

## LETTER TO THE EDITORS

**Salvage transjugular intrahepatic portosystemic shunt followed by early transplantation in patients with Child C14-15 cirrhosis and refractory variceal bleeding: a strategy improving survival**

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Sirs,

Variceal bleeding is a major complication of cirrhosis [1, 2], with mortality of about 15% at 6 weeks [3]. International recommendations include treatment with vasoactive drugs, band ligation and prophylactic antibiotics [4]. In patients with refractory bleeding, salvage transjugular intrahepatic portosystemic shunt (TIPS) placement has been efficacious in controlling bleeding [5]. However, 1-year mortality is about 50% [5], mainly because of further deterioration of liver function; moreover, TIPS is generally contraindicated in patients with Child-Pugh C14-15 cirrhosis. Since 2007, with the implementation of the French Model for End-stage Liver Disease (MELD)/in France [6], most patients with severe disease may have access to liver transplantation (LT) quickly after being put on the waiting list for transplantation ("sickest first policy"). We hypothesized that LT may improve survival in patients with Child-Pugh C14-15 cirrhosis with deterioration/no improvement of liver function after salvage TIPS.

Therefore, from March 2007 to May 2011, patients referred to the Intensive Care Unit (ICU) of Hepatology and Gastroenterology in La Pitié-Salpêtrière Hospital and displaying the following features were considered for LT: 1) Child-Pugh C14-15 cirrhosis; 2) refractory variceal bleeding requiring salvage TIPS placement; 3) control of bleeding after TIPS; 4) development of liver failure during hospitalization with increased MELD score or persistence of liver failure after control of bleeding; and 5) no contraindication for LT (TIPS/LT group). We compared this group to historical controls with Child-Pugh C14-15 cirrhosis admitted to the ICU before March 2007 and who underwent salvage TIPS (Table 1). At the time LT was not considered because patients had limited access to organs (TIPS alone group). Placement of TIPS (e-PTFE-covered stent: Viatorr TIPS endoprosthesis, dilated to 8 mm, Gore) was performed within 4 hr after the diagnosis of refractory haemorrhage. When possible, treatment of underlying disease was started. If severe alcoholic hepatitis (AH) was suspected, liver biopsy

was performed, and prednisolone was administered if AH features were retrieved (40 mg/day). In TIPS/LT group, a rapid preoperative check-up was performed to seek for contraindication for LT (echocardiography, full-body scan, screening for neoplasia). Patients displaying alcohol-related cirrhosis with AH were considered for LT only, if they met the criteria previously described by the Lille team [7]. Patients were put on the waiting list for LT as soon as possible. Deceased-donor orthotopic LT was then performed.

Between March 2007 and March 2011, 372 patients with cirrhosis and variceal bleeding were hospitalized in the ICU; 31 patients underwent salvage TIPS, 10 of them displaying Child-Pugh C14-15 cirrhosis. Bleeding stopped after TIPS in 8/10 patients, but only 1 patient showed improvement of liver function. Among the 7 patients without improvement, 2 were not considered for LT because they displayed alcoholic cirrhosis without meeting the criteria for early transplantation for severe AH [7]; those 2 patients died. Five patients with Child-Pugh C14-15 cirrhosis were considered for LT (TIPS/LT group). The aetiology of cirrhosis was alcohol consumption with severe AH (meeting Lille criteria) ( $n = 2$ ), Wilson disease ( $n = 1$ ), and chronic hepatitis C ( $n = 2$ ). The MELD score at the time of listing for LT ranged from 29 to 40. The median delay between TIPS placement and LT was 8 days (range 3–17 days).

Between April 2004 and March 2007, 251 patients were hospitalized for variceal bleeding. Among those patients, 18 patients underwent salvage TIPS (Child A/B/C = 2/6/10); 8 had Child-Pugh C 14-15 cirrhosis. Bleeding stopped in 5 (TIPS alone group). Three displayed features of AH at liver biopsy, and were treated by corticosteroids. None of the 5 patients improved their liver function.

The 6-month survival was 100% in the TIPS/LT group and 0% in the TIPS alone group ( $P < 10^{-4}$ ). In the TIPS/LT group, two patients underwent re-transplantation (1 hepatic artery thrombosis and 1 acute rejection refractory to medical treatment). All transplanted patients were alive and at home with normal liver function with a median

follow-up of 18 months. In the TIPS alone group, septic shock developed in 4 patients within 2 weeks after TIPS placement and died. One patient died from invasive aspergillus infection 6 weeks after TIPS.

The high risk of death in patients with salvage TIPS placement justifies considering more aggressive treatment such as LT in patients with the most severe liver function. In many centres, patients with Child-Pugh C14-15 cirrhosis and refractory bleeding are not considered for salvage TIPS because mortality is about 100%. In our centre, we never defer patients for salvage TIPS; this might explain the lower proportion of patients displaying control of bleeding in our salvage TIPS series as compared to already described in the literature.

Here, we report the first data from salvage TIPS followed by rapid LT in patients with Child C14-15 cirrhosis. These results are encouraging, because among patients with controlled bleeding after TIPS and rapid placement on the waiting list, all underwent transplantation and were alive, as compared with none of the matched patients who did not undergo LT. The “sickest first policy” implemented in France since March 2007 [6] allowed us to consider patients for LT in case of variceal bleeding with very poor outcome. Therefore, in patients with the most severe disease, salvage TIPS should probably be considered only if LT is envisioned. Our results may be related to the rapid decision of LT after TIPS. Four of five patients in the TIPS alone group died within 2 weeks after salvage TIPS placement. In contrast, none of the patients listed for LT after TIPS died, because of rapid access to organ in case of worsening of MELD. These

**Table 1.** Clinical and biochemical characteristics of patients undergoing salvage transjugular intrahepatic portosystemic shunt (TIPS) with (TIPS/LT group) or without liver transplantation (TIPS alone group).

Variable	TIPS/LT group (n = 5)	TIPS alone group (n = 5)	P
Age (year)	44.8 ± 11.4	51.2 ± 8.7	0.27
Sex distribution (M/F)	5/0	5/0	0.41
Aetiology of cirrhosis			
Alcohol	2	3	0.34
Hepatitis C	2	1	
Hepatitis C and alcohol	0	1	
Wilson disease	1	0	
Previous history of variceal bleeding	2/5	3/5	0.93
Vasopressors	5/5	5/5	0.22
Mechanical ventilation	5/5	5/5	
Meld score	31.2 ± 4	31.5 ± 7	0.94
Bilirubin (µmol/l) [2–17]	228 ± 49	125 ± 56	0.27
INR	4.1 ± 2	3.1 ± 1.3	0.28
Albumin (g/l) [37–50]	23.2 ± 3.5	20.5 ± 3.7	0.21
AST (U/l) [20–32]	456 ± 639	121 ± 100	0.27
ALT (U/l) [16–35]	151 ± 175	60 ± 46	0.28
Creatinin (µmol/l) [62–106]	95 ± 25	84 ± 21	0.29

results are in line with recent results in patients with AH, suggesting that early LT was beneficial for survival [7]. Overall, our strategy strengthens the recent idea of early management of decompensated cirrhosis.

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