

Short-term independent mortality risk factors in patients with cirrhosis undergoing cardiac surgery

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Abstract

OBJECTIVES: Cirrhosis represents a serious risk in patients undergoing cardiac surgery. Several preoperative factors identify cirrhotic patients as high risk for cardiac surgery; however, a patient's preoperative status may be modified by surgical intervention and, as yet, no independent postoperative mortality risk factors have been identified in this setting. The objective of this study was to identify preoperative and postoperative mortality risk factors and the scores that are the best predictors of short-term risk.

METHODS: Fifty-eight consecutive cirrhotic patients requiring cardiac surgery between January 2004 and January 2009 were prospectively studied at our institution. Forty-two (72%) patients were operated on for valve replacement, 9 (16%) for a CABG and 7 (12%) for both (CABG and valve replacement). Thirty-four (58%) patients were classified as Child-Turcotte-Pugh class A, 21 (36%) as class B and 3 (5%) as class C. We evaluated the variables that are usually measured on admission and during the first 24 h of the postoperative period together with potential operative predictors of outcome, such as cardiac surgery scores (Parsonnet, EuroSCORE), liver scores (Child-Turcotte-Pugh, model for end-stage liver disease, United Kingdom end-stage liver disease score) and ICU scores (acute physiology and chronic health evaluation II and III, simplified acute physiology score II and III, sequential organ failure assessment).

RESULTS: Seven patients (12%) died in-hospital, of whom 5 were Child-Turcotte-Pugh class B and 2 class C. Comparing survivors vs non-survivors, univariate analysis revealed that variables associated with short-term outcome were international normalized ratio (1.5 ± 0.24 vs 2.2 ± 0.11 , $P < 0.0001$), presurgery platelet count (171 ± 87 vs 113 ± 52 nl^{-1} , $P = 0.031$), presurgery haemoglobin count (11.8 ± 1.8 vs 10.2 ± 1.4 g dl^{-1} , $P = 0.021$), total need for erythrocyte concentrates (2 ± 3.4 vs 8.5 ± 8 units, $P < 0.0001$), $\text{PaO}_2/\text{FiO}_2$ at 12 h after ICU admission (327 ± 84 vs 257 ± 78 , $P = 0.04$), initial central venous pressure (11 ± 3 vs 16 ± 4 mmHg, $P = 0.02$) and arterial blood lactate concentration 24 h after admission (1.8 ± 0.5 vs 2.5 ± 1.3 mmol l^{-1} , $P = 0.019$). Multivariate analysis identified initial central venous pressure as the only independent factor associated with short-term outcome ($P = 0.027$). The receiver operating characteristic curve showed that the model for end-stage Liver disease score had a better predictive value for short-term outcome than other scores (AUC: $90.5 \pm 4.4\%$; sensitivity: 85.7%; specificity: 83.7%), although simplified acute physiology score III was acceptable.

CONCLUSIONS: We conclude that central venous pressure could be a valuable predictor of short-term outcome in patients with cirrhosis undergoing cardiac surgery. The model for end-stage liver disease score is the best predictor of cirrhotic patients who are at high risk for cardiac surgery. Sequential organ failure assessment and simplified acute physiology score III are also valuable predictors.

Keywords: Liver cirrhosis • Cardiac surgery • Short-term outcome • Mortality scores

INTRODUCTION

Liver cirrhosis (LC) is a major preoperative risk factor in general surgery, especially in cardiac surgery, and the outcome is strongly related to the severity of liver disease in those patients [1]. While in patients without advanced cirrhosis, cardiac surgery can be done safely, the risk of mortality is higher in patients with Child-Turcotte-Pugh (CTP) class B and C or with a model for end-stage liver disease score (MELD) >13 [1, 2]. Preoperative total plasma bilirubin, cholinesterase concentrations, the European

system for cardiac operative risk evaluation (EuroSCORE), and the cardiopulmonary bypass (CPB) time have all been identified as potential predictors of mortality after cardiac surgery in those patients [3]. However, evidence comes mainly from several small studies; due to the lack of evidence from larger pools of data, postoperative risk factors remain unidentified.

At the same time, the option of liver transplantation as a treatment for patients with LC has produced an increase in survival rate and the evaluation of concomitant cardiac diseases, which increase post-liver transplantation complications, is crucial for

preoperative risk assessment [4]. Thus, cardiac surgery is increasing in those patients awaiting liver transplantation.

Consequently, identifying independent cardiac surgery post-operative risk factors for these patients is an area of interest if we want to optimize post-surgical management and improve outcome, especially post-surgical short-term outcome. In this study, we also wanted to evaluate different score systems to identify the best predictors of mortality.

MATERIALS AND METHODS

This study is a prospective single-centre observational study performed between January 2004 and January 2009. Data were included from 58 patients of 2825 (2.05%) consecutive patients with LC who underwent cardiac surgery in our hospital. The study was approved by the Institutional Ethics Committee. All of the patients had previously granted permission for their medical records to be used for research purposes.

LC was confirmed either by a liver biopsy or by clinical, laboratory and radiographical findings showing impaired hepatic function and portal hypertension. The CTP classification score was calculated for each patient (CTP A: 7 points; CTP B: 8–10 points; CTP C >11 points); 58.6% ($n = 34$) were classified as class A, 36.2% ($n = 21$) as class B and 5.2% ($n = 3$) as class C.

We evaluated demographical data and comorbidities, treatment before surgery, bedside variables currently measured during the first 24 h of postoperative clinical care and complications/mortality during their admission. We calculated different prognosis scores for each patient: cardiac surgery scores (Parsonnet and EuroSCORE), liver scores (CTP, MELD and United Kingdom end-stage liver disease (UKELD)), ICU scores (sequential organ failure assessment (SOFA), acute physiology and chronic health evaluation (APACHE II and III) and simplified acute physiology score (SAPS II and III). Finally, survival of the different CTP groups was shown to allow a comparison with previous studies.

Cardiac surgical procedures were performed in all patients using median sternotomy, standard cardiopulmonary bypass (CPB) with moderate hypothermia (34°C) and antegrade cardioplegia. A mean aortic pressure of >60 mmHg was maintained during surgery. For revascularization, we used the internal thoracic artery (or bilateral if possible) and saphenous vein grafts. Bypass graft flow was assessed for each graft by Doppler transit time flowmetry. Protamine was administered to reverse heparin according to standard practice. For CABG surgery, aspirin was routinely administered within the first 6 h after surgery following local protocol.

Statistical analysis

Statistical analysis was carried out using PASW statistics 13.0 (SPSS, Inc., Chicago, IL, USA). Data are expressed as mean \pm standard deviation. We analyzed differences in data between survivors and non-survivors. For the comparisons between the two groups, the Mann–Whitney *U*-test was used or, when appropriate (after applying the one-sample Kolmogorov–Smirnov test), the two-sample *t*-test was used. The χ^2 test was used to evaluate categorical prognostic factors. A multivariate analysis was carried out using Cox regression model to show independent risk mortality factors for short-term outcome. Finally, the survival analysis

of the CTP group was carried out with the Kaplan–Meier estimator for comparison with previous studies. Receiver operating characteristic (ROC) curve analyses were applied to determine optimal cut-off values of the different scores for short-term outcome and to further evaluate the predictive power between them, considering the differences of the areas under the empirical ROC curves. A *P*-value of 0.05 was considered statistically significant in all cases.

RESULTS

Forty-one patients (70.7%) were operated on for valve replacement, 10 (17.2%) for CABG, 6 of them off-pump, and 7 (12.1%) were both CABG and valve replacement. Only 3 patients underwent urgent surgery for CABG and there were no mortalities. All valve replacement operations were isolated: 34 (70.83%) were mitral valve and 14 (29.17%) aortic. None of the patients had previously undergone cardiac surgery.

Aetiologies for LC were predominantly infective hepatitis in 37.9% (hepatitis C, 31% ($n = 18$); hepatitis B, 6.9% ($n = 4$)), alcohol-induced in 34.48% ($n = 20$) and both hepatitis C and alcohol-induced in 13.8% ($n = 8$). The other were cryptogenic cirrhosis/others (13.8% ($n = 8$)) and in 10 patients, it was because of hepatocellular carcinoma.

The preoperative characteristics of the patients, including treatment before surgery, presented differences between groups in platelet and haemoglobin counts (see Table 1). Three patients were admitted previously at the cardiology department for acute myocardial infarction and underwent urgent cardiac surgery during the same admission. None of them died and their post-operative course did not differ from the other patients. Six patients (10.3%) were treated with aspirin before going into theatre. None of them died and there was no significant increase in terms of postoperative bleeding or the requirement for blood products. Despite there being a considerable prevalence of pre-operative risk factors in these patients in terms of LC complications due to end-stage liver disease, there was no significant difference between survivors and non-survivors.

There were no differences in intraoperative data, such as CPB time and aortic cross-clamping (ACC), between groups (see Table 2). Differences in postoperative data were observed for arterial oxygen pressure of O₂ and the fraction of inspired oxygen ratio (PaO₂/FiO₂), which was higher in survivors, while central venous pressure (CVP) on admission and 24 h after admission and arterial lactate (AL) 24 h after admission were all lower in survivors. With regard to postoperative morbidities, patients who died required a large amount of erythrocyte concentrates during admission, but there were no differences in terms of post-surgical bleeding. They also required a longer period on mechanical ventilation, and had a greater need for renal replacement therapies (RRT) and an increased need for vasopressors.

The median ICU stay was 9 \pm 10 days, with a difference between groups (7.7 \pm 1 in the survival group vs 13 \pm 5 in the non-survival group, $P = 0.002$). However, the median hospital stay was 34 \pm 20 days, and there were no differences between groups (21 \pm 3 vs 14.8 \pm 5.6 days).

Mortality was 12.1% ($n = 7$); 5 patients were CTP class B and 2 class C. The class C died of multi-systemic organ failure (MSOF), and the class B MSOF (3 patients) and septic shock (2). Short-term survival evaluated by Kaplan–Meier in Fig. 1 showed differences between CTP class groups (log-rank test, $P = 0.035$).

Table 1: Demographics and baseline data

| | All patients (n = 58) | Survivors (n = 51) | Non-survivors (n = 7) | P |
|---|--------------------------|-----------------------|--------------------------|-------------|
| Sex (male) | 69% (40) | 70.6% (36) | 57.1% (4) | 0.66 |
| Age (years) | 64.9 ± 11.6 | 64.6 ± 9.6 | 66.9 ± 10.3 | 0.92 |
| Body mass index (kg m ⁻²) | 27 ± 4.2 | 27.6 ± 4.6 | 26.6 ± 4.2 | 0.54 |
| Hypertension | 56.9% (33) | 54.9% (28) | 71.4% (5) | 0.68 |
| Diabetes mellitus | 32.8% (19) | 33.3% (17) | 28.6% (2) | 0.99 |
| Dyslipidaemia | 34.5% (20) | 33.3% (17) | 42.9% (3) | 0.68 |
| Chronic renal insufficiency | 8.6% (5) | 7.8% (4) | 14.3% (1) | 0.12 |
| Renal failure (on dialysis) | 19% (11) | 19.6% (10) | 14.3% (1) | 0.60 |
| Creatinine before surgery (mmol l ⁻¹) | 114.4 ± 100.8 | 106.4 ± 93.7 | 170.3 ± 136.3 | 0.15 |
| Previous stroke | 12.1% (7) | 12.1% (7) | 0% | 0.23 |
| Chronic obstructive pulmonary disease | 17.2% (10) | 17.6% (9) | 14.3% (1) | 0.85 |
| Active smokers | 19% (11) | 19.6% (10) | 14.3% (1) | 0.64 |
| Active alcohol consumption | 3.4% (2) | 3.9% (2) | 0% | 0.84 |
| Previous atrial fibrillation | 31% (18) | 33.3% (17) | 14.3% (1) | 0.78 |
| Previous myocardial infarction | 12.1% (7) | 11.8% (6) | 14.3% (1) | 0.53 |
| NYHA class III-IV | 34.5% (20) | 35.3% (18) | 28.6% (2) | 0.58 |
| On B-blockers | 39.7% (23) | 41.2% (21) | 28.6% (2) | 0.69 |
| On statins | 25.9% (15) | 25.5% (13) | 28.6% (2) | 0.92 |
| Ascites (moderate to severe) | 69% (40) | 70.6% (36) | 57.1% (4) | 0.45 |
| Oesophageal varices | 31% (18) | 25.5% (13) | 71.4% (5) | 0.26 |
| Variceal bleeding | 17.2% (10) | 17.6% (9) | 14.3% (1) | 0.14 |
| Encephalopathy | 34.5% (20) | 33.3% (17) | 42.9% (3) | 0.32 |
| Hypertrophic cardiomyopathy | 31% (18) | 31.4% (16) | 28.6% (2) | 0.68 |
| Dilated cardiomyopathy | 27.6% (16) | 27.5% (14) | 28.6% (2) | 0.91 |
| Left ventricular ejection fraction (%) | 60.3 ± 11.2 | 59.3 ± 11.7 | 62.6 ± 10.1 | 0.71 |
| Pulmonary arterial pressure (mmHg) | 48.7 ± 15.4 | 48.6 ± 15.6 | 49.4 ± 14.7 | 0.58 |
| Haemoglobin before surgery (g dl ⁻¹) | 11.67 ± 1.82 | 11.8 ± 1.8 | 10.2 ± 1.05 | 0.02 |
| Platelet count before surgery (1 nl ⁻¹) | 164 ± 85 | 171 ± 87 | 113 ± 52 | 0.03 |
| International normalized ratio before surgery | 1.5 ± 0.83 | 1.45 ± 0.15 | 1.85 ± 0.76 | 0.18 |

NYHA: New York Heart Association classification. Results are expressed as mean ± standard deviation or percentage.

Some scores revealed significant differences between groups: only SAPS II and III and SOFA showed a significant predictive power similar to that of UKELD and CTP. However, the other ICU scores and cardiac surgery scores were not as useful (Table 3). In order to compare differences between potential preoperative (liver and cardiac surgery scores) and postoperative (ICU scores) predictions, predictors of outcome for short-term survival were analysed using the ROC curve. The MELD score was the most predictive for in-hospital mortality. The optimal cut-off level for the MELD score was 18.5, with a sensitivity of 85.7% and a specificity of 83.7% (Fig. 2).

To evaluate preoperative and postoperative predictors of death for all patients, a multivariate analysis was conducted (See Table 4). We included those univariate factors that showed significant differences between groups in a Cox regression model. After risk adjustment, the multivariate analysis revealed initial CVP as the only independent factor associated with short-term outcome.

DISCUSSION

The most important finding of the current study was that in terms of predicting short-term mortality, both the CVP and the SAPS III and SOFA postoperative scores proved effective. We also confirm that the MELD score is the most effective predictor for the short-term outcome of these patients and that the CTP is a valuable score.

In view of the complexity of the procedure, the postoperative morbidity and mortality rates reported in the literature are considerably higher for cirrhotic patients undergoing cardiac surgery. [1]. The mortality risk in CTP class B patients is around 32.2% and increases to 66.6% in CTP class C patients [2]; even when there is a minimal degree of impaired liver function in combination with elective surgery, the incidence of complications significantly increases [5]. Careful patient selection is critical to improve surgical outcome in patients with cirrhosis [6]; however, there is a lack of factors that can be used to identify the mortality risk in those patients, especially after surgery. The lower incidence of comorbidities, the low number of urgent procedures and the low mortality rate found highlight the importance of our aim to select and prepare those patients for surgery carefully. Despite the differences in haemoglobin and platelets, the groups of survivors and non-survivors were comparable in almost all presurgery risk factors except the grade of liver disease. The major need for erythrocyte concentrates and RRT needs in non-survivors can be explained by initial presurgical lower haemoglobin, post-surgical INR differences and larger ICU admission and presence of MSOF as a cause of mortality, respectively. In any case, the risk of mortality increases with the deterioration of liver function [1–6].

In this scenario, INR progressively worsens during cirrhosis, also reflecting the current status of end-stage liver disease [7]. The replenishment of vitamin K-dependent factors beyond a normal INR has not proven its efficacy; however, individualized heparin and protamine dosing, antifibrinolytic drug administration,

Table 2: Intraoperative and postoperative data

| | All patients (n = 58) | Survivors (n = 51) | Non-survivors (n = 7) | P |
|---|--------------------------|-----------------------|--------------------------|-------------------|
| Intraoperative data | | | | |
| Isolated CABG | 15.5% (9) | 15.7% (8) | 14.3% (1) | 0.95 |
| Isolated valve surgery | 72.4% (42) | 72.50% (37) | 71.4% (5) | 0.97 |
| CABG + valve surgery | 12.1% (7) | 11.76% (6) | 14.3% (1) | 0.78 |
| Fluid balance during surgery (ml) | 1325 ± 850 | 1250 ± 980 | 1350 ± 785 | 0.58 |
| Aortic cross-clamping time (min) | 72 ± 44 | 74 ± 41 | 69 ± 50 | 0.85 |
| Cardiopulmonary bypass time (min) | 107 ± 37 | 106 ± 48 | 108 ± 53 | 0.35 |
| Postoperative data and major postoperative complications | | | | |
| Ventilation time (days) | 5.3 ± 10.2 | 3.16 ± 7.7 | 21 ± 12 | 0.01 |
| PaO ₂ /FiO ₂ on admission | 287 ± 95 | 293 ± 93 | 245 ± 110 | 0.28 |
| PaO ₂ /FiO ₂ 12 h after admission | 318 ± 86 | 327 ± 84 | 257 ± 78 | 0.04 |
| PaO ₂ /FiO ₂ 24 h after admission | 307 ± 75 | 315 ± 70 | 253 ± 96 | 0.23 |
| MAP on admission (mmHg) | 83 ± 15 | 85 ± 15 | 74 ± 18 | 0.72 |
| MAP 24 h after admission (mmHg) | 80 ± 10 | 80 ± 9 | 75 ± 11 | 0.51 |
| CVP on admission (mmHg) | 12 ± 3.6 | 11.4 ± 3 | 16.5 ± 4.4 | 0.02 |
| CVP 24 h after admission (mmHg) | 12.5 ± 3.6 | 12 ± 2.8 | 16.3 ± 6 | 0.002 |
| Need of vasoactive drugs (h) | 165 ± 197 | 112 ± 109 | 490 ± 304 | 0.016 |
| Low cardiac output syndrome | 31% (18) | 34% (17) | 14.3% (1) | 0.25 |
| Perioperative myocardial infarction | 7.1% (4) | 6.1% (3) | 14.3% (1) | 0.18 |
| Arterial lactate on admission (mmol l ⁻¹) | 2.6 ± 1.4 | 2.45 ± 1.3 | 3.6 ± 1.5 | 0.22 |
| Arterial lactate 24 h after admission (mmol l ⁻¹) | 1.9 ± 0.7 | 1.8 ± 0.5 | 2.5 ± 1.3 | 0.02 |
| Creatinine 24 h after surgery (mmol l ⁻¹) | 129 ± 108 | 118 ± 101 | 207 ± 138 | 0.15 |
| Urine output first 24 h (ml) | 1860 ± 650 | 1920 ± 570 | 1444 ± 1066 | 0.28 |
| Need for renal replacement therapy | 8.9% (5) | 2% (1) | 57.1% (4) | <0.0001 |
| Albumin (g l ⁻¹) | 27 ± 4 | 27.9 ± 4 | 27.8 ± 4.5 | 0.97 |
| International normalized ratio on admission | 1.8 ± 0.32 | 1.5 ± 0.24 | 2.2 ± 0.11 | <0.0001 |
| Drainage loss first 12 h (ml) | 464 ± 308 | 446 ± 299 | 595 ± 369 | 0.34 |
| Major bleeding | 1.7% (1) | 2% (1) | 0% | 0.85 |
| Re-exploration | 19% (11) | 21.6% (11) | 0% | 0.15 |
| Erythrocyte concentrates (units) | 3 ± 4.6 | 2 ± 30.4 | 8.5 ± 8 | <0.0001 |

CABG: coronary artery bypass graft; PaO₂/FiO₂: arterial partial pressure of O₂ and fraction of inspired oxygen ratio; MAP: mean arterial pressure; CVP: central venous pressure. Results are expressed as mean ± standard deviation or percentage.

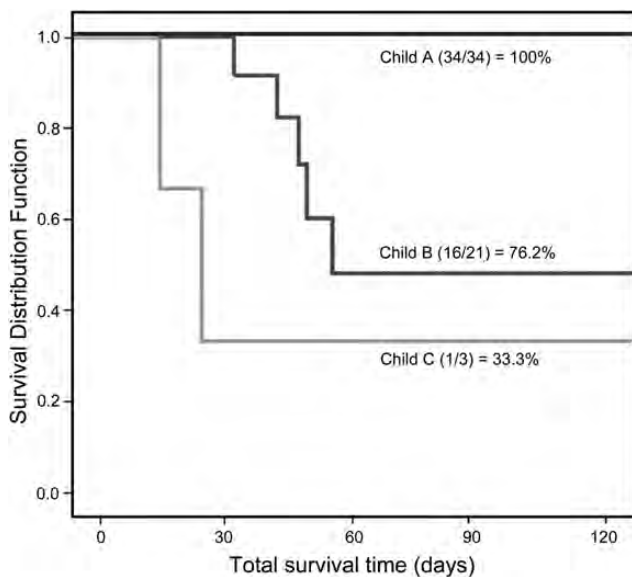


Figure 1: Short-term survival rate according to Child-Turcotte-Pugh score.

minimization of blood loss and dilution, and minimal CPB time could still potentially help achieve surgical homeostasis [8]. All these efforts are reflected in our results, in that drainage loss was similar between the groups despite postoperative INR differences.

Table 3: Evaluation scores for risk assessment

| | All patients (n = 58) | Survivors (n = 51) | Non-survivors (n = 7) | P |
|-----------------|--------------------------|-----------------------|--------------------------|-------------------|
| SAPS II | 25.2 ± 10.4 | 24 ± 9.4 | 33.7 ± 14 | 0.02 |
| SAPS III | 45.9 ± 10.8 | 44.7 ± 10.4 | 54.7 ± 10.4 | 0.045 |
| APACHE II | 13.9 ± 4.4 | 13.5 ± 4.1 | 16.8 ± 6 | 0.19 |
| APACHE III | 56.6 ± 18 | 55.2 ± 17.7 | 66.7 ± 19 | 0.17 |
| SOFA | 5.41 ± 2.72 | 6.6 ± 2.7 | 9.4 ± 1.8 | 0.005 |
| EuroSCORE | 6.48 ± 3 | 6.2 ± 2.9 | 8.8 ± 3.7 | 0.12 |
| Parsonnet score | 9.43 ± 6.42 | 9.2 ± 6.4 | 11.4 ± 6.8 | 0.43 |
| MELD | 16 ± 5.4 | 15 ± 4.57 | 23 ± 5.4 | 0.005 |
| UKELD | 49.8 ± 4 | 49.6 ± 4 | 52.6 ± 3.3 | 0.044 |
| CTP class A | 58.6% (n = 34) | 66.7% (n = 34) | 0% | <0.0001 |
| CTP class B | 36.2% (n = 21) | 31.4% (n = 16) | 71.4% (n = 5) | <0.0001 |
| CTP class C | 5.2% (n = 3) | 2% (n = 1) | 28.6% (n = 2) | 0.045 |

SAPS: simplified acute physiology score; APACHE: acute physiology and chronic health evaluation; SOFA: sequential organ failure assessment; EuroSCORE: European system for cardiac operative risk evaluation; MELD: model for end-stage liver disease score; UKELD: United Kingdom end-stage liver disease; CTP: Child-Turcotte-Pugh. Results are expressed as mean ± standard deviation or percentage.

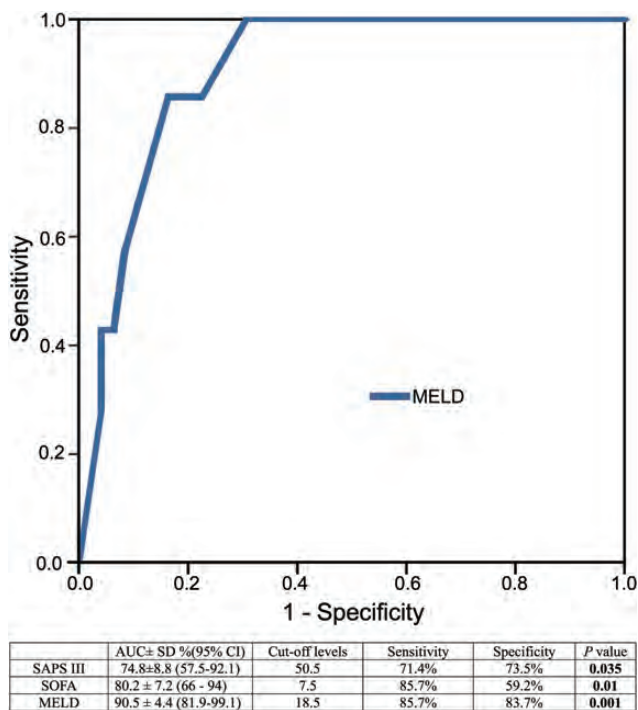


Figure 2: ROC curve for MELD. Comparison of AUC for MELD, SAPS III and SOFA scores. AUC: area under curve; ROC: receiver operating characteristic curve; SAPS: simplified acute physiology score; SOFA: sequential organ failure assessment; MELD: model for end-stage liver disease score; NS: non-statistically significant. Results are expressed as mean ± standard deviation or percentage.

Table 4: Multivariate analysis-dependent variable deceased during admission

| | Hazards ratio (95% CI) | P |
|---|------------------------|--------------|
| Age | 0.99 (0.94-1.036) | 0.69 |
| Platelets before surgery | 0.96 (0.79-1.164) | 0.68 |
| Haemoglobin before surgery | 1.13 (0.65-1.97) | 0.66 |
| INR after surgery | 0.65 (0.17-2.51) | 0.53 |
| CVP on admission | 0.88 (0.78-0.98) | 0.027 |
| SOFA score | 1.02 (0.86-1.195) | 0.82 |
| AL 24 h after admission | 0.81 (0.60-1.094) | 0.17 |
| PaO ₂ /FiO ₂ 12 h | 1.00 (0.99-1.004) | 0.91 |
| MELD score | 0.96 (0.87-1.068) | 0.48 |

PaO₂/FiO₂: arterial partial pressure of O₂ and fraction of inspired oxygen ratio; AL: arterial lactate; INR: international normalized ratio; CVP: central venous pressure; SOFA: sequential organ failure assessment; MELD: model for end-stage liver disease score.

Hyperlactataemia in the ICU, which is caused mainly by shock, is associated with increased mortality and is more frequent when respiratory and/or renal failures are/is present [9]. It predicts postoperative mortality after cardiac surgery with a maximum lactate threshold of ≥ 4.4 mmol l⁻¹ in the first 10 h after operation [10]. Arterial lactate tends to be higher in non-survivors, though it could be a reflection of a presurgery poorer liver function or an exacerbation of liver dysfunction in the setting of CPB.

Arterial partial pressure of O₂ and fraction of inspired oxygen ratio (PaO₂/FiO₂) is a new marker for outcome in some types of cardiac surgery [11]. Hypoxaemia depicted by low PaO₂/FiO₂ is common after CPB, and is associated with different variables, which are preoperative factors (age, obesity, chest X-ray with alveolar oedema 1 h after surgery, decreased baseline PaO₂/FiO₂, previous myocardial infarction), operative factors (emergency surgery, prolonged CPB) and postoperative factors (low cardiac output syndrome (LCOS), renal failure, persistent hypothermia 2-6 h after surgery, requirement for re-exploration). A lower PaO₂/FiO₂ ratio correlated significantly with the time required to carry out extubation and also to lung injury. However, in these patients, it had minimal effect on the postoperative clinical course [12]. Although PaO₂/FiO₂ 12 h after admission was lower in non-survivors, it did not have an independent significant impact on the outcome of surgery.

Central venous pressure (CVP) is used almost universally to guide fluid therapy in hospitalized patients. Some authors argue that there is a very poor relationship between CVP and blood volume as well as the inability to predict the haemodynamic response to a fluid challenge, being a good indicator of blood volume only at the extreme values [13]. Nevertheless, the conditions that influence CVP are well known, and as such, CVP remains a useful tool for evaluating haemodynamic status if it is performed under controlled conditions. CVP has the great advantage of being able to be measured at the patient's bedside without the need of invasive methods [14]. Dynamic evaluation of CVP could be a reliable predictor of fluid responsiveness in patients under mechanical ventilation, similar to the variation of arterial pulse pressure after cardiac surgery [15]. The proper use of CVP requires a good understanding of the waveform because higher values and CVP tracing are concordant with rhythm disorders, tricuspid regurgitation, cardiac tamponade, cardiac restriction and decreased thoracic compliance [16]. Limitations of CVP as a surrogate variable of preload are caused by the influence of intrathoracic and intra-abdominal pressures. However, these limitations do not impair the importance of CVP as the downstream pressure of the systemic venous system [15, 16]. We found CVP on admission to be the only independent factor for short-term outcome in the multivariate analysis. We hypothesize that CVP could be a surrogate marker of underscoring right ventricular failure, which can ultimately explain the higher mortality, but we cannot confirm our suspicions [17]. However, non-survivors did not receive larger amount of fluids in the operating theatre and did not have higher incidences of low cardiac output syndrome, which could have biased the CVP measurement.

Although EuroSCORE is widely accepted in Europe as a valuable score in cardiac surgery, in some populations, it does not have acceptable discriminatory ability. The development of local mortality risk scores corresponding to local epidemiological characteristics may improve the prediction of outcome [18]. In addition, it does not take into account surgical prognosis factors such as CPB time, and there is a lack of postoperative factors to determine short-term mortality [19]. Furthermore, the Parsonnet score does not consider specific liver variables. However, some authors suggest that it can be used to predict 3-month mortality, prolonged length of stay and specific postoperative complications such as renal failure, sepsis and respiratory failure in the whole context of cardiac surgery [20]. Because mortality in cirrhotic patients undergoing cardiac surgery is associated with liver function, liver scores such as the MELD or CTP score are

associated with outcome [1–3]. Our results confirm that the MELD score most reliably identifies cirrhotic patients at high risk for cardiac surgery, with better results than in previous studies [1]. In our study, the MELD values are higher than in previous studies, which is likely due to the high number of patients awaiting liver transplantations. With regard to CTP class scores, mortality was higher in postoperative cardiac surgery in patients with a CTP score of class C [1–3, 6]. With a lack of a large data series in previous research or a significant number of CTP class C patients described in the literature, there is no basis for comparison. The UKELD score can be used as a local score for end-stage liver disease, but unlike the MELD, it has never been evaluated in cardiac surgery. It evaluates sodium as well as INR, creatinine and bilirubin, identifying cirrhotic patients with the poorest quality of life and the highest complication rates [21]. The results for UKELD were statistically significant in the univariate analysis, though the ROC analysis raised doubts about its clinical relevance. ICU scores such as SOFA have been previously evaluated in cardiac surgery for the same purpose [22]. We also evaluated other ICU scores such as SAPS and APACHE. SAPS scores provided an estimate of the risk of death without having to specify a primary diagnosis, including liver failure and cardiac insufficiency grade [23]. Furthermore, higher SAPS scores have been associated with a poor quality of life, with the worst outcome occurring both before and after general surgery [24]; additionally, a higher mortality rate was found in elderly patients (>70 years) who required dialysis after cardiac surgery [25]. In our series, SAPS III provided an acceptable level of sensitivity and specificity, comparable with MELD results of other series [1]. APACHE scores were not found to be valuable tools.

Our study presents certain limitations. The most important are that it was a single-centre observational study. Results should be viewed cautiously due to the low number of patients and events. However, we have shown a larger number of patients than any other study of this kind to date, and observed a low mortality rate despite the level of end-stage liver disease.

We conclude that cardiac surgery can be performed safely in CTP class A and in some class B patients. Regarding CTP class C patients, due to the higher mortality in these patients, we think that liver function should be optimized prior to cardiac surgery, perhaps even performing liver transplantation. Indeed, synchronous surgery has modestly improved survival in some patients with cirrhosis when cardiac surgery is needed [4]. We recommend proper preoperative selection of patients and apply careful operative and postoperative management, especially in terms of fluid balance, in order to increase the short-term survival rate. A higher CVP at ICU admission may make physicians aware of a patient's prognosis, but its efficacy as a valuable predictor of short-term outcome must be shown in future studies. MELD score and postoperative ICU scores such as SAPS III and SOFA can be used to predict short-term outcome in those patients. In our opinion, in the setting of end-stage liver disease and cardiac surgery, postoperative evaluation is as important as preoperative evaluation in terms of predicting short-term outcome.

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eComment. The prognostic role of the MELD score in cardiac surgery patients with cirrhosis

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We read with great interest the recent article from Lopez-Delgado and colleagues [1], addressing the very relevant issue of risk prediction of short-term outcome in cirrhotic patients undergoing cardiac surgery. However, we believe that some aspects of the article require further comment.

The Model for End-stage Liver Disease (MELD) score has gained increased popularity over recent years in predicting the risk of mortality in patients with liver cirrhosis undergoing cardiac surgery. We agree that the MELD score improves prognostic assessment of those cirrhotic patients who are at an extraordinary high risk for major postoperative complications and in-hospital mortality after conventional cardiac surgery. Crucially, the mean preoperative MELD score is usually significantly lower among survivors compared to non-survivors. In a recent article [2], our group showed that in 57 cirrhotic patients, those with a MELD score of 13.5 points or higher had a significantly higher risk of dying within 30 days of cardiac surgery (mortality: 56%) than patients with a MELD score less than 13.5 (mortality: 9%) with a sensitivity of 82.0% and a specificity of 78.5%. With an even better discriminative power, Lopez-Delgado and colleagues [1] demonstrate the prognostic strength of the MELD score for in-hospital mortality with a cut-off value of 18.5. In this study of 58 patients who underwent cardiac surgery, predominantly for

isolated primary valve replacement (71%), the overall mortality rate was 12% at 4 months. This figure consisted exclusively of in-hospital mortality, without any further documentation of deaths in the early period after discharge from the cardiac surgery clinic. These promising results are inconsistent with our data [2] and those of another recently published retrospective study of 109 such patients from Germany [3], in which the overall in-hospital mortality was found to be 29.8% and 26%, respectively. Unfortunately, the work of Lopez-Delgado and colleagues [1] focused only on short-term outcome, with a follow-up of just four months. Therefore, their work contributes no additional knowledge to this field, as they simply did not incorporate a long enough follow-up period to enable comparison with other studies in this area. In addition, the authors state that, "... the MELD values are higher than in previous studies, which is likely due to the high number of patients awaiting liver transplantation ..." It would be interesting to know if and how many of these cirrhotic patients indeed underwent liver transplantation after successful cardiac surgery, and particularly whether this institutional strategy could have influenced short-term survival. Clarity on this specific issue and a better longitudinal data collection would add important information to the study. However, irrespective of early outcomes achieved, it is clear that 1-year survival rate drops significantly in cirrhotic patients considered to be at elevated operative risk. In our study [2] and according to the MELD score, 1-year survival was 23.8% with MELD score >13.5 as compared to 74.6% with MELD score <13.5. Roughly 75% of our high-risk cirrhotic population died after conventional cardiac surgery, despite adherence to strict preventive and postoperative management strategies, and expert consultation before and up to one year after surgery. Disappointingly, cardiac surgery in such individuals is performed before liver transplantation candidacy and often on an emergency basis with little if any impact on long-term survival.

Although liver cirrhosis alone is not considered a contraindication for surgery, cirrhotic patients with a high preoperative MELD score, in whom life expectancy per se is also limited by non-cardiac comorbidities, should be treated with caution. In this sub-group of cirrhotic patients, we believe that conventional cardiac surgery should not be performed.

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