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Case Report

Off-pump coronary artery bypass grafting in a patient with Child class C liver cirrhosis awaiting liver transplantation

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We report the case of a Child class C cirrhotic patient who was diagnosed with coronary artery disease in the course of his pretransplantation evaluation. He underwent off-pump coronary artery bypass grafting (OPCAB), which was complicated with acute renal failure. The morbidity and mortality associated with cardiac operation in patients with cirrhosis is discussed, and the potential advantage of OPCAB in this patient population is emphasized.

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The morbidity and mortality associated with liver transplantation is significantly increased in patients with coronary artery disease (CAD).[1] Therefore, the presence of severe CAD has traditionally been considered an absolute contraindication to liver transplantation.[2] For this reason, a revascularization procedure is needed for patients undergoing liver transplantation in whom significant CAD exists. However, previous studies reported that in the presence of cirrhosis, cardiac surgery with the use of cardiopulmonary bypass carries a very high risk of morbidity (in Child class A, B and C) and mortality (in Child class B and C),[3–11] and hence it was recommended that patients with advanced liver cirrhosis not be offered cardiac surgery.[11] Recent attempts to solve this problem involved combined sequential cardiac surgery and liver transplantation.[12 13] With the improvements in surgical and anaesthetic techniques, and specifically with the advent of off-pump coronary artery bypass grafting (OPCAB), it was suggested that the risk may be lowered.[3–6 8] The literature discussing cirrhotic patients undergoing OPCAB is scarce and includes a handful of Child class A and B patients. This is the first report to describe the outcome of a patient with Child class C liver cirrhosis who underwent OPCAB procedure before liver transplantation.

Case history

A 60-yr-old Caucasian male was diagnosed with non-alcoholic steatohepatitis (NASH) cirrhosis. In the year earlier to his admission he developed severe hepatic decompensation, manifested by progressive fatigue, tense ascites, and several episodes of hepatic encephalopathy and spontaneous bacterial peritonitis. In addition, he had progressive hepatic synthetic dysfunction, with an international normalized ratio (INR) of 2.26, serum albumin of 27 g litre^{-1} and serum ammonia of 90 μmol litre^{-1}. The patient's clinical and laboratory deterioration persisted despite treatment with high dose spironolactone, furosamide and propranolol. He was classified as suffering from Child class C cirrhosis, and was offered liver transplantation.

During the patient's pretransplantation evaluation he reported new onset dyspnoea and chest pain on mild exertion. Ischaemic risk factors included non-insulin-dependent diabetes mellitus, morbid obesity (body mass index of 41) and essential hypertension. SPECT-Dipyridamole scan revealed ischaemia of the apex, inferobasal and basal septal walls. On cardiac catheterization a 95% stenosis of left main artery and 70% stenosis of first marginal coronary artery were documented. Echocardiography revealed normal sized left ventricle with good function. The patient's advanced cirrhotic complications and background illnesses made him a poor candidate for coronary artery bypass grafting, while his coronary anatomy was unsuitable for percutaneous revascularization. After extensive interdisciplinary consultation he was offered OPCAB surgery.

During the two preoperative days, and during the first two postoperative days, the patient received i.v. albumin (40 mg kg^{-1} three times daily). There was no attempt to correct coagulopathy preoperatively, as INR was only mildly elevated the day before operation (Table 1). General anaesthesia was induced with fentanyl, midazolam and vecuronium, and after tracheal intubation, maintained

Table 1 Perioperative laboratory results. OPCAB, off-pump coronary artery bypass; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio

Parameter (normal range)	PreOPCAB	PostOPCAB	Postoperative day 2	Postoperative day 7
Gamma-GT (10–80) u litre^{-1}	108	57	76	84
Alkaline phosphatase (40–130) u litre^{-1}	161	64	72	118
AST (2–60) u litre^{-1}	62	43	41	39
ALT (6–53) u litre^{-1}	27	16	16	11
Bilirubin (0–17) μmol litre^{-1}	41	67	82	66
INR (0.9–1.4)	1.65	1.93	1.74	1.77
Serum albumin (3.5–5) g dl^{-1}	2.9	2.5	2.8	3.2
Creatinine (60–120) μmol litre^{-1}	87	71	110	304
Thrombocytes (140–400×1000 ml^{-1})	163	121	122	181

with continuous infusion of remifentanil and midazolam. Additional remifentanil and vecuronium were administered as appropriate and a bolus of morphine was administered at the end of the operation. Minute ventilation was titrated to maintain normocarbia. Intraoperative monitoring included, in addition to the standard monitors, intra-arterial (via radial artery catheter) and central venous (via an internal jugular catheter) pressure monitoring, and electrocardiogram (ECG; 5-lead) with continuous ST-segment trends. The use of aprotinin was seriously discussed preoperatively; however, a decision was made not to administer it because of Mangano and colleagues'[14] recent study showing that aprotinin administered during CABG increases the risk of developing renal failure, stroke encephalopathy, myocardial infarct and heart failure. Moreover, recent reports have raised concerns about the existence of a relative hypercoagulable or prothrombotic state after OPCAB and its possible consequences on graft patency.[15 16]

After midline sternotomy the left thoracic artery and left saphenous vein were harvested. After a dose of 1.5 mg kg^{-1} heparin OPCAB was performed. The left internal thoracic artery was anastomosed to the left anterior descending artery and the vein was anastomosed to the first diagonal and than to the aorta with good flow. Reversal of heparin was than carried out with protamin (1 mg kg^{-1}). The patient was haemodynamically stable throughout the operation. Total surgery time was 2 h and 35 min and total blood loss was approximately 250 ml.

In the intensive care unit the patient was extubated within 8 h. Pain was treated with morphine (2 mg h^{-1}). Chest drains were removed on the second postoperative day. Twenty-four hours after surgery the patient developed oliguric renal failure, which was treated aggressively with fluids and diuretics. The serum creatinine concentration increased from a baseline of 87 μmol litre^{-1} to a maximum of 304 μmol litre^{-1} on the 7th postoperative day (Table 1) and decreased gradually thereafter (discharge creatinine concentration of 154 μmol litre^{-1}). There was no excessive bleeding and no new abnormality in liver function (Table 1). The patient was discharged from the intensive care unit on the 10th postoperative day and from the hospital after 14 days of hospitalization.

Table 2 In-hospital morbidity and mortality of patients with liver cirrhosis undergoing CABG or OPCAB surgery. CABG, coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass; *n*, number of patients; NA, not available

Classification	Morbidity, % (number of patients)	Mortality, % (number of patients)
CABG surgery		
Child class A		
n=11[3]	45 (5)	8 (1)
n=10[4]	40 (4)	0
n=2[6]	100 (2)	0
n=3[7]	NA	0
n=31[9]	10 (3)	3 (1)
n=10[10]	50 (5)	0
n=8[11]	25 (2)	0
Child class B		
n=4[3]	75 (3)	0
n=4[4]	100 (4)	50 (2)
n=6[6]	100 (6)	50 (3)
n=12[9]	66 (8)	44 (5)
n=2[10]	100 (2)	50 (1)
n=5[11]	100 (5)	80 (4)
Child class C		
n=1[3]	100 (1)	0
n=1[4]		100 (1)
n=1[9]		100 (1)
OPCAB surgery		
Child class A		
n=2[3]	0	0
n=2[6]	0	0
n=1[5]	0	0
Child class B		
n=3[4]	33 (1)	0
n=1[8]	0	0

Discussion

Published data report very high perioperative mortality (50%) and morbidity (80%) for patients with CAD undergoing liver transplantation.[1] For this reason, identifying CAD in patients undergoing liver transplantation is crucial. Morbidity and mortality rates after cardiac operation with cardiopulmonary bypass in patients with cirrhosis are high (Table 2). Major morbidity has been reported to be 10–100%, 66–100% and 100% for Child class A, B and C, respectively, mostly attributable to cirrhotic complications rather than impaired cardiac function. Mortality has been reported to average 3% (2 out of 75 patients), 45%

(15 out of 33 patients) and 66% (2 out of 3 patients) for Child class A, B and C, respectively.[3–11] None of the reported patients died postoperatively as a result of cardiac failure. Major perioperative complications include infections (mainly mediastinitis, sternal wound infection and sepsis), renal failure, bleeding (gastrointestinal bleeding, cardiac tamponade, mediastinal bleeding as suggested by increased haemorrhagic chest tube output), fluid retention (including ascites, pleural and pericardial effusion) and hepatic decompensation. Possible pathophysiological features of cirrhosis that contribute to the development of the above-mentioned complications have been recently reviewed.[17] Cirrhotic patients have decreased reticuloendothelial function and impaired immune function. This, in addition to poor nutritional status, increase their susceptibility to infections which are much more prevalent in the cirrhotic patient undergoing operation, and are the leading cause of death in this patient population. Cirrhosis is also associated with coagulopathy that results from decreased synthesis of coagulation factors, splenic sequestration of platelets with thrombocytopenia and fibrinolysis because of low concentration of antiplasmin and inadequate clearance of tissue plasminogen activator. A decrease in hepatic blood flow observed during anaesthesia and surgery causes further liver damage with deterioration of liver function. The pulmonary complications associated with liver diseases which include restrictive lung disease, hepatopulmonary syndrome, intrapulmonary shunts, ventilation-perfusion abnormalities and pulmonary hypertension further increase the risk of surgery. Fluid balance is significantly impaired in the cirrhotic patient. Together with renal failure, which is prevalent in this group of patients, the development or worsening of fluid retention (in the form of ascites and pleural effusion), and electrolyte and acid–base abnormalities, may expose the patient to rhythm disturbances, aspiration, sepsis and haemodynamic instability. These complications translate into increased transfusion requirements, long-period dependency on mechanical ventilation, need for re-exploration and prolonged postoperative intensive care unit and hospital stay. Because of this very high morbidity and mortality, it is generally agreed that elective cardiac operations using cardiopulmonary bypass are contraindicated in patients with moderate to severe cirrhosis.[2]

The pathogenesis of adverse outcome after the use of cardiopulmonary bypass is complex and multifactorial and includes non-pulsatile flow, haemodilution, haemolysis, activation of the inflammatory cascade, anticoagulation, hypothermia and reduced end-organ perfusion.[18] Consequently, coagulation, vascular permeability, fluid balance and organ function may be affected. Thus, avoidance of cardiopulmonary bypass use in cirrhotic patients may theoretically lower the risk of perioperative morbidity, and indeed performing coronary revascularization on a beating heart was reserved for a subset of patients who were at a higher risk to develop complications. In a recent study, on-pump coronary artery bypass grafting (CABG) was associated with more chest drainage, blood and blood products transfusion and longer duration of dopamine infusion compared with OPCAB surgery.[19] Current best available evidence from randomized control trials suggests that OPCAB reduces bleeding and need of allogeneic transfusion.[20] This is perhaps because of less disturbed equilibrium between procoagulant and anticoagulant activity in patients operated with OPCAB technique. Neurocognitive function was also better preserved in OPCAB compared with CABG patients both immediately postoperatively and at 6 months after the operation.[19 21] These authors suggested that the observed reduced cerebral perfusion during the operation and the higher incidence of microembolization in CABG patients play a role in the development of cognitive dysfunction. The effect of OPCAB on postoperative renal function is controversial with studies suggesting that OPCAB has no beneficial effect[22] *vs* exerts protective effect[23] on adverse renal outcome when compared with CABG. Regarding pulmonary function, prospective trials comparing pulmonary complications between OPCAB and CABG patients reported shorter time to extubation with OPCAB; however, no significant differences between the groups was found in the incidence of pleural effusion, pneumonia, need for reintubation and mortality because of pulmonary causes.[24 25] Although Cleveland and colleagues[26] reported that OPCAB decreases risk-adjusted mortality and morbidity, two meta-analysis found lack of substantial evidence to support the notion that OPCAB has better clinical outcome than standard cardiopulmonary bypass.[27 28] Significant advantage for OPCAB was reported only for the prevention of atrial fibrillation. Yet, only a trend towards an advantage in terms of short term morbidity and mortality for OPCAB *vs* CPB was found.

Only nine cases of cirrhotic patients undergoing OPCAB surgery, all of whom were suffering Child A and B cirrhosis, have been previously described (Table 2). The data from these reports suggest that OPCAB surgery may be associated with lower morbidity and mortality compared with on-pump surgery.[3–6 8] In Child class A and B patients, the reported morbidity was 0% (0 out of 5 patients) and 25% (1 out of 4 patients), respectively, and none of the patients died. Our report is the first to describe the outcome of OPCAB surgery in a patient with Child class C cirrhosis. Similar to the one morbidity reported in a Child class B patient undergoing OPCAB surgery,[4] the patient in the current report developed postoperative renal failure. Acute renal failure is one of the most common complications after cardiac surgery in cirrhotic patients.[4 9 11] Moreover, our patient had diabetes mellitus and hypertension, both of which have been demonstrated to be independent predictors of renal adverse outcome in patients undergoing cardiac surgery.[29] In the presented patient, acute renal failure although necessitating a prolonged intensive care unit stay, ultimately resolved after aggressive fluid and diuretic treatment. Treatment of hepatorenal syndrome with terlipressin has been reported to improve renal function in patients with cirrhosis.[30] This is particularly important in light of the fact that an association between improved renal function and survival was suggested.[31] In our patient, the use of terlipressin was seriously weighted because of the deteriorating renal function, but eventually the patient responded to fluid and diuretic therapy, obviating the need for terlipressin.

In the present case albumin was administered during the perioperative period. Recent meta-analysis of trials (71 trials, 44 of which involved surgical patients) that evaluated albumin administration to acutely ill patients found that albumin significantly lowered morbidity in patients suffering from ascites.[32] In a systematic review, Haynes and colleagues[33] showed that patients receiving albumin in cardiac surgery developed less pulmonary oedema, and required less fluids. In patients with ascites, albumin prevented haemodynamic derangements, shortened hospital stay, lowered morbidity and improved survival after spontaneous bacterial peritonitis.

In summary, the relatively favourable outcome of our patient may suggest that OPCAB surgery may be feasible in selective patients with Child C cirrhosis diagnosed with CAD. Further studies are needed to evaluate the perioperative use of albumin in this group of patients.

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