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Cardiac Operations for Patients with Chronic Liver Disease

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ABSTRACT

Background: Due to the systemic and hepatic effects of cardiopulmonary bypass (CPB), open-heart surgery for patients with chronic liver disease is associated with high mortality and morbidity. In this retrospective study, we present our results of cardiac surgery on patients with non-cardiac cirrhosis.

Methods: Between March 1996 and April 2000, 10 patients with chronic liver disease had open-heart surgery in our institution. Six patients were male and four were female, with a mean age of 57.1 ± 6.85 years. Preoperative severity of liver disease was determined according to Child classification. Four cases (40%) were Child class A and six (60%) were class B. Coronary artery bypass grafting was performed in four cases, and the remaining six operations were for aortic valve replacement (AVR) and/or mitral valve replacement (MVR). Eight of the operations (80%) were performed by using cardiopulmonary bypass and two (20%) were performed as beating heart surgery.

Results: Chest tube drainage and transfusion needs of these patients were three times the average normal values. Three of the patients for whom CPB was used, all of them in Child class B, died. None of the patients in Child class A died. This resulted in an overall mortality rate of 30%, with mortality of 50% for the Child B group. There was no mortality for any patient who underwent cardiac surgery on the beating heart or cardiac surgery of short duration on CPB. Common characteristics of cases that were associated with high morbidity and mortality included increased postoperative hemorrhagic chest tube output, dependency on mechanical ventilation, hepatic and renal failure, gastrointestinal bleeding, and sepsis. None of the patients died of cardiac failure.

Conclusions: Our findings indicate that cardiac operations may be performed with good results for patients suffering from liver disease of mild severity (Child A), but cardiac interventions that include CPB in conjunction with advanced hepatic pathologies are associated with high mortality and morbidity. Cardiac surgery (whether valvular or coronary artery surgery) for patients with chronic liver disease should be carried out with a short duration of CPB or should be done on the beating heart, if possible, in the case of coronary artery surgery.

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INTRODUCTION

The use of cardiopulmonary bypass (CPB) in open-heart operations has systemic effects and particular effects on the liver. Mortality and morbidity (postoperative bleeding, extended duration of endotracheal intubation, difficulty in awakening, hepatorenal syndrome, infection) of elective cardiac surgery is increased for patients with abnormal preoperative liver function tests and with chronic liver disease. These cases necessitate a thorough preoperative preparation, an adequate perioperative management, and postoperative care that is well-organized and sufficient for management of possible complications [Bizouarn 1999, Hirata 1999].

In this article we present the results of our open-heart operations on patients with chronic liver disease and cardiac pathology, and compare these results with the current literature.

MATERIALS AND METHODS

Between March 1996 and April 2000, 10 patients with abnormal liver function tests or chronic liver disease underwent cardiac surgery at our institution. Six of the patients were male and four were female, with an average age of 57.1 ± 6.85 years. In terms of liver pathology, according to Child classification (Table 1, ◎), four (40%) of the patients were Child class A and six (60%) were Child class B. Liver pathology was due to alcohol in five cases (50%), hepatitis in four (40%), and primary biliary cirrhosis in one. Preoperatively, thrombocytopenia was found in six patients (60%). Data on patients are summarized in Table 2 (◎) and Table 3 (◎).

Diagnosis of cirrhosis was established with biopsy in two cases, and in eight cases diagnosis was established clinically according to the presence of the following indications and pathologies: findings related to portal hypertension (esophageal varices, gastric lesions), thrombocytopenia, congestive splenomegaly, ascites, presence of etiologic factor, and nonspecific biochemical abnormalities (hyperbilirubinemia, elevated serum transaminases).

Intraoperative heparinization was done so that activated clotting time (ACT) was 400 seconds. A membrane oxygenator was used and mild hypothermia was applied (for coronary

Table 1. Child Classification

	Class A	Class B	Class C
Bilirubin (mg/dl)	< 2.0	2-3	> 3
Albumin (g/dl)	> 3.5	3-3.5	< 3
Ascites	—	Readily controllable	Uncontrollable
Encephalopathy	—	Mild	Advanced
Nutritional Status	Excellent	Good	Poor
Surgical Risk	Favorable (mortality < 10%)	Moderate (mortality approximately 30%)	Poor (mortality > 40)

artery surgery 32°C and for valvular surgery 28°C). Mean pump flow was 3.0 l/min./m^2. Hematocrit was kept level at 25% during CPB. Fresh whole blood, erythrocyte, fresh frozen plasma and, when necessary, platelet transfusions were administered.

The primary cardiac pathology was coronary artery disease in four patients (40%) and aortic and/or mitral valve disease in six patients (60%). Surgical interventions performed were coronary artery bypass grafting (CABG) in four cases and aortic (AVR) and/or mitral valve replacement (MVR) in three cases. The valve replacements consisted of MVR in two cases and AVR + MVR in one case. In two patients (20%) with coronary artery disease, CABG was performed on the beating heart due to the presence of abnormalities in liver function tests (Table 4, ◎).

Statistical Analysis

Statistical calculations were performed by using SPSS® version 10.0 (SPSS Inc., Chicago, IL). Data are expressed as means ± standard deviations. Fisher's exact test was used in statistical evaluation of data. A p value of less than 0.05 was considered significant.

RESULTS

Mean durations of cross-clamping (CC) and cardiopulmonary bypass (CPB) were 51 ± 14.27 min. and 93 ± 33.10 min., respectively. Postoperative bleeding and requirements for blood and blood products were three times the standard amounts. Average chest tube output within the first 24 hours was 1300 ± 80 ml in Child A group, whereas this value was 1650 ± 150 ml in Child B group. Average 3 ± 1.2 U fresh whole blood, 3 ± 1.4 U erythrocyte, 2 ± 0.9 U platelet, and 4 ± 1.4 U fresh frozen plasma transfusions were administered due to bleeding. Transfusion requirements in Child B group were significantly higher than in Child A group. Aprotinin (kallikrein inhibitor) was administered to six patients who had thrombocytopenia and/or a likelihood of coagulation problems (2 million U infusion following induction of anesthesia and addition of 2 million U into the priming solution). Revision due to bleeding was required in one of four patients in Child A group and in two of six patients in Child B group, but this difference was not statistically significant (Fisher's exact test, $p > 0.05$).

The following categories of complications were observed postoperatively: hemorrhagic (high output from chest tubes), neurologic (stroke, tonic-clonic convulsions, encephalopathy), pulmonary (dependency on ventilation, pneumonia), infectious (sternal wound infection, sepsis), gastrointestinal (bleeding), and renal (renal failure, requirement for dialysis).

Overall mean durations of intensive care unit (ICU) stay and hospitalization were 5.1 ± 4.06 days and 10.5 ± 7.83 days, respectively. Those values were 3.25 ± 0.95 days and 9.5 ± 1.29 days for Child A group and 6.33 ± 4.96 days and 11.16 ± 10.43 days for Child B group. There was no mortality in Child A group, but three of the patients (50%) in Child B

Table 2. Preoperative Characteristics of Patients

Patients	Age	Gender	Liver Pathology (Child class)	Etiology	Thrombocytopenia	Cardiac Disease
1	60	Female	Child B	Primary biliary cirrhosis	Present	AS+MS+MI
2	68	Male	Child B	Hepatitis	Present	CAD+PAD
3	59	Male	Child B	Alcohol	Present	AS+AI+MS+MI
4	56	Female	Child A	Hepatitis	—	CAD
5	48	Male	Child B	Alcohol	Present	AS+AI
6	66	Male	Child B	Hepatitis	Present	MS+MI+TI
7	52	Female	Child A	Alcohol	—	CAD
8	51	Female	Child A	Alcohol	—	CAD
9	50	Male	Child B	Hepatitis	—	MS+MI+TI
10	61	Male	Child A	Alcohol	Present	AI

AI = aortic insufficiency, AS = aortic stenosis, CAD = coronary artery disease, MI = mitral insufficiency, MS = mitral stenosis, PAD = peripheral arterial disease, TI = tricuspid insufficiency.

Table 3. Preoperative Liver Function Tests

Patients	Bilirubin (mg/dL)	Albumin (g/L)	Ascites	Encephalopathy	Finding related to portal hypertension
1: Child B	2.8	3.0	+	–	Esophageal varices
2: Child B	2.9	3.1	+	–	Esophageal varices, Gastritis
3: Child B	2.6	3.1	+	–	Esophageal varices
4: Child A	1.7	3.6	–	–	–
5: Child B	2.8	3.3	+	–	Gastritis
6: Child B	2.2	2.8	+	–	Gastritis
7: Child A	1.8	3.7	–	–	Gastritis
8: Child A	1.9	3.6	–	–	–
9: Child B	1.6	3.4	+	–	Gastritis
10: Child A	1.5	3.8	–	–	–

group died. Causes of mortality were hepatorenal syndrome, respiratory failure, renal failure, sepsis, gastrointestinal bleeding, and hepatic encephalopathy. Mean duration of follow-up for surviving patients was 30.85 ± 12.21 months. During long-term follow-up there was no mortality, but two patients exhibited jaundice with ascites, and two patients were observed to have jaundice without ascites and ascites without jaundice, respectively. Patients are still under follow-up.

DISCUSSION

Most surgical interventions performed under general anesthesia affect liver functions. Anesthetic agents decrease liver blood flow and oxygen utilization. In addition, CPB has some effects on the liver. Heparin prevents coagulation within the perfusion system, but it does not inhibit consumption and surface activation of coagulation factors. Hemodilution decreases the level of all coagulation proteins. A decrease in the number of platelets and loss of platelet function increases postoperative bleeding time. Although CPB does not change total renal blood flow, it decreases the blood flow to the outer renal cortex. In patients with hepatorenal syndrome, due to the decrease in prostaglandins, which are renal vasodilators, there is a significant decrease in renal cortical flow and urinary output [Mathie 1993].

Risk factors in liver diseases are determined according to Child classification (Table 1, ◉). In Child class A, there is no limitation of liver function that would inhibit an operation, and regeneration capability is normal. In class B, there are certain limitations of liver functions and there is a variable response in all operations. Although regeneration capability of the liver is limited in class B, a good tolerance is observed following a thorough preoperative preparation. There are advanced limitations of liver functions in class C. The regeneration capability of the liver is either minimal or absent. Outcomes of operations for this class are unfavorable regardless of the adequacy of preoperative preparation [Ota 1996, Klemperer 1998, Bizouarn 1999].

Table 4. Surgical Operations and Postoperative Course

Patient	Operation	Complications	CC-CPB Time (min.)	ICU Stay (days)	Hospital Stay (days)	Result
1: Child B	AVR+MVR/CPB	High chest tube output, revision due to hemorrhage, further hepatic dysfunction, hepatorenal syndrome, extended intubation, GIS bleeding	82-164	6	6	Exitus
2: Child B	CABGx3/CPB	High chest tube output,extended intubation, GIS bleeding, sepsis	54-90	4	4	Exitus
3: Child B	AVR/CPB	Elevation of serum transaminases	45-78	6	6	Alive
4: Child A	CABGx2/Beating Heart	Hepatic dysfunction, extended intubation	–	4	10	Alive
5: Child B	AVR/CPB	Extended intubation, GIS bleeding, sepsis	52-120	16	32	Exitus
6: Child B	MVR+Tricuspid De Vega/CPB	High chest tube output, revision due to hemorrhage	47-78	4	10	Alive
7: Child A	CABGx3/CPB	Pleural effusion	38-75	3	9	Alive
8: Child A	CABGx1/Beating Heart	High chest tube output, revision due to hemorrhage	–	4	11	Alive
9: Child B	MVR+TricuspidDe Vega/CPB	Extended intubation	54-72	2	9	Alive
10: Child A	AVR/CPB	Elevation of serum transaminases	36-67	2	8	Alive

AVR = aortic valve replacement, CABG = coronary artery bypass graft, CC = cross-clamping, CPB = cardiopulmonary bypass, GIS = gastrointestinal system, ICU = intensive care unit, MVR = mitral valve replacement.

Preoperative evaluation and preparation are important for the success of the operation. Nutritional status should be corrected with preoperative alimentation. For the caloric requirements of the patient, branched-chain amino acids and low concentration aromatic amino acids may be given instead of proteins because of potential hepatic encephalopathy. Caloric supplementation with fat is restricted due to decreased bile salt excretion and impaired lipid absorption. Medium-chain triglycerides, which do not need bile salts for absorption, may be used. Lipid soluble vitamins A, D, and E are also necessary, in addition to vitamin K. Due to the possibility of hepatic encephalopathy, necessary precautions for esophageal varices and ulcer bleeding should be taken. Prophylactic endoscopic sclerosis may be performed for gastroesophageal varices, and antihypertensive treatment is also important. Daily protein intake of the diet should be lowered (20-30 g/day) and a lactulose enema should be administered. Lactulose converts intestinal ammonia to an ammonium ion, which is not absorbed. Close monitoring of glucose levels and infusion of glucose solutions are of vital importance in patients with fulminant hepatic failure and end stage cirrhosis [Friedman 1987, Ota 1996].

It is difficult to predict the response of a patient with chronic liver disease to the stress of anesthesia and surgery. Although anesthetic agents are not directly hepatotoxic, they decrease liver blood flow and oxygen intake. Halothane, enflurane, and isoflurane lead to systemic vasodilatation and decrease in cardiac output. Isoflurane is preferred in liver disease patients, as it is the least metabolized volatile anesthetic agent in the liver [Friedman 1987].

Hypoalbuminemia is a feature of liver diseases. Binding to albumin and biliary excretion is decreased in hypoalbuminemia. Sedatives like diazepam, narcotics like meperidine, and induction agents like phenobarbital may result in extended depression of consciousness and acceleration of hepatic encephalopathy. However, narcotics like fentanyl, which has been shown in studies to have unaltered pharmacokinetics in liver disease, and hypnotic agents like low-dose propofol that lose their effect by redistribution, are appropriate for use. Resistance to curare-like muscle relaxants due to low levels of pseudocholinesterase has been reported; therefore atracurium, which is not metabolized in the liver, should be preferred [Friedman 1987, Maze 1994].

Transfusions of coagulation factors, fresh frozen plasma, whole blood, and platelets are important in the management of postoperative hepatocellular dysfunction. Plasma is effective in returning prothrombin time to normal levels. In addition, there is published data suggesting that desmopressin shortens bleeding time in cirrhosis patients. [Friedman 1987, Ota 1996, Yaku 2000].

Diuretic use, paracentesis, and a low protein and carbohydrate diet with restricted sodium are recommended for patients with ascites. Because patients with ascites are very sensitive to potassium decreases, potassium-sparing aldosterone antagonist diuretics like spironolactone (if necessary in combination with a potent loop diuretic like furosemide) should be used. In order to avoid excessive salt intake, albumin with low salt, fresh frozen plasma, and glucose solutions are recommended for preoperative volume replacement. Water restriction is required for hyponatremia, and potassium, phosphate, and magnesium deficits should be corrected. [Friedman 1987, Yaku 2000].

The postoperative complication rate is increased for patients with abnormal liver functions and for patients with chronic liver disease [Hirata 1997, Yaku 2000]. We observed the following categories of complications postoperatively: hepatic, hemorrhagic (due to thrombocytopenia, thrombocyte dysfunction, decreased hepatic synthesis of coagulation factors, and fibrinolysis), infectious, respiratory, renal, and gastrointestinal.

Bizouarn and colleagues reported that, following elective cardiac operations performed on patients with mild to moderate cirrhosis, the rate of postoperative complications was increased and durations of ICU stay and hospitalization were extended [Bizouarn 1999].

In order to improve preoperative status and to decrease postoperative complications in these patients, assurance of good nutritional status (particularly when infectious complications are concerned) is important. Good nutritional status also provides hemostatic stability. Hirata and colleagues reported that preoperative serum transaminase and hematocrit levels, as well as good nutritional status, were of significant importance in terms of postoperative prognosis [Hirata 1997].

In our study we observed gastrointestinal hemorrhage in three patients due to preoperative esophageal varices, postoperative extended duration of intubation, and coagulation problems. Hemorrhagic drainage through chest tubes was high in four patients, and three of these required surgical revision. For postoperative bleeding we administered aprotinin (perioperatively and postoperatively), fresh frozen plasma, fresh whole blood, erythrocytes, and platelets. Administration of fresh frozen plasma is important in instances of hepatocellular dysfunction and coagulopathy, as it is effective in returning prothrombin time to normal. However, reports have suggested that administration of aprotinin, fresh frozen plasma, and platelets may have a decreasing effect over time [Bizouarn 1999, Yaku 2000].

Hepatorenal syndrome is often seen in the terminal stage of patients with decompensated cirrhosis. Hepatorenal syndrome is characterized by azotemia, oliguria, hyponatremia and hypotension that is unresponsive to volume replacement. Shunting of portal venous blood to the systemic circulation in hepatocellular dysfunction and entrance of toxic agents rescued from hepatic detoxification (e.g., ammonia) into the central nervous system play a role in the pathogenesis of hepatorenal syndrome. Factors that precipitate hepatic encephalopathy are gastrointestinal hemorrhage, constipation, azotemia, hypokalemic alkalosis, sepsis, hypoxia, and administration of drugs that inhibit central nervous system function [Mathie 1993, Ota 1996].

In patients with cirrhosis, low partial arterial oxygen pressure (PaO_2) due to intrapulmonary shunts is as significant as the other characteristic signs of liver disease, such as ascites, splenomegaly, and distal clubbing. Seventy percent of total cardiac output may be shunted [Mathie 1993]. All these factors lead to a troublesome postoperative course for these patients. We observed oxygenation problems and extended intubation in five of our cases (50%) postoperatively.

Postoperative jaundice may be caused by preoperative high right-atrial pressure, hypoxia during the operation, early postoperative hypotension, perioperative transfusions, and hemolysis [Mathie 1993]. We found that a bilirubin level above 2.8 mg/dl was associated with a higher mortality ($p < 0.05$). In addition, hepatic microemboli and variations in hepatic blood flow during CPB also affect liver functions [Mathie 1993, Klemperer 1998]. High flow rate during CPB, hypothermia, and pulsatile flow are found to be helpful in protecting the liver, but low perfusion pressure and hypoxia during CPB increase hepatic damage [Mathie 1993, Toyoda 1996].

Chronic liver disease patients cannot well tolerate the inflammatory reaction caused by extracorporeal circulation because of their poor general health status and the presence of a severe liver pathology. Therefore, in cardiac surgical interventions for patients with chronic liver disease, the duration of extracorporeal circulation should be as short as possible. If CABG is to be performed, surgical intervention on the beating heart should be preferred when appropriate so that the patient will be protected from the unfavorable effects of cardiopulmonary bypass.

Gaudino and colleagues performed CABG on eight patients with concomitant noncardiac disease and reported that they had operated on two patients with hepatic cirrhosis without using CPB. Both of the cirrhosis patients had angina pectoris, one stable and the other unstable, and neither had postoperative problems [Gaudino 1997]. On the other hand, Klemperer and colleagues reported that one of six liver cirrhosis patients on whom they performed CABG with CPB died during the postoperative period due to renal and pulmonary complications [Klemperer 1998]. Sakakibara and colleagues reported a successful redo CABG operation on the beating heart via thoracotomy in a coronary artery disease patient [Sakakibara 1998].

For our patients, we used the beating-heart method for two of four coronary artery disease patients with chronic liver disease. For the other two patients, who were operated upon with CPB, the durations of CC and CPB were 54-90 min. and 38-75 min., respectively. The patient with the longer CC and CPB durations had high chest tube output, extended duration of intubation, gastrointestinal system bleeding, and sepsis. This patient died postoperatively. The postoperative phase was less problematic for the two patients who were operated upon with the beating-heart method. In one of these patients, liver enzymes increased early in the postoperative period. The other patient experienced pleural effusion postoperatively. Both recovered and were discharged from the hospital without further problems.

Uchida and colleagues reported a re-replacement of a tricuspid valve in a liver cirrhosis patient by means of the right heart bypass technique. The apparatus included a centrifugal pump, heparin-coated circuits, and a blood reservoir. It did not have a membranous oxygenator that would activate chemical mediators and lead to postoperative liver dysfunction. The patient had no postoperative problems and is still under follow-up [Uchida 2001].

Major causes of death for cirrhosis patients who have undergone surgery are infection, hemorrhage, renal failure, hepatic failure, and encephalopathy. Postoperative care is highly important. Hypotension, hemorrhage, hypoxia, hypercapnia, use of vasoactive drugs, intermittent positive pressure ventilation (IPPV), and particularly positive end-expiratory pressure (PEEP) decrease hepatic blood flow and increase splanchnic vascular resistance throughout the surgical procedure and postoperatively [Ota 1996]. Respiratory alkalosis should be avoided, and adequate fluid replacement and nutrition should be provided. Crystalloid solutions like lactated ringer and, as a diuretic, mannitol should be preferred for provision of sufficient urinary output. Mannitol is especially helpful when the serum bilirubin level is above 300 mmol/L. Intravenous mannitol decreases the postoperative incidence of renal failure in patients with obstructive jaundice [Ota 1996].

In our study, causes of postoperative death were hepatorenal syndrome, inability to wean from ventilation, gastrointestinal hemorrhage, and sepsis. Univariate analysis showed that predictors of postoperative hepatic dysfunction were New York Heart Association (NYHA) class, type of cardiac surgical intervention, duration of operation (duration of cross-clamping and CPB), low cardiac output syndrome, hemorrhage, transfusion amounts of blood and blood products, extended duration of intubation, and infection.

Surviving patients are still receiving follow-up, with a mean duration of 30.85 ± 12.21 months at present. During the late postoperative period, two cases of jaundice with ascites were observed, and one case each of jaundice without ascites and ascites without jaundice. No mortality has occurred in the late postoperative period.

CONCLUSION

Klemperer and colleagues have stated that patients with mild signs of cirrhosis may tolerate a cardiac operation but that elective cardiac surgery for patients with advanced liver disease is not recommended [Klemperer 1998]. Likewise, our findings indicate that patients with mild liver disease (Child class A) may tolerate cardiac surgery but patients with advanced liver pathologies (Child class B) should not undergo elective surgery unless there is an absolute indication for it. In order to avoid postoperative mortality and morbidity, the duration of CPB should be kept shorter in cardiac operations for patients with chronic liver disease. If possible, surgical intervention on the beating heart should be preferred where CABG is to be performed. We suggest that urgent and emergent cases among Child class B patients should proceed to operation only with the provision of adequate preoperative preparation and perioperative management, and with postoperative care adequate to overcome challenging complications. The high morbidity and mortality associated with such operations should always be kept in mind.

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