Editorial

Early versus rescue transjugular intrahepatic portosystemic shunt in patients with acute variceal bleeding

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In patients with liver cirrhosis, acute variceal bleeding has a considerable risk of death. Mortality increases dramatically if bleeding persists or early rebleeding occurs after endoscopic and drug treatments have been applied. This almost fatal situation occurs in 10–20% of patients with variceal bleeding which are now candidates for treatment with the transjugular intrahepatic portosystemic shunt (TIPS) (1,2).

Numerous cohort studies (3-10) have been performed in the past to evaluate the benefit of rescue TIPS. They predominantly included patients in Child-Pugh class B and C and the technical success rate was close to 100%. Primary hemostasis was achieved in almost all patients but 16% to 30% rebled mostly from ulcers due to previous endoscopic treatments. The 30-day mortality ranged between 17% and 55%. Since studies were not comparative and mortality after rescue TIPS is considerable, the benefit of this measure remains obscure.

In the intention to avoid death from rapid disease progression by rebleeding, studies have been performed applying the TIPS as early as possible after admission. The first randomized study selected patients with an increased risk of early rebleeding indicated by a high portal-hepatic venous pressure gradient of ≥20 mmHg (11). A subsequent study selected patients according to clinical risk factors predicting early rebleeding such as the Child score and the presence of active variceal bleeding at initial endoscopy (12). Patients with Child Pugh class B and active bleeding at initial endoscopy or those with Child-Pugh class C were randomized to receive early TIPS or standard treatment. TIPS significantly reduced rebleeding and improved survival without increasing the risk of hepatic encephalopathy. A later observational study from the same centers confirmed the previous results (13). As shown in *Table 1*, in comparison with the studies using the TIPS as a rescue treatment after failure of more than one endoscopic approach (3-10), results after early TIPS seem to be favourable showing lower in-hospital rebleeding and mortality rates of 3–12% and 3–8%, respectively. However, comparison of cohort studies on rescue and early TIPS may be biased by various confounders, including the time of the study and the stent-type. The earlier rescue studies exclusively used bare stents, while the later early TIPS studies predominantly implanted covered stents.

Njei *et al.* addressed this problem by comparing outcomes in patients with variceal bleeding not receiving a TIPS with those receiving rescue or early TIPS (14). This 10-year retrospective population-based study queried the US Nationwide Inpatient Sample database to identify 142,539 patients with cirrhosis, decompensated by variceal bleeding. The primary outcome variable was in-hospital death and secondary outcome variables included early rebleeding and hepatic encephalopathy. A total of 5,844 patients (4.1%) received rescue TIPS and 713 patients (0.5%) received early TIPS treatment. Thereby, early preventive TIPS was defined by placement within 3 days of hospitalization for acute variceal bleeding after one session of endoscopic therapy, whereas rescue TIPS was defined as

Table 1 Outcome variable of studies on rescue and early TIPS and of the study by Njei *et al.*

Modality	No. of studies	Patients	Stents	In-hospital rebleeding (%)	In-hospital mortality (%)
Rescue TIPS (3-10)	8	296	Bare stents	16.0–30.0	17.0–55.0
Njei rescue (14)	1	5,844	Not given	2.2	8.1
Early TIPS (11-13)	3	103	Covered stents*	3.0–12.0	3.0–8.0
Njei early (14)	1	713	Not given	0.5	1.5

*, type of stent not given in (11).

TIPS implantation after two endoscopic interventions for variceal bleeding. On multivariate analysis adjusted for age, ethnicity, sex, comorbidities, and severity of liver disease, early TIPS showed decreased inpatient mortality (1.5%) when compared to no TIPS (5.6%, P<0.01) and rescue TIPS (8.1%, P<0.01). In addition, in-hospital rebleeding was significantly reduced by early TIPS (0.5%, P<0.01) when compared to no TIPS (15.4%, P<0.01) or rescue TIPS (2.2%, P<0.01), respectively, without a difference in the occurrence of hepatic encephalopathy. Comparing the results of the study by Njei *et al.* with the results of the previous studies on rescue or early TIPS, the in-hospital mortality and rebleeding rates differ considerably (*Table 1*).

Multiple reasons may explain the divergent findings.

(I) The study by Njei *et al.* selected patients with "decompensated" cirrhosis using the definition of Baveno V (1). Accordingly, any patient with variceal bleeding was regarded as decompensated and was included. Computation of the Child-Pugh and MELD scores could not be obtained. Thus, in comparison with the randomized studies on rescue and early TIPS which included exclusively Child-Pugh class B and C patients (3-13), Njei *et al.* included a moiety of roughly 50% of Child-Pugh class A patients. This may explain the low in-hospital mortality rates in patients with no TIPS of 5.6%.

(II) The result may be biased by the fact that many patients with a greater risk of rebleeding and death did not receive early or rescue TIPS because hospitals did not provide the procedure. This may be the reason why, in the Njei study, mortality was lower in patients receiving an early TIPS than in patients not receiving a TIPS, a finding which may postulate to recommend early TIPS in any patient with variceal bleeding.

(III) Data of the Inpatient Sample may be incomplete. This may explain why patients receiving rescue TIPS had a much lower in-hospital mortality (8.1%) than in previous comparable studies (about 50%) (*Table 1*).

(IV) Results of the Njei study may be confounded by indication. The group of patients receiving early TIPS may have a considerable risk of rebleeding, e.g., larger varices, higher Child-Pugh class, which prompted the physician to recommend the more invasive treatment. However, patients receiving rescue TIPS definitely rebled and can, therefore, be regarded as the group with the most serious condition. Post hoc comparison of these groups may, therefore be inaccurate. In addition, the study by Monescillo (11) showing a beneficial effect of early TIPS in patients with portosystemic pressure gradients of ≥20 mmHg, has been published in 2004, and the study by Garcia-Pagan showing a benefit of early TIPS in patients with Child-Pugh B cirrhosis and active bleeding at endoscopy or Child-Pugh C cirrhosis has been published in 2010 (12). Thus, the presently used and proven criteria to select patients for early TIPS implantation have not or only partially existed during the time of the generation of the database [2000–2010].

Does the study contribute to the timing of the TIPS implantation in patients with variceal bleeding?

The answer may be yes because the study evaluated data of a huge database demonstrating significant superiority of early TIPS over rescue TIPS (and no TIPS) with respect to in-hospital variceal rebleeding and in-hospital mortality. However, the answer may be no, since the observational character of the study with its inherent issues of confounding and bias, delivers questionable results. One major problem may be the comparability of groups which is affected by various potential confounders. If there is still a need to clarify the roles of early and rescue-TIPS, a randomized study is required.

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Footnote

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