

Cirrhotic Patients Undergoing Cardiac Surgery: Why Not to Develop a More Specific Heart-Liver Score?

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Abstract

Despite not included in the traditional risk scores before surgery, liver cirrhosis, especially in advanced stages, has always influenced strongly final outcome both on short and mid-term in patients undergoing cardiac surgery. Growing incidence of non-alcoholic fatty liver disease interlinked with metabolic syndrome and significant advancements in medical therapy have actually increased the likelihood of cardiac surgery in cirrhotic patients. To date, Child-Pugh and MELD scores have been commonly used to predict mortality and postoperative hepatic decompensation, but on the other hand, both traditional risk scores show some limitations for evaluation of hepatopathic patients undergoing specifically cardiac surgery. In this context, a specific Heart-Liver score hasn't been developed yet in the attempt to outline a patient profile able to face surgery, therefore addressing us to adopt the best strategy possible for each case. If CP class A or low MELD score (<11) patients tolerate cardiac surgery with a mild increase in mortality and morbidity, currently state of art recommends particular caution towards surgery idea in presence of advanced hepatic disease. As far as cardiac surgery represents the unique therapeutic strategy in several life-threatening cases, anyway surgical correction of cardiac pathology won't guarantee an increased life expectancy in accordance with the persistent liver dysfunction. Hereby, this paper will focus on preoperative parameters that should be considered in the future realization of a Heart-Liver prognostic score for overcoming limitations and difficulties related to the impact of liver disease on final clinical outcome.

Keywords

Liver Cirrhosis, Cardiac Surgery, Risk Score

1. Background

Nowadays, we more and more often may deal with cirrhotic patients having to undergo cardiac surgery, because of growing incidence of non-alcoholic fatty liver disease (NAFLD) and significant advancements in medical therapy (**Figure 1**), that have actually improved life expectancy of a cirrhotic patient.

NAFLD is becoming the most frequent cause of chronic liver disease, showing a pandemic prevalence of about 25%, arising from the western countries with progressive global involvement; patients affected from NAFLD are characterized by higher cardiovascular burden because of interconnections with diabetes and metabolic syndrome (the so-called “meta-inflammation”), more frequently as a consequence of increasing sedentary lifestyle and wrong eating habits.

Absence of liver cirrhosis within traditional risk score calculators after cardiac surgery doesn't rule out clinical dogma that so far an advanced hepatic disease has always influenced strongly final outcome both on short and mid-term.

Recent studies have underlined and reinforced the prognostic role of MELD score [1], commonly used together to Child-Pugh (CP) classification in order to predict mortality and postoperative hepatic decompensation (**Table 1**). Regardless of easy application, nonetheless both traditional risk scores show some limitations for specific evaluation of hepatopathic patients undergoing cardiac surgery, as listed in **Table 2**.

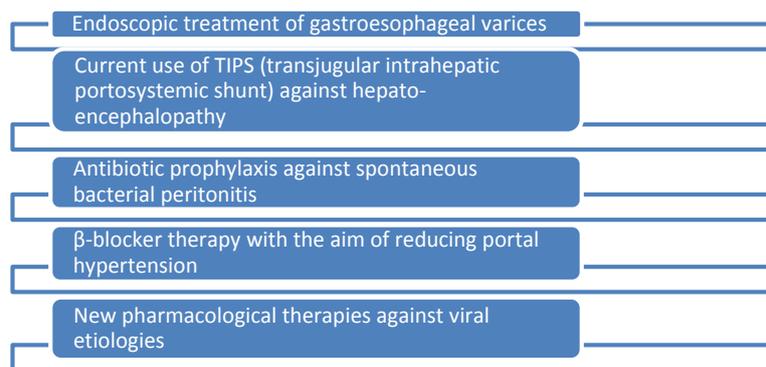


Figure 1. The picture illustrates the most important improvements that have been made over the last decades in the clinical management of cirrhotic patients.

Table 1. Common main risk scores in liver cirrhosis.

| Child Pugh Classification | 1 pt | 2 pts | 3 pts |
|---------------------------|------|-------------------|-------------------|
| Serum Bilirubin (mg/dL) | <2.0 | 2.0 - 3.0 | >3 |
| Serum Albumin (g/dL) | >3.5 | 2.8 - 3.5 | <2.8 |
| INR | <1.7 | 1.7 - 2.3 | >2.3 |
| Ascites | None | Easily controlled | Poorly controlled |
| Hepatic Encephalopathy | None | Minimal | Advanced |

CP class A (score of 5 - 6) - Class B (7 - 9) - Class C (>10). MELD score includes total bilirubin, INR, creatinine and hemodialysis performed twice at least in the week prior; recently serum sodium has been added (**MELD-Na Score**). MELD score is usually categorized into three functional classes: **Low MELD (6 - 14) - Intermediate MELD (15 - 24) - High MELD (25 - 40).**

Table 2. Disadvantages of traditional risk scores used before surgery (Child-Pugh and MELD scores).

| |
|---|
| No evaluation of immune dysfunction → infectious complications |
| Incomplete assessment of coagulopathy degree (thrombocytopenia/responsiveness INR to vitamin K administration) → bleeding |
| No mentioning of gastro-esophageal varices → rupture risk → life-threatening bleeding |
| No evaluation of serum cholinesterasis |
| No evaluation of cardiac disease related to liver cirrhosis |

Postoperative hepatic decompensation, frequent cause of hospital readmission with higher death risk, is commonly expressed from occurrence within three months after cardiac surgery of the following conditions:

- new-onset ascites and jaundice,
- encephalopathy porto-systemic,
- coagulopathy,
- variceal haemorrhage,
- hepato-renal syndrome.

2. Caveats

Currently, state of art recommends particular caution towards cardiac surgery idea in presence of an advanced hepatic disease, since the risk of mortality and liver-related complications for patients CP class B or C and MELD score > 13 is mostly considered too high, except for some selected CP Class B patients [2]; indeed, assessing what parameter increases final score within CP class B (*i.e.* encephalopathy has a prognostic burden more relevant than hypoalbuminemia) and learning to quantify the real impact of each clinical measure on prognosis, new subtypes of patients with different functional implications will be identified.

Nevertheless, the impact of preoperative hepatic and cardiac functional status on the final outcome is a so crucial issue that the idea emerges about a more specific new score taking into account both hepatic and cardiac parameters, in the respect of *Heart-Liver axis* that reflects close clinical relationship between the two organs in case of cirrhosis. In **Table 3** are resumed preoperative parameters (general, cardiac and hepatic) that might be analyzed by logistic regression models and thus included in the future realization of a Heart-Liver score with the aim of improving final outcome and facilitating new guidelines.

Indeed, the importance of a complete cardiac assessment in concomitant liver cirrhosis before surgery is a key factor for enhancing prognosis; in this regard myocardial performance indexes (such as a Tei index close to dobutamine stress echocardiography) can lead to better diagnostic conclusions than B-type natriuretic peptide aspecific dosages. A significant systo-diastolic dysfunction following a cirrhotic cardiomyopathy linked to hyperdynamic circulation can explain the potential pathogenesis of a dangerous hepatorenal syndrome or AKI, as well as a low cardiac output syndrome after surgery. Beyond the left ventricle

Table 3. Preoperative parameters predictive of clinical outcome in a Heart-Liver prognostic score.

| |
|---|
| Age at cardiac surgery |
| Reduced creatinine clearance (GFR < 45 mL/min) |
| High central venous pressure (≥ 15 mmHg) |
| Severe tricuspid regurgitation associated to low TAPSE (<16 mm) |
| Depressed ejection fraction (<50%) |
| Presence of esophagogastric varices (F3) |
| Conjugated hyperbilirubinemia (>2.5 mg/dL) |
| Low serum Cholinesterasis (CHE < 2000 UI/L) |
| Hypoalbuminemia (<3 g/dL) |
| Basal leucopenia (WBC < 2000 μ L) |
| INR correction unresponsive to vitamin K administration |
| Low ICG-PDR value (<8.2%/min) |
| Thrombocytopenia (Platelet < 100.000 μ L) |

diastolic dysfunction, it's a crucial issue to focus on right ventricle study since a significant tricuspid valve regurgitation due to hepatic venous congestion is a common finding; moreover, higher central venous pressure (CVP) values and a low TAPSE (<16 mm) before surgery may reflect an underscored right ventricular failure in this special subtype of patients. Furthermore, analysis of volemic status is often complex in the cirrhotic patient, who shows peripheral fluids overload linked to hypoalbuminemia but is actually depleted at intravascular level; an exact evaluation of CVP values allows to overcome this clinical paradox.

Close to cardiac study, hepatic functional reserve must be simultaneously studied before cardiac surgery and in this perspective low values of indocyanine green plasma disappearance rate (ICG-PDR) represent independent predictors of surgical mortality and postoperative complications [3]. Then, in alternative to hepatic venous pressure gradient measurement, ICG 15-minute retention (ICG-r15) describes an interesting tool that evaluates the presence and grading of portal hypertension (PH) ruling out the presence of esophageal varices with ICGr15 values < 10%, while values < 7% exclude a clinically significant PH [4]. Nevertheless, early identification of patients who must perform a digestive endoscopic study is essential to ward off dramatic complications related to a perioperative bleeding of unknown esophago-gastric varices; large size (Grade F3) of esophageal varices and presence of red color signs, especially red wale markings, represent endoscopic features associated to higher risk of rupture. Nowadays, role and degree of gastroesophageal varices never have been included in the widely accepted risk scores before cardiac surgery in patients with more advanced liver disease. Once evaluated, preoperative hepatic status [5] should be optimized in order to choose the right surgical timing and reduce postoperative complications by:

- enhancing hydro-electrolytic balance,
- improving the nutritional status,
- correcting coagulation disturbances.

How to assess and manage coagulopathy in a cirrhotic patient undergoing open heart surgery? Up to now both CP and MELD scores have referred only to INR values without taking into consideration responsive capacity to the correction through vitamin K or the severity of thrombocytopenia.

Poorer prognosis is observed in case of unresponsiveness to vitamin K administration in terms of improvement of PT-INR; besides, a thrombocytopenia (PLT < 100.000 μ L), that often reflects a hypersplenism condition, represents a marker of PH degree leading, in absence of correction, to dangerous bleedings in patients who even don't synthesize correctly various coagulation factors, have vitamin K deficiency and a reduced clearance of tissue plasminogen activator. Managing perioperative bleeding, a thromboelastography-guided transfusional therapy according to platelet functional status comes up beside the traditional support based upon fresh frozen plasma and packed red blood cells, whilst Recombinant factor VII A or Desmopressin are alternative and interesting pharmacological strategies to manage intractable perioperative bleedings.

Furthermore, CP and MELD scores are lacking evaluation of immune dysfunction linked to hepatic disease; high incidence of various infections (*i.e.* mediastinitis, bacterial spontaneous peritonitis up to sepsis leading to potential onset of multiple organ failure) suggests a proper analysis of each patient from an immune point of view. Thereby, recurrent basal leucopenia (WBC < 2000 μ L) should be considered a real contraindication to cardiac surgery, in accordance with the invasiveness of surgical procedure too.

Before cardiac surgery, lower cholinesterasis values and conjugated hyperbilirubinemia reflect respectively inability of hepatic protidosynthetic and excretory function representing useful biomarkers of liver cirrhosis and predictors of worse clinical outcomes in terms of morbidity and mortality; on the other hand, a low colloid oncotic pressure related to a severe disprotidemia or hypoalbuminemia implies higher incidence of pleural-pericardial effusions or ascites, without neglecting a potential massive fluids shift towards lungs or peripheral districts as limbs.

Also a preoperative reduced creatinine clearance represents an important prognostic marker; within the first 24 hours after surgery, low or absent urine output frequently occurred (almost 80% of incidence) with a following positive hydric balance that might lead to dangerous pulmonary edema.

Early identification of oliguria and immediate adoption of a pharmacological therapy or hydration, according to central or renal cause of AKI, may avoid dialysis that really must be the last step, anyway characterized by higher overall rates of mortality.

Despite potential use of MECC or a dilutional ultrafiltration during cardiopulmonary bypass (CBP), the negative impact of On-pump surgery on cirrhotic

patient is an incontrovertible evidence in terms of complications and mortality; hepatic hypoperfusion and ischemia-reperfusion damages or an incoming inflammatory response related to CPB may be offset by Off-Pump surgery, especially in CAD patients, or minimally invasive procedures. Of note, CPB is able to emphasize baseline coagulopathy of a cirrhotic patient through platelet dysfunction, fibrinolysis and hypocalcemia. If then On-Pump surgery is so unavoidable, CPB and cross-clamp times shouldn't be too long [6] trying to keep a cardiac index > 2.0 L/min/m² with higher pump flows (≥ 2.3 L/min) and adequate hematocrit values preventing hemodilutional anemia.

A “*post-pump jaundice syndrome*” causes frequently cholestasis, the earliest marker of ischemic hepatic damage, expressed by higher ALP and γ -GT rates more significant than hypertransaminasemia; although less common, other clinical scenarios, such as a bowel ischemia or gastrointestinal hemorrhage, stand out among the postoperative gastrointestinal complications in a cirrhotic patient, conversely associated to higher lethality.

3. Conclusions

As far as cardiac surgery represents the unique therapeutic strategy in several life-threatening cases, anyway surgical correction of cardiac pathology doesn't guarantee an increased longevity in accordance with the persistent liver dysfunction; indeed, new-onset hepatic decompensation within three months after successful cardiac surgery implies a survival of a CP class B patient around 50% after 8 months, while only half of patients in Class C survives after 4 months. Thereby, in case of advanced cirrhosis, a best medical therapy, shift towards percutaneous techniques (angioplasty or valvuloplasty) or minimal hybrid strategies should be considered effective therapeutic options for achieving better final outcomes.

Apart from complex and highly impracticable synchronous hepatic transplant and cardiac surgery, managing a cirrhotic patient undergoing cardiac surgery, the first and critical step is the preoperative patient selection close to a multidisciplinary approach in order to enhance final outcome; a new Heart-Liver prognostic score development would help us to predict properly the risk of mortality/complications after cardiac surgery and adopt the best strategy possible, especially in those “grey” patients CP class B or with a MELD cut-off 13 - 18, since CP class C or high MELD patients are nearly inoperable.

Eventually, despite especially MELD score gives indisputably useful precepts to quantify the severity of chronic hepatopathy, it seems necessary to develop a more specific new risk score dedicated to cirrhotic patients having to undergo cardiac surgery in the respect of the impact of liver disease on final clinical outcome [7].

Conflicts of Interest

The author declares no conflict of interest relevant to this publication.

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