Chapter 19
Cardiac Surgical Procedures in Patients with Cirrhosis

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Introduction

Cardiac surgery in patients with cirrhosis is fraught with high mortality and morbidity rates. Hepatic decompensation is common after cardiac surgery with cardiopulmonary bypass (CPB). The mortality rates in some studies were so high that cardiac surgery was contraindicated in patients with Child–Pugh (CP) Classes B and C cirrhosis [1–3]. A recent Cleveland Clinic study showed that the patients with liver cirrhosis had a five times higher mortality rate after cardiac surgery than the matched controls [4]. A large population-based study showed increased mortality, postoperative complications, length of stay, and hospital charges associated with coronary artery bypass grafting (CABG) in patients with cirrhosis [5]. Despite the general consensus of an associated higher risk, liver cirrhosis does not preclude cardiac surgery in carefully selected patients [4, 6].

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Risk Stratification for Cardiac Surgery in Patients with Cirrhosis

Utility of Various Scores

Various scoring systems have been employed to predict postoperative mortality and morbidity in patients with liver cirrhosis. These include CP score, Model for End-stage Liver Disease (MELD) score, Society of Thoracic Surgeons (STS) score, European System for Cardiac Operative Risk Evaluation (EuroSCORE), and Simplified Acute Physiology Score (SAPS) III. The CP Classification was initially developed empirically for patients with bleeding esophageal varices. It uses the albumin, prothrombin time, serum bilirubin, degree of ascites, and presence of encephalopathy to characterize the severity of liver cirrhosis. It has been found to be a reliable predictor of functional status of liver and overall survival [7]. It correlates strongly with postoperative mortality and morbidity in the patients who underwent cardiac surgery [2–5, 7, 8]. MELD score was developed in 2000 to stratify survival of patients after transjugular intrahepatic portosystemic shunt (TIPS) procedure. It is validated for predicting survival of patients with end-stage liver disease [4, 7, 9].

Filsoufi et al. did not find MELD scores to be significantly associated with hospital mortality [3], while the CP classification and its associated numerical score appropriately predicted mortality and morbidity [1–4, 7, 10]. Their study confirmed the predicted value of CP Classification; albeit, the sample size was small. On the other hand, Thielmann et al. found the MELD score to be the most predictive risk evaluation model with clear superiority to CP Classification and EuroSCORE. The best value for MELD score was found to be 13.5 with a sensitivity of 52% and specificity of 79%. CP Classification was found to be useful as well. The hospital and long term outcomes were better with CP Class A as compared to Classes B and C. Class C fared the worst [9].

CP Classification remains the best means for predicting mortality after cardiac surgery [3]. In the current literature, CP Classification is used most commonly. The numerical score associated with CP Classification is considered particularly helpful in stratifying the risk for cardiac surgery with CPB in patients with liver cirrhosis [4, 7].

Cirrhosis is not considered a risk factor in the STS score and EuroSCORE. EuroSCORE was not particularly useful in predicting the risk in patients with cirrhosis requiring cardiac surgery [9, 11]. However, a recent German study demonstrated a significant predictive power of EuroSCORE for 30 day mortality [12]. Simplified Acute Physiology Score (SAPS) III has been noted to have the best predictive value for long term outcomes [10].

Beyond the Scores

If carefully examined, most of these risk scores rely on the synthetic function of the liver measured by serum bilirubin, prothrombin time, and international normalized ratio (INR); the stigmata of advanced liver disease like presence of ascites and encephalopathy; and the markers of end organ dysfunction like serum creatinine. Any patient with a high CP or MELD score reflects the advanced liver dysfunction with the derangements of coagulation, renal function, and portal hypertension associated with ascites and splenomegaly. Blood tests to estimate hepatic functional reserve, like indocyanine green clearance and asialoscintigraphy may augment the evaluation of hepatic function; but, their use as a preoperative risk evaluation tool has not been well characterized [13, 14].

Thrombocytopenia associated with splenomegaly is also considered to be a significant predictor of risk in patients with cirrhosis undergoing cardiac surgery. Filsoufi et al. reported a statistically significant in-hospital mortality associated with a low preoperative platelet count [3]. Thielmann et al. similarly noted that preoperative thrombocytopenia is adversely associated with survival after cardiac surgery in patients with cirrhosis [3, 9].

A Cleveland Clinic study by Suman et al. further delineated the correlation of a higher CP and MELD scores to hepatic decompensation after cardiac surgery with CPB. For patients with a CP score >7, there is an association of hepatic decompensation and mortality with a 86% sensitivity and 92% specificity for predicting mortality in addition to a 66% sensitivity and 97% specificity for predicting hepatic decompensation. MELD score with a value of >13 offered a 71% sensitivity and 89% specificity for mortality. Hepatic decompensation under the receiver operative curve (ROC) for mortality was similar for both scores. The best values for predicting mortality and hepatic decompensation were determined to be >7 for CP and >13 for MELD score. These findings confirm the poor prognosis noted in patients with CP Classes B and C in other studies [7]. The individual parameters of serum bilirubin, albumin, and INR were not strongly associated with mortality. This Cleveland Clinic study concluded that the risk for postoperative mortality in patients with cirrhosis considered for cardiac surgery with CPB was assessed accurately by using the numerical CP score and a score >7 was associated with higher mortality [7].

Contemporary Outcomes

Short-Term Outcomes

The risk of complications is high in all CP Classes; but, some studies report a comparable or acceptable risk in propensity matched population in patients with a CP score <8 [4]. Klemperer et al. noted that 100% of patients with CP Class B and 25% of those with CP Class A had major complications [1]. Arif et al. noted longer intensive care unit stay, longer duration of invasive ventilation, tracheostomy, and demand for red blood cells, plasma, and platelets in patients with cirrhosis who did not survive 30 days after cardiac surgery [12]. In this group, renal failure, neurological complications, sepsis, and gastrointestinal complications were higher. The patients with liver cirrhosis stayed twice as long in the hospital as compared to their matched controls. Prolonged hospital stay was primarily due to hepatic decompensation and renal failure rather than the need for mechanical ventilation and pressor support requiring [4]. Length of stay was substantially higher for patients with cirrhosis versus those without cirrhosis (9 vs. 6 days). Similarly, patients with cirrhosis accrued up to 34% higher hospital charges [5].

Common postoperative complications include coagulopathy and thrombocytopenia, resulting in increased postoperative bleeding. An early complication after CPB is a lack of vascular tone. It is unclear why this happens; but, most of the patients with cirrhosis show very low systemic vascular resistance (SVR) requiring high-dose vasoactive agents to maintain systemic blood pressure.

A number of studies demonstrated the high risk associated with open heart surgery in patients with liver cirrhosis [1–12]. Overall in-hospital mortality is high among patients with liver cirrhosis. Various single institution studies have reported 17–31% in-hospital mortality (Arif et al.: 30-day mortality 26% [12]; Shaheen et al.: 17.2% [5]; Filsoufi et al.: 26% [3]; Klemperer et al.: 31% [1]). Most of these studies had a small number of patients precluding definitive conclusions being drawn. Definitive conclusions could not be drawn from these studies due to small sample sizes. However, one common theme emerges that CP Classes B and C have a very high risk of mortality and morbidity. Patients with CP Class C have up to a 100% mortality associated with open heart surgery [1–12]. Mortality rates of 0–20%, 18–50%, and 67–100% have been reported in patients with CP Classes A, B, and C, respectively [1–12].

Long-Term Outcomes

The overall 5-year survival rate is noted to be 19% for all CP Classes. Patients with CP Class C had a 0% 5-year survival, while patients with CP Class A had a 25% 5-year survival. In Arif et al.'s study, 1-year and 5-year survival rates of CP Class A patients were 70% and 26%, CP Class B patients 33% and 5%, and CP Class C patients 33% and 0%, respectively, suggesting a somewhat prohibitively high risk for elective cardiac surgery in CP Class C patients [12]. Another study shows excellent long-term survival for all CP Classes of 78.6% at 3 years and 70.2% at 5 years [8]. Their findings suggest that the survival after 3 years becomes similar to the survival in the general population undergoing cardiac surgery. In another study, long-term survival was 82.4% for CP Class A, 47.6% for CP Class B, and 33.3% for CP Class C patients [10].

Preoperative Evaluation for Cardiac Surgery in Patients with Cirrhosis

Typical stigmata of liver cirrhosis, such as bleeding esophageal varices and ascites, may result in a complicated postoperative course due to severe hepatic decompensation. A careful diagnostic evaluation by a hepatologist should be performed before the operation [8]. Patients with a CP score of <8 may safely undergo cardiac surgery with CPB [4]. This is consistent with documented lower mortality rates for patients with CP Classes A and B. The presence of ascites or hepatic encephalopathy is associated with nearly a fivefold increase in mortality [5].

Patients with CP Class B should be thoroughly evaluated prior to any surgery. According to the current data, surgery in patients with CP Class C is contraindicated because most studies report a 100% mortality. In rare cases, an off pump coronary artery bypass grafting (OPCAB) may be possible. In high-risk patients, a combined OLT and cardiac surgery are performed with success [8].

One may wonder if a TIPS is feasible and useful in patients with cirrhosis who are to undergo elective cardiac surgery and result in a decrease in the incidence of postoperative complications [15].

Patients with CP Class C have a prohibitively high risk of mortality and morbidity. Elective cardiac surgery should be avoided in these patients, if possible. Urgent operations, like aortic valve and mitral valve replacement for endocarditis, should be carefully considered. For patients requiring emergency operations, the risk of mortality may be the same regardless of having surgery or not. Emergency procedures, such as an open repair of ruptured type A or B aortic dissection, CABG for unstable angina with multivessel coronary artery disease, and placement of left ventricular assist devices for low cardiac output state, are contraindicated due to a 100% mortality. In CP Class C patients, OPCAB, TAVR, transcatheter mitral valve repair, transcatheter endovascular aortic repair (TEVAR), and high-risk percutaneous coronary interventions (PCI) should be considered favorably to open heart surgery with CPB [3, 16, 17]. The use of a transesophageal echocardiography probe may cause injury to preexisting esophageal varices. Thus, a preoperative esophagogastroscopy may be particularly necessary in case a TAVR is planned [18].

Intraoperative Considerations while Performing Cardiac Surgery in Patients with Cirrhosis

Longer mean operative time is associated with higher mortality [12]. An off pump approach for a CABG is associated with a lower risk of complications [3]. A longer cross clamp time is associated with adverse outcomes [9].

If CPB is used, a high pump flow specifically more than 2.4 L/min/m^2 with associated moderate hypothermia down to 28 °C is associated with less hepatic dysfunction. There are numerous factors that adversely affect the liver function during CPB including hypoxia, hemodilution with anemia, hypotension, and hypothermia. Additionally, hypercarbia and metabolic acidosis result in sympathetically mediated hepatic artery vasoconstriction with decreased blood flow in both hepatic artery and portal vein [19].

In a canine study, the total hepatic blood flow decreased by 50% during pulsatile flow at a perfusion pressure of 60 mmHg. Pulsatile blood flow is considered superior to nonpulsatile normothermic perfusion. A pump flow of 2.4 L/min/m^2 does not significantly impact hepatic blood flow (approximately a 20% decrease). This is consistent with the clinical observation of relatively lower complication rate with hypothermic, high flow CPB for routine cardiac surgery. The bottom line is hepatic blood flow is better maintained during CPB with high flows and hypothermic CPB [19].

It is important to realize that there is an increased in hepatic decompensation with the use of CPB. Probably, this occurs as a result of the inflammatory mediators released during CPB in combination with the compromised coagulation profile and related hepatic dysfunctions. This results in severe acidosis, loss of vasomotor tone, and coagulopathy. It is not the cardiac procedure itself; but, the presence or absence of the CPB that has a deleterious effect on the postoperative mortality and morbidity in patients with cirrhosis [3]. This is reflected in the outcomes associated with on pump CABG and AVR [3, 6, 9, 16].

Postoperative Considerations after Cardiac Surgery in Patients with Cirrhosis

Careful hemodynamic management is critical in the early postoperative phase. Prompt correction of metabolic acidosis, coagulopathy, and fluid balance are essential for a good outcome. Better long-term outcomes are associated with lower arterial lactate and good urine output in the first 24 hours [10].

Bleeding and Coagulopathy

High postoperative chest tube output due to bleeding is a common complication. The coagulation tests are abnormal and thrombocytopenia is universally present. Most patients require blood transfusions with red blood cells, fresh frozen plasma, platelets, and cryoprecipitate [5, 8, 11, 20]. Factor VII has been used in selected settings. In a center where cardiac surgery is performed on patients with liver cirrhosis, robust blood bank support should be available and utilized. It is important that the blood products are available on a short notice to prevent catastrophic complications. Long-term bleeding complications usually do not occur even under continuous therapy with platelet inhibitors [8].

Worsening of Hepatic Function after CPB

Incidence of significant hepatic dysfunction after CPB is about 3% in the general population [21]. Risk factors associated are New York Heart Association functional class, sex, type of operation performed, operative time, low cardiac output state, cardiac arrest, and blood transfusions. Patients with cirrhosis are particularly vulnerable to hepatic decompensation because of their limited hepatocyte reserve. The above mentioned risk factors can be mitigated to a certain degree by vigilant postoperative management. It is hard to completely eliminate all the risk factors but an attempt can be made for a positive outcome in patients with CP Class A [21].

Gastrointestinal Bleeding

Although not very common, gastrointestinal bleeding can be worrisome and sometimes even fatal in patients with cirrhosis undergoing cardiac surgery. The exact incidence of gastrointestinal bleeding after cardiac surgery is unknown. Yet, the preoperative presence of esophageal varices and portal hypertension with advanced cirrhosis may herald the gastrointestinal bleeding. In select patients, TIPS placement could decrease the incidence of postoperative gastrointestinal bleeding [15]; however, it is associated with shunt thrombosis, encephalopathy, and hemodynamic changes likely to increase cardiac output and systemic vascular resistance.

Coronary Artery Bypass Grafting (CABG)

Cirrhosis has a significant effect on mortality and morbidity in patients undergoing CABG. Gopaldas et al. reported increased mortality (adjusted odds ratio [AOR] 6.9, 95% confidence interval [CI]: 2.8–17), morbidity (AOR: 1.6, 95% CI: 1.3–2.0), length of stay (+1.2 days; $p < 0.001$), and hospital expenses (+$22,491; $p < 0.001$). In patients, who underwent OPCAB, mortality was only effected by severe liver dysfunction (mortality: AOR: 5.1, 95% CI 3.7–6.9; morbidity: AOR 2.1, 95% CI: 1.6–2.4). On pump patients had a higher mortality (4.6 fold) and morbidity regardless of the severity of cirrhosis. Authors concluded that a CABG should only be performed in carefully selected patients and preferably without the use of CPB [6]. Marui et al. from Japan reported a lower adjusted in-hospital mortality after OPCAB as compared with on pump CABG. Although the same study reported an adjusted overall mortality to be similar between the two groups of patients with hepatic cirrhosis. In this study, no optimal revascularization strategies for patients with liver cirrhosis were suggested and a need for a randomized controlled trial was emphasized [16]. Filsoufi et al. and Hayashida et al. reported a 0% mortality in patients with CP Class B who underwent OPCAB. This contrasts with the high mortality rate for on pump CABG for this same patient group. These studies suggest that OPCAB should be attempted in patients with CP Class B, when feasible [2, 3].

Whereas, in a large population based study, Shaheen et al. reported that OPCAB was not associated with decreased mortality. This is in contrast with the above conclusions. In this study, patients older than 60 years, presence of congestive heart failure, and being female were associated with increased in-hospital mortality after CABG in patients with liver cirrhosis. The presence of ascites and hepatic encephalopathy was associated with three times increase in mortality [5]. Ben Ari et al. reported a single case of a 60-year-old male with CP Class C, who survived an OPCAB [17]. The above mentioned studies point towards the utility of OPCAB in select patients with CP Classes B and C. Careful consideration of the overall clinical picture should be made by a hepatologist and a cardiac surgeon. Referral to a tertiary care center for a combined CABG and OLT should be considered for patients with CP Class C.

Aortic Valve Surgery

Surgical aortic valve replacement (SAVR) is uncommon in patients with cirrhosis due to high risk. Petress et al. reported seven patients with CP Class B and a median MELD score of 14 who underwent AVR using minimized extracorporeal perfusion circuits (MECC). Perioperative management included digestive decontamination, antioxidant supplements, and adjusted antibiotics. There was no mortality at 30, 60, and 90 days postoperatively with a median intensive care unit length of stay of 3 days. Only one patient required re-exploration for bleeding and another one suffered from temporary seizures. Authors concluded that the SAVR with vigilant postoperative management is feasible [22]. Nemati et al. reported a patient with CP score of 10 (Class B) who underwent a successful SAVR with a mechanical valve and then a subsequent liver transplant 2 months after the SAVR [23].

Due to the invasive nature of traditional cardiac surgery and the association of adverse outcomes with CPB in patients with liver cirrhosis, TAVR is an appealing alternative. Shah et al. reported a study of TAVR being performed in 17 patients with chronic liver disease (11 CP Class A and 6 CP Class B). TAVR was performed successfully in these patients with in-hospital mortality of 5.88% and a 90 day mortality of 17.65%. The authors concluded that TAVR is a feasible method for treating aortic stenosis in patients with chronic liver disease. The procedure associated risk is low in patients with CP Classes A and B. Patients in CP Class C warrant further study to assess the feasibility of TAVR [18].

Greason et al. reported a complication rate of 33% after TAVR as compared to 67% with SAVR. No mortality was noted in the TAVR group, while 17% of patient died in SAVR group. The authors concluded that in patients with liver cirrhosis TAVR may be a viable alternative to SAVR [24].

Simultaneous Liver Transplant and Elective Cardiac Surgery

Due to the high mortality associated with CP Classes B and C, most cardiac surgeons are reluctant to offer elective procedures to these patients. A viable option is to perform these procedures in tandem with OLT. In a Cleveland Clinic study, Lima et al. reported the outcomes of 10 patients with preserved left ventricular function (7 in CP Class B and 3 in CP Class C) who underwent elective cardiac procedures in combination with OLT. In-hospital mortality was 20% and actuarial survival was

70% at 3 years. Mean postoperative length of stay was 23 ± 8 days. Both in-hospital deaths had a CP Class C and underwent SAVR. The addition of a cardiac surgical procedure to OLT did not have a long-term effect on survival (70% actuarial survival at 3 years). The authors concluded that the elimination of hepatic dysfunction as a postoperative issue improves outcomes, especially in patients with CP Class B. Patients with CP Class C did not receive any additional survival benefit from a cardiac procedure in conjunction with an OLT [25].

Conclusion

Liver cirrhosis poses a challenging problem in patients requiring cardiac surgery. Patients with CP Class A have acceptable outcomes after open heart surgery regardless of the usage of CPB. Advanced cirrhosis with CP Classes B and C and higher MELD scores are associated with higher mortality and morbidity. Techniques that obviate the need for CPB, such as OPCAB and TAVR, may provide favorable outcomes in this high-risk patient population. Further, combined cardiac procedures and OLT may be the optimal treatment for patients with advanced cirrhosis.

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