Liver Transplant for Fulminant Hepatic Failure: A Single-Center Experience

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Abstract

Objectives: Acute liver failure is a life-threatening condition with sudden onset liver injury, decreased liver functions, hepatic encephalopathy, and coagulopathy in patients without preexisting liver disease. In this study, we sought to evaluate the results of liver transplant as a treatment for acute liver failure.

Materials and Methods: Between November 1988 and March 2015, we performed 482 liver transplants in 471 patients. We performed 36 liver transplants in 35 patients because of acute liver failure. Only 5 of these were from deceased donors. Thirty of those 34 patients were pediatric (85%) and 5 were adults (15%).

Results: Five patients died (4 in early postoperative period and 1 during the 18th month of living-donor liver transplant). We diagnosed 11 acute rejections (32%); 6 biliary leaks (17%); 6 intraabdominal hemorrhage (17%); 5 hepatic arterial thromboses (15%), and 1 venous complication (3%) during the early postoperative period. We have no morbidity or mortality in living-donor liver transplants.

Conclusions: Living-donor liver transplants are an efficient and successful treatment for acute liver failure patients. In our center, we mostly consider and prefer living-donor liver transplants to deceased-donor liver transplant because of the paucity of organ donation, especially for pediatric patients. Considering acceptable postoperative complications, living-donor liver transplant is a lifesaving treatment for acute liver failure.

Key words: Liver dysfunction, Acute liver failure, Hepatic coma, Liver transplantation

Introduction

Acute liver failure (ALF) is a life-threatening condition with sudden onset liver injury, decreased liver functions, hepatic encephalopathy (HE) and coagulopathy in patients without preexisting liver disease. Etiologic factors change with regard to geographic location, age, and socioeconomic status of countries. Although viral agents and drugs mostly cause ALF, no etiologic factors can be found in 19% of patients.1,2 Viral causes are mostly seen in developing countries (especially hepatitis A, B, E); whereas drug-induced liver injury is the primary cause of ALF in Europe and the United States. In our country, the most common cause of ALF is a virus followed by toxic- and drug-induced liver injury.3,4

When ALF is diagnosed, cause of liver injury should be determined immediately. Cases with deteriorated mental status and prolonged prothrombin time (> 4-6 sec) and international normalized ratio (> 1.5) should be hospitalized. Blood ammonia level, and the lactate level of arterial blood gas analyses are important predictive factors in prognosis.5

The staging of hepatic encephalopathy of ALF patients were done by West-Haven Criteria for Hepatic Encephalopathy: grade 0, normal; grade 1, mild lack of awareness; grade 2, lethargic; grade 3, somnolent but arousable; grade 4, coma. The definition and classification of fulminant liver failure patients were diagnosed as having fulminant hepatitis when they developed grade 2 or worse hepatic encephalopathy because of severe liver damage, as represented by prothrombin time values of 40% of the standardized value within 8 weeks of the onset of hepatic symptoms. Fulminant hepatitis was further classified into 2 clinical types: acute and subacute.
types, based on the hepatic encephalopathy developing within 10 days, or between 11 and 56 days, after the onset of the hepatitis symptoms. Fulminant hepatitis is defined as histologic evidence of hepatic inflammation, characterized by lymphocytic infiltration of the liver, associated with acute liver failure.

Living-donor liver transplant is an efficient and successful treatment for ALF patients. In our center, we prefer LDLT to deceased-donor liver transplant (DDLT) because of the scarcity of organ donation, especially for pediatric patients. Considering acceptable postoperative complications, LDLT is a lifesaving treatment for ALF. We aimed to evaluate the results of liver transplant as a treatment choice for ALF in our study.

**Materials and Methods**

Between November 1988 and March 2015, we performed 482 liver transplants in 471 patients (283 adults, 188 pediatric). Thirty-five patients (8%) had liver transplants due to ALF (30 pediatric, 5 adult). All patients were followed in the intensive care unit. Patients who had a life expectancy of less than 7 days without a liver transplant, were announced to national organ transplant coordination center as high-urgency candidates for liver transplant. Plasmapheresis was performed in all patients until a donor liver was available (Figure 1).

Between 1988 and 2015, ninety-seven ALF patients were admitted to our center (83 pediatric, 14 adult). After diagnosis of ALF, need for urgent liver transplant was established in 35 patients. Forty of the rest of the patients (36 pediatric, 4 adult) were treated without transplant. We lost 22 patients before urgent liver transplant.

For each ALF patient, urgent announcement for a deceased donor was made for every patient via national transplant coordination center. Living-donor liver transplant was performed in 30 patients with living donors. All LDLTs were examined according to a previously reported algorithm for living-related liver donor evaluation that includes the results for donor liver biopsy and hepatic angiographic studies. Donors were selected based on the results of blood tests and graft/recipient size matching from family members who had volunteered to give liver grafts. Blood tests consisted of ABO blood typing, liver function test (ie, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, total bilirubin, direct bilirubin, cholinesterase), complete blood cell count (ie, white blood cells, red blood cells, hemoglobin, hematocrit, platelets), coagulation test (ie, prothrombin time, fibrinogen, antithrombin-III activity), renal function test (ie, creatinine, blood urea nitrogen), glucose, amylase and electrolytes measurements, and serology of hepatitis (ie, hepatitis B surface antigen, hepatitis C antibody). Special evaluations including Doppler ultrasonography and computed tomography (CT) scans were done in emergencies.

After donors were made aware of possible complications for donors and recipients, operative outcomes, and long-standing problems for recipients associated with LDLT, written informed consent was obtained from all subjects or their legal guardians. During the preoperative evaluation by hepatologists and surgeons, donor candidates also were evaluated by anesthesiologists for donor operation risk. As a rule, authorization for surgery was obtained from the Ethics Committee of our university. For the donor operations, no blood was obtained from blood banks or preoperative autologous blood from the donors. The type of donor operation (ie, lateral segmentectomy, left lobectomy, or right lobectomy) was decided according to the ratio between the estimated liver graft weight established on the basis of CT scan volumetry and recipient body weight (estimated graft-to-recipient weight ratio). An estimated graft-to-recipient weight ratio of more than 1.0% was considered optimal, and a ratio of 0.8% minimally acceptable. All of the protocols conformed to the ethical guidelines of the 1975 Helsinki Declaration.

All patients were treated with the same immunosuppression protocols after transplant. The standard immunosuppression protocol comprised tacrolimus
and low-dose steroid. The target blood level for tacrolimus was 10 to 15 ng/mL during the first 2 weeks, approximately 10 ng/mL thereafter, and 5 to 8 ng/mL after the second month.

No protocol liver biopsy was performed. We performed liver biopsies only for investigation of biochemical abnormalities (elevated serum transaminase or bilirubin levels). Acute rejection episodes were documented by means of liver histology and treated with methylprednisolone boluses.

**Results**

We performed 36 liver transplants in 35 patients (16 female, 19 male) due to ALF. Thirty (85%) of those 35 patients were pediatric and 5 were adults (15%). We performed 5 DDLTs (15%) and 30 LDLTs (85%). The mean age of the patients was 9.5 years (range, 0.6-42 y). The causes of ALF and the patient demographic data are listed in Tables 1 and 2.

The donors were 5 deceased donors, 19 mothers, 9 fathers, 1 brother, and 1 aunt’s husband. The mean age of the donors was 35.1 ± 8.5 years (range, 23-53 years). No donor required a blood transfusion. During the immediate postoperative period, the results of liver function tests were elevated in all donors, but those values returned to normal after a mean of 9.6 ± 3.7 days (range, 6-25 d). Although most donors were well within 5 days after surgery and were eligible for discharge from the hospital, parents who served as donors preferred to stay in the hospital with their child (the recipient), often for an extended period. No donor experienced early or late postoperative complications. At this time, all donors have returned to their normal preoperative activities.

We detected 6 biliary leaks (17%) during the early postoperative period. We revised duct-to-duct anastomosis to hepaticojejunostomy in 2 patients. We treated 4 biliary leakages by percutaneous biliary drainage. Hepatic arterial thromboses were seen in 5 patients (all pediatric). We performed urgent deceased-donor retransplant in 1 patient. We treated the remaining 4 patients by a reanastomosis under loop. We detected acute rejection in 11 patients (one patient had 5, two patients had 3, two patients had 2, and six patients had 1 acute rejection episodes; Table 3). All 11 patients received pulse steroid for rejection treatment. However, we had to treat 2 patients died because of chronic rejection in the 18th month posttransplant. We had 1 hepatic arterial thrombosis that was treated with urgent retransplant from deceased donor.

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The mean intensive care unit stay for the recipients was 3.1 days (range, 2-8 d) and 1 day for the donors. The mean hospital stay of recipient was 19 days (range, 12-60 d). Thirty-two patients recovered from hepatic coma during the early postoperative period. One patient died because of chronic rejection in the 18th month posttransplant. We had 1 hepatic arterial thrombosis that was treated with urgent retransplant from deceased donor.

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<table>
<thead>
<tr>
<th>Complications</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Biliary leak</td>
<td>6 (17)</td>
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<tr>
<td>Bleeding</td>
<td>6 (17)</td>
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<tr>
<td>Arterial complications (hepatic arterial thromboses)</td>
<td>5 (15)</td>
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<tr>
<td>Venous complications (portal vein aneurism)</td>
<td>1 (3)</td>
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<tr>
<td>Acute rejections</td>
<td>11 (32)</td>
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patients with antithymocyte globulin because of steroid-resistant acute rejection. Among all ALF patients, 5 patients died. Two were due to chronic rejection and the remaining 3 were due to pneumonia. Our 5-year survival rate is 85%.

Discussion

The first study about ALF was reported by Tanaka and colleagues in 1994 finding LDLT in 3 ALF cases. The investigators suggested that LDLT was feasible in patients with ALF and determined that with a partial liver graft weighing approximately 1% of the recipient's body weight. After that, Hattori and colleagues expanded their study to 11 LDLTs in pediatric ALF. They increased the survival rate from 28% to 73%. In a previous study from our center, previously our center reported LT in 12 ALF pediatric patients and increased the survival up to 75% in 2007.

Acute liver failure is considered a high-urgency qualification for liver transplant, which is the only treatment option for most patients with that disorder (although a few may recover with medical treatment). Most transplant centers rely on clinical and biochemical parameters to determine the proper time for and validate the decision to perform liver transplant in patients with ALF.

Uemoto and colleagues reported high acute rejection rates in their ALF series. They reported acute rejection in 6 of their 19 ALF patients that they performed LT due to non A/non B hepatitis. The authors considered that non A/non B hepatitis might lead to accelerate the immune response in patients with ALF. We diagnosed 16 acute rejection episodes in 11 patients. In 2 of them, we applied antithymocyte globulin for steroid-resistant acute rejection. One of these patients recovered from rejection with antithymocyte globulin therapy. The other patient developed chronic rejection 18 months after transplant, and we lost the patient while waiting for a deceased donor. Both patients had non A/non B ALF.

Donor hepatectomy is reported with morbidity in various studies in literature. However, all donors in our study were well and were discharged from the hospital within 5 days after the operation. We had no postoperative complications in donors.

The mortality rate of patients with ALF who are waiting for deceased donors is as high as 50% because of the paucity organ donation in Eastern countries. In Western countries, it is a big deal for pediatric ALF patients because of the shortage of appropriate deceased donors for them, and the mortality rate has been reported to be 20%. Before organ failure and permanent irreversible neurologic damage, liver transplant from living donors should be performed in pediatric patients with ALF.

While waiting for deceased donors admitted to our center, 22 patients grade 4 HE with AFL (23%) died during medical because there were no donors. However, this problem can be solved by increasing the number of deceased donors.

Ee and colleagues reported the survival of ALF patients who were waiting for deceased donors as 27%. In our center, we lost 4 of 22 ALF patients while waiting for deceased donors in last 10 years because we had no living-related or deceased donors for them.

Because of the scarcity of organ donation in pediatric patients, LDLT is reasonable. In our center we performed liver transplant from living donors in 30 patients (28 pediatric, 2 adults; 85%). We lost 4 only these patients (14%) during the early postoperative period. When compared with the literature, LDLT is proper for ALF patients.

Living-donor liver transplant is an effective and successful treatment for ALF patients. In our center, we mostly prefer LDLT to DDLT because of the paucity of organ donation, especially for pediatric patients.

References


