psychometric performance and reducing the incidence of HE post TIPS. Possible explanations could be, beyond the pathophysiological mechanism underlying the development of HE post TIPS, the reduced number of patients enrolled and the different dosage of infused albumin comparing to those used in the Fagan’s trial. Moreover, also the evidence and the grade of a persistent cognitive impairment after TIPS could be different and heavy than those observed in cirrhotic patients [5, 6]. However, the evidence of a non-worsening of PHES after TIPS as well as an overt post TIPS HE incidence lower than that reported in literature [3, 7] seems to suggests that, even in this particular subset of patients at high risk of HE, the use of human albumin may be effective and, in our opinion, opens a new perspective. Therefore, further studies, specifically designed on this outcome, will be necessary to clarify this unmet need. Finally, a series of considerations regarding the design of RCT on patients with cognitive impairment and MHE should be made.
In fact, changes of psychometric performance could be considered as a useful tool to enroll comparable patients but should not be only chosen as the main endpoint of the study as well as the calculation of sample size should consider clinically relevant endpoints (safety due to prolonged use, quality of life, the occurrence of OHE during the follow up, falls) [8].

References


