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Prognostic factors in patients with refractory ascites treated by transjugular intrahepatic porto-systemic shunt: From the liver to the kidney

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ABSTRACT

Background: The aim of this retrospective study was to evaluate the prognostic value of different scores (including Child–Pugh and Model for End Stage Liver Diseases) in cirrhotic patients treated with transjugular intrahepatic porto-systemic shunt for refractory ascites.
Methods: Overall, 111 patients with transjugular intrahepatic porto-systemic shunt insertion between January 1998 and July 2012 were included.
Results: Survival rates (without transplantation) were 82.0% at 3 months, and 59.4% at 1 year. In addition to standard parameters, a new simple classification based on platelet count and glomerular filtration rate showed strong prognostic ability and could distinguish 3 groups of patients (Log-rank test, $p < 0.001$): a "good-prognosis" group with platelet counts above $125 \times 10^9\ L^{-1}$ and a glomerular filtration rate above 90 mL/min (1-year survival rate 92%), a "poor-prognosis" group with platelet counts below $125 \times 10^9\ L^{-1}$ and a glomerular filtration rate below 90 mL/min (1-year survival rate 34.8%), and an "intermediate-prognosis" group (1-year survival rate 58.2%). Multivariate analysis showed a hazard ratio of 6.34 for the intermediate class and of 12.623 for the high class.
Conclusions: A new and simple classification including platelet count and glomerular filtration rate is highly predictive of survival in patients with refractory ascites treated with transjugular intrahepatic porto-systemic shunt and could be used to select patients for this procedure.

1. Introduction

Ascites is the most frequent complication of liver cirrhosis, especially if compared to jaundice, gastrointestinal bleeding, or hepatic encephalopathy [1]. Approximately 50% of cirrhotic patients present with ascites during 10 years of observation [1]. The prognosis for patients with newly established ascites is a 1 and 5-year survival of 85% and 56%, respectively [2]. Life-threatening complications of refractory ascites include spontaneous bacterial peritonitis, abdominal wall hernia (with the risk of incarceration, skin ulceration, or rupture), hepatic hydrothorax, denutrition, and impaired renal function leading to hepatorenal syndrome (HRS). In addition, chronic ascites also strongly affects quality of life [3]. Approximately 90% of cases could be controlled by a combination of optimal diuretic treatment and dietetic rules [1]. The treatment options for diuretic-resistant ascites include therapeutic paracentesis with intravenous albumin infusion, peritoneo-venous shunting, transjugular intrahepatic porto-systemic shunt (TIPS) and liver transplantation (LT) [4]. LT is the only curative treatment, but cannot be largely used because of organ scarcity and extrahepatic contraindications.

Several large-scale, randomized, controlled trials of TIPS compared with large-volume paracentesis have demonstrated that TIPS significantly improves the transplant-free survival of cirrhotic patients with refractory ascites [5]. Nevertheless, there is a significant risk of mortality in the first year following TIPS insertion, especially due to worsening of liver function [6]. Therefore, it has been a challenging issue for physicians to elaborate reliable tools for predicting the outcome of patients with refractory ascites and who

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are candidates for TIPS placement. The Model for End Stage Liver Diseases (MELD) score was initially specifically designed to predict the 3-month mortality risk of patients undergoing elective TIPS [7]. During the past 10 years, in addition to MELD, the prognostic value of several scores has been investigated in this field, including Child–Pugh score, creatinine-modified Child–Pugh score I and II, MELD-Na, iMELD, MESO, and REFIT-MELD. Recently, it has been suggested that a simple score, calculated from bilirubin level and platelet count, could be very efficient for the prediction of survival for patients with refractory ascites treated by TIPS [8].

The aims of the present retrospective study were [1] to evaluate the reliability of different scores (including the standard Child–Pugh and MELD scores and the simple "bilirubin-platelets" score) for the prediction of mortality after TIPS insertion in cirrhotic patients presenting refractory ascites, and [2] to investigate the ability of the same scores to predict ascites control.

2. Patients and methods

2.1. Study population

One hundred and eleven consecutive patients who had undergone TIPS placement for refractory ascites complicating liver cirrhosis were included in our centre (Edouard Herriot Hospital, Lyon, France) between January 1998 and July 2012. Refractory ascites was defined as ascites that does not respond to sodium restriction and high-dose diuretic treatment (400 mg/d spironolactone and 160 mg/d furosemide) or that reoccurs rapidly after therapeutic paracentesis or associated with diuretic-induced complications, as proposed by the International Ascites Club [9].

Patients' demographic characteristics (gender, age) and information on the type of cirrhosis were available for all patients. Baseline biological patients' characteristics were recorded within one week before TIPS placement and were available for all the patients. Glomerular filtration rate (GFR) was calculated by using the MDRD (Modification of Diet in Renal Disease) simplified formula as follows: $186 \times (\text{creatinine}/88.4) - 1.154 \times \text{age} - 0.203 \times (0.742$ if female gender$) \times (1.212$ if African descent) [10].

2.2. Calculation of scores

The Child–Pugh score was calculated in accordance to Pugh et al. [11].

The other scores were calculated as follows:

MELD = $9.6 \times \log_e$ [creatinine (mg/dL)] + $3.8 \times \log_e$ [bilirubin (mg/dL)] + $11.2 \times \log_e$ (INR) + 6.43 [6] [INR: international normalized ratio]

MELD-Na = MELD + $1.59 \times$ [135 − Na (mmol/L)]; Na range = 125–140 mmol/L [12]

iMELD = MELD + [$0.3 \times$ age (years)] − [$0.7 \times$ Na (mmol/L) + 100] [13]

MESO = [MELD/Na (mmol/L)] × 100 [14]

REFIT MELD = $4.082 \times \log$ bilirubin (mg/dL) + $8.485 \times \log$ creatinine (mg/dL) + $10.671 \times \log$ INR + 7.432 [15]

REFIT MELD Na = $4.258 \times \log$ bilirubin (mg/dL) + $6.792 \times \log$ creatinine (mg/dL) + $8.290 \times \log$ INR + 0.652 log (140 − Na) − $0.194 \times 140 - \text{Na} \times$ bilirubin + 6.327 [15]

Modified creatinine Child–Pugh score-I (range: 5–19) was derived from the original CP score by adding 0 points for creatinine <1.3 mg/dL and 4 points for creatinine > or = 1.3 mg/dL [16].

Modified creatinine Child–Pugh score-II (range: 5–19) was derived from the original CP score by adding 0 points for creatinine <1.3 mg/dL, 2 points for creatinine 1.3–1.8 mg/dL and 4 points for creatinine >1.8 mg/dL [15].

2.3. Patients' outcome

All patients were followed after TIPS insertion.

For the analysis of TIPS effectiveness, ascites was considered controlled if patients did not need paracenteses at 6 months. The presence of ascites was assessed and recorded after TIPS revision when this was necessary.

For the survival analysis, the follow-up time was defined from the TIPS placement up to death, LT, or last visit (patients who underwent LT were censored as dead).

Follow-up was complete through June 30, 2013.

2.4. Statistical analysis

Quantitative variables were described using mean, median, range, and standard deviation (SD). Qualitative values were tabulated and percentages were calculated. Quantitative variables were compared using the Student's *t*-test or Mann–Whitney test. Qualitative variables were compared using the χ^2 test.

The concordance statistic was calculated both for the scores and tests predicting mortality (at 3 and 12 months), and for those predicting TIPS efficacy (at 6 months). The concordance statistic, *c*, is identical to the area under the receiver operating characteristic (ROC) curve. The *c*-statistic varies between 0.5 and 1.0 for sensible models; the higher the value, the better. Only the results of *c*-statistics above 0.5 were considered as statistically significant.

Kaplan–Meier curves were used to represent survival according to the levels of scores and tests. The purpose of the univariate analysis was to select potentially explanatory variables. The continuous variables were dichotomised, by splitting at their median or upper normal value or at previously proposed values, and then compared. A Cox regression model was used to test the significance of these scores and tests as predictors of survival. All tests with a $p < 0.1$ at univariate analysis were included in the Cox Model.

Statistical tests were considered as significant if $p < 0.05$. All analyses were performed using SPSS (version 18).

3. Results

3.1. Patients' characteristics

The main characteristics of the patients included in the study group are summarized in Table 1. From the whole cohort of 111 patients, 36 subjects were considered to present resistant ascites (no response to high doses of diuretics) and the other 75 presented intractable ascites (with impossibility to give diuretics because of severe side effects or complications). Most of the patients were male, had alcoholic cirrhosis (78.4%), and had a mean age of 56.8 ± 10.7 years. The mean Child–Pugh score was 9 ± 1.45 and mean MELD score was 14 ± 6. No TIPS insertion failure was recorded during the study period for this specific indication.

3.2. TIPS effectiveness

After TIPS placement, 24.3% of patients (27/111) underwent a TIPS revision for stenosis and/or thrombosis. The presence of ascites was evaluated and recorded after TIPS revision when this was necessary. The persistence rate of ascites was 45.9% (51/111) at 6 months.

None of the biological or clinical parameters considered (including stent type, covered or uncovered) were significantly different when comparing patients with or without ascites persistence. Only