Orthotopic Liver Transplant for Budd-Chiari Syndrome: An Analysis of 14 Cases

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Abstract

Objectives: Budd-Chiari syndrome is a low-prevalence, life-threatening disorder characterized by hepatic venous outflow obstruction at the hepatic venules, the large hepatic veins, the inferior vena cava, or the right atrium. Orthotopic liver transplant should be considered for patients with fulminant and chronic forms of the syndrome.

Materials and Methods: Fourteen patients received 15 orthotopic liver transplants at our center from September 2006 to March 2013. This study retrospectively reviewed the prospectively collected data from these 14 patients.

Results: The mean age of the patients was 33 years; only 1 patient was female. The severity of liver disease was Child-Pugh score A in 1 patient, B in 4 patients, and C in 9 patients. Mean calculated Model for End-Stage Liver Disease score was 18 (range, 6-30). The cause of Budd-Chiari syndrome was factor V Leiden mutation in 3 patients, polycythemia vera in 2 patients, factor 2 and 3 deficiency in 1 patient, fulminant essential thrombocytosis in 1 patient, and protein C deficiency in 2 patients. We performed 15 transplants in 14 patients. Five grafts were obtained from deceased donors, and 10 grafts were from living-related donors. Mean graft-to-recipient weight ratio was 1.12 for patients receiving a living-donor liver transplant. Median follow-up was 29 months. Patient survival rates were 87%, 71%, and 71% at 1, 3, and 5 years.

Conclusions: Liver transplant is an option for treating Budd-Chiari syndrome in cases of fulminant presentation and cirrhosis. Living-donor liver transplant is a viable choice in countries where procuring organ donations is still a problem. To manage the long-term medical therapy and follow-up for these patients, a careful evaluation is necessary to determine the cause of Budd-Chiari syndrome. Anticoagulant and antiaggregant therapy remains the mainstay of treatment for this syndrome.

Key words: Antiaggregant and anticoagulant therapy, Factor V Leiden mutation, Myeloproliferative disorders, Living-donor liver transplant, Budd-Chiari syndrome

Introduction

Budd-Chiari Syndrome (BCS) is an uncommon, life-threatening disorder characterized by hepatic venous outflow obstruction at the level of the hepatic venules, the large hepatic veins, the inferior vena cava, or the right atrium.1 Obstruction of the hepatic venous outflow tract results in increased hepatic sinusoidal pressure and portal hypertension. Later on, venous stasis and congestion lead to hypoxic damage to the hepatic parenchymal cells.2,3 In this disease process, free radicals are released and sinusoidal lining cells are injured. As a result, progressive centrilobular fibrosis, nodular regenerative hyperplasia, and cirrhosis ultimately develop.1,3

In most cases of BCS (75%), at least 1 inherited or acquired prothrombotic risk factor is identified as a cause.1,2 The most common underlying disorders are myeloproliferative, such as polycythemia vera and essential thrombocytosis.4,5 Other causes include factor V Leiden mutation, oral contraceptive use, protein C and S deficiencies, antiphospholipid syndrome, antithrombin III deficiency, paroxysmal nocturnal hemoglobinuria, cancer, Behçet syndrome, trauma, and idiopathic disorders.4,6

Treatment options for BCS include anticoagulation, percutaneous interventional techniques, transjugular intrahepatic portosystemic shunt (TIPS), surgical shunts, and liver transplant.4 Therapeutic procedures...
are introduced in order of increasing invasiveness, based on the patient’s response to previous therapy.\textsuperscript{1,7-9} Orthotopic liver transplant (OLT) should be considered in patients with fulminant BCS with irreparable necrosis of the liver parenchyma, as well as in patients with chronic forms of BCS accompanied by established cirrhosis and hepatic decompensation.\textsuperscript{5,7}

The aim of this study was to evaluate the results of 15 OLTs over a period of 7 years in 14 patients diagnosed with BCS.

Materials and Methods

Fourteen patients received OLT at our center from September 2006 to March 2013. This population constituted 2.7\% of 519 liver transplants performed at our center during that period. In this study, we retrospectively reviewed the prospectively collected data from these 14 patients. The diagnosis of BCS was confirmed by Doppler ultrasound examination, computerized tomography scan, and histopathologic examination of the explanted liver.

Most of the patients were referred to our center for OLT. In these patients, diagnosis had already been done by the referring center, and causative factors had already been identified. For patients admitted to our center without an evaluation of the underlying cause, we performed bone marrow biopsy to exclude a myeloproliferative disorder (MPD) in addition to performing a routine preoperative evaluation. We obtained informed consent from all of our patients before any invasive procedure and OLT. All of the protocols conformed to the ethical guidelines of the 1975 Helsinki Declaration.

Surgical technique

The transplant operations were performed by the same surgical team. A piggyback technique was performed in all deceased-donor liver transplant (DDLT) cases except 1, in whom we used the classic technique. For living-donor liver transplant (LDLT), we used the right lobe of the recipient and reconstructed the segment 5 or segment 8 vein using a polytetrafluoroethylene vascular graft. There was no need to reconstruct the inferior vena cava in any case.

Postoperative follow-up

Postoperative immunosuppression was achieved using a regimen of tacrolimus and mycophenolate mofetil orally, and steroids intravenously for the first 7 days and orally after the first week of transplant. After discharge, patients were followed up in the clinic once weekly during month 1, then once every 2 weeks during months 2 and 3. Subsequently, follow-up took place once per month until the end of month 6. If the patient’s condition was stable, then follow-up visits gradually became less frequent. Liver function tests, complete blood counts, and tacrolimus levels were evaluated at each visit. After 6 months, patients were evaluated by their family physician and stayed in contact with our clinic. All patients were treated with anticoagulant drugs after transplant. Antiaggregant therapy was given during the early period posttransplant to all patients, and the decision to discontinue it was made based on the cause of BCS.

Statistical analyses

Statistical analyses were performed with SPSS software for Windows (SPSS: An IBM Company, version 13.0, IBM Corporation, Chicago, IL, USA). Survival rates were estimated using the Kaplan-Meier method.

Results

Patient age ranged from 17 to 62 years (median age, 33 y); 1 patient was female. The severity of liver disease was Child-Pugh score A in 1 patient, B in 4 patients, and C in 9 patients. Mean calculated Model for End-Stage Liver Disease (MELD) score was 18 (range, 6-30) (Figure 1). The cause of BCS was factor 5 Leiden mutation in 3 patients, polycythemia vera in 2 patients, factor 2 and 3 deficiency in 1 patient, fulminant essential thrombocytosis in 1 patient, and

![Figure 1. Patient Survival After Liver Transplant](image)
protein C deficiency in 2 patients. The cause of BCS could not be determined in 5 patients, even though we performed bone marrow biopsy in 2 patients (Table 1).

We performed 15 OLTs in 14 patients. Five grafts were from brain-dead deceased donors, and 10 grafts were from a living-related donor. Mean graft-to-recipient weight ratio was 1.12 for LDLT patients. Only 2 patients had a history of previous abdominal surgery, comprising appendectomy, hidatid cyst surgery, and laparoscopic cholecystectomy. In 1 patient, we performed portal vein anastomosis between the portal vein graft and 1 of the branches of the mesenteric vein because the recipient’s portal vein was completely occluded. Hepatocellular carcinoma was found in the explanted liver of 1 patient.

Average follow-up was 33 months (range, 0-68 mo). Patient survival rates were 87%, 71%, and 71% at 1, 3, and 5 years in the BCS group (Figure 1) compared with 87.8%, 85.0%, and 71.4% at these time points for patients who received OLT for other indications. Three postoperative deaths were caused by primary nonfunction of the graft, cardiac failure, and intra-abdominal sepsis; an additional patient died due to recurrent BCS 19 months after transplant while waiting on the national organ allocation list for retransplant.

Early complications included cholangitis, mechanical ileus, gastrointestinal system bleeding from Roux-en-Y anastomosis that required sclerotherapy, biliary fistula and intra-abdominal abscess, pleural effusion, and surgical site infection. Three patients developed biliary leakage that was managed by percutaneous catheterization and endoscopic retrograde cholangiopancreatography and stenting. One of these patients died due to multiorgan failure secondary to intra-abdominal infection.

Three patients had acute graft rejection, confirmed by biopsy, 2 of which responded well to steroid therapy. One patient refused this therapy and was discharged from the hospital at his request and was lost to follow-up. He had traveled from abroad, and we could not locate any further information about this patient. Late complications included cytomegalovirus colitis, subclavian vein thrombosis, and recurrent BCS. One patient required retransplant on postoperative day 7 owing to primary graft nonfunction. This patient’s first transplant was from a living-related donor, but for retransplant, we used a graft from a deceased donor.

**Discussion**

Budd-Chiari syndrome results from the obstruction of hepatic venous outflow at the hepatic venules to the entrance of the inferior vena cava into the right atrium. This obstruction results in venous stasis, centrilobular congestion, and hepatocyte necrosis, which lead to centrilobular fibrosis and cirrhosis of the liver.5,8 Potential causes of BCS in Asia and South Africa include calcification of the caval membranes, on the other hand in Western countries, MPDs and prothrombotic conditions are the main cause of BCS. Idiopathic cases constitute 25% of cases in the west and approximately 60% of cases in Asian countries.2,5,10,11 In our study, 21% of patients had an MPD, 42% had BCS due to a prothrombic state, and 5 patients (36%) had idiopathic BCS.

In BCS, treatment should follow a stepwise strategy in which OLT is indicated as a rescue
therapy. Medical therapy is the first-line treatment, angioplasty with stenting is second line, and TIPS and liver transplant are third-line treatments. The indications for transplant include fulminant hepatic failure, cirrhosis, and failure of other strategies. We performed OLT in patients who had a mean MELD score of 18. In addition, 13 of our patients' (93%) liver disease severity was Child-Pugh score B or C. Only 1 patient with a calculated MELD score of 6 received OLT. However, because this patient had ascites that were resistant to medical therapy and liver disease severity of Child-Pugh score B, OLT was considered before other treatment strategies.

Mentha and associates reported on one of the largest series of patients (n = 248) receiving transplants for BCS. They reported 1-, 5-, and 10-year survival rates of 76%, 71%, and 68%. In these patients, most deaths occurred in the first 3 months after transplant owing to infection, multiorgan failure and graft failure, or hepatic artery thrombosis. Late mortality resulted from recurrent BCS in 9 patients (13%). In contrast, Ulrich and colleagues reported 89.4% and 83.5% five- and ten-year survival rates in their patient population. They found higher rates of vascular complications in patients who had received a transplant for BCS than for other indications. In our study, overall patient survival rates were 87%, 71%, and 71% at 1-, 3-, and 5-year follow-up, and 3 of 4 patient deaths (75%) occurred in the early postoperative period. In this study, the causes of mortality were primary graft nonfunction, cardiac failure, and intra-abdominal sepsis. No BCS-related complications occurred during the early postoperative period. However, 1 patient (7.1%) died from recurrent BCS 19 months after transplant while waiting on the national organ allocation list for retransplant. These findings are similar to those from larger series of patients published in this era. Ulrich and associates also reported the same rate of recurrent BCS in their study (7.1%), whereas Yamada and colleagues reported a higher rate of recurrence in their series (33.3%).

After OLT, the most important strategy for preventing recurrent BCS is anticoagulant or anti-aggregant therapy, depending on the underlying cause of BCS. In 2011, Chinnakotla’s group reported on their 23 years of experience with OLT for BCS. They found that MPD was the most common cause of BCS in their series. They managed their patients diagnosed with BCS secondary to MPD by using hydroxyurea and aspirin rather than anticoagulation therapy. They reported that their approach resulted in excellent long-term outcomes and a 15-year survival rate of 73%. Even so, it is important to keep in mind that multiple causative factors may be present in patients with BCS, and therefore, it may be reasonable to recommend long-term anticoagulant therapy after liver transplant. We prescribe anticoagulant therapy, as well as antiplatelet therapy, to all our transplant patients. In our practice, we also give antiplatelet therapy for other OLT indications for at least 3 months because most of our grafts are from a living donor, and the arteries are most often small and can be reconstructed only under a surgical microscope. Among our patients who underwent OLT for BCS, none experienced portal vein or hepatic artery thrombosis during the early postoperative period, although 1 patient developed recurrent BCS in the longer term.

Most of the studies concerning BCS and liver transplant have reported on the results of DDLT. However, LDLT for BCS has been reported by only a few studies consisting mostly of case reports. Yamada and associates reported on 9 LDLTs for BCS in 2006. They performed patch plasty for inferior vena cava reconstruction in 4 patients, and 5 patients required a replacement vein graft. Other successful LDLTs for BCS have been reported in the literature. In this study, we performed 10 LDLTs and 5 DDLTs at our center. We did not need to use cavoplasty for LDLT. Our results were comparable with those of other centers in terms of mortality, early complications, disease recurrence, and other outcomes. To the best of our knowledge, this is the largest series of patients who have received LDLT for BCS. One limitation of this study is that it lacks long-term results because of its retrospective design.

In conclusion, we reaffirm that OLT for BCS is a viable option for treating this disease. It should be considered in cases of BCS with fulminant presentation and cirrhosis. One of the options for treating BCS is LDLT, particularly in countries where procuring organ donations is still a problem. To manage long-term medical therapy and follow-up protocols in these patients, a careful evaluation is necessary to determine the underlying cause of BCS. In addition to immunosuppressive therapy, anticoagulation and anti-aggregant therapy is the mainstay of treatment after liver transplant for BCS.
References


