

SURVIVAL AFTER LIVER TRANSPLANTATION: EXPERIENCE WITH 89 CASES

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Background: Liver transplantation has become an accepted clinical modality in the treatment of end-stage liver disease since the early eighties. In this paper, the result of liver transplantation at the largest liver transplant center in Saudi Arabia is presented with a special emphasis on the difficulties hindering the expansion of such programs.

Patients and Methods: A series of 89 liver transplant procedures was performed between January 1994 and June 1998. This is the largest series of liver transplant cases reported to date in Saudi Arabia. Patient data were retrospectively analyzed with a special emphasis on mortality and morbidity. Kaplan-Meier technique was used to compute patient survival.

Result: The final outcome of the transplants was found to be comparable to that of well-established programs in Western Europe and North America. The actuarial survival rate at three months and one year was 98% and 89%, respectively. The long-term survival rate (>3 years) was 67%. Technical complications were well below average. The dominating cause of early death was sepsis. Late death was generally due to disease recurrence and chronic rejection.

Conclusion: Liver transplantation has been successful in Saudi Arabia. However, the main obstacle to program expansion and, therefore, the salvage of patients with end-stage organ failure, is lack of organs. This situation can be resolved only if all parties involved in organ transplantation in Saudi Arabia take serious steps towards the alleviation of the problem of organ shortage. Improvement in the donor situation in the Kingdom should result in timely retransplantation of patients with primary graft non-function and hepatic artery thrombosis, and will certainly enhance their chances of survival.

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Liver disease is a major health problem in Saudi Arabia, resulting in a substantial number of patients suffering from life-threatening complications of end-stage organ failure. The estimated number of patients requiring transplantation in the Kingdom is between 300 and 500 annually.¹ With liver transplantation becoming the standard treatment for end-stage liver disease over the past two decades,² there was an obvious need for a liver transplant program in the Kingdom of Saudi Arabia.

The first successful liver transplant procedure in Saudi Arabia was performed in June 1990.³ In February 1994, the first liver transplant procedure was performed at the King Fahad National Guard Hospital. This program continues to date, with a total of 100 procedures having been performed so far. Two other programs were also begun in 1994 but were later discontinued. These two programs performed a total of 50 cases.

In this article, the author reports his personal experience in 89 procedures performed, with special emphasis on the final outcome and the technical complications encountered.

Patients and Methods

From January 1994 until June 1998, a total of 89 liver transplant procedures were performed on 83 patients by the author. There were 28 females and 55 males. The age of the recipients ranged between 4 and 66 years, with the average being 45 years. All patients underwent a thorough pre-transplant workup, as per an established protocol. Table 1 illustrates the etiology of their liver disease.

Following their confirmed candidacy for liver transplant, patients are placed on a list which is sent to the Saudi Center for Organ Transplantation (SCOT), awaiting the availability of donors. Determination of donor organ suitability is based on blood group, size, and medical urgency. Most of these patients are followed while on the waiting period as outpatients. Once a suitable organ becomes available, the patient is called and the procedure performed. The standard surgical procedure⁴ was utilized

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in 85 of the transplant cases. In four cases, a modification of the piggybank technique⁵ was performed, whereby the native inferior vena cava was preserved. In 64 procedures, venovenous bypass was used,⁶ and in 25 cases, bypass was omitted⁷ following confirmation that the patient was able to tolerate inferior vena cava clamping. The operating time ranged from 4 hours and 15 minutes to 15 hours and 15 minutes, with an average time of 9 hours and 3 minutes. Cold ischemia time (the time from clamping the aorta in the donor to the time when the liver is brought out of the ice to be transplanted) ranged from 3 hours and 52 minutes to 17 hours and 22 minutes, with an average time of 9 hours and 21 minutes. Warm ischemia time (time from which the liver is brought out of the ice until perfused by the recipient blood) ranged from 27 minutes to 1 hour and 8 minutes, with an average of 46 minutes. Following surgery, patients were taken to an isolated intensive care unit where hemodynamic and respiratory monitoring were carried out in a standard post-surgical manner.

Cyclosporin-based immunosuppression was given initially, and several months into the program this was changed to the new formulation of Cyclosporin Neoral[®] (Sandoz Pharmaceutical), which is given orally 24 to 48 hours post-transplant when the renal function is determined to be normal. Two years into the program, immunosuppression was changed to Tacrolimus[®] (Fujisawa Pharmaceutical), with the drug being given orally 24 to 48 hours post-transplant, at a dose of 0.05 to 0.1 mg/kg twice a day to achieve a therapeutic whole blood level of 7-10 ng/mL. One gram methylprednisolone was given preoperatively, followed by a tapering dose of 100 mg down to 20 mg in the first postoperative week. The 20-mg dose was tapered beginning one month post-transplant, until the steroid was weaned off completely by the end of the third postoperative month.

Following transfer from the intensive care unit, patients were cared for in the liver transplant ward for an average period of two to three weeks. The patients were discharged with follow-up blood work twice weekly for the first three months, and a weekly outpatient visit. Liver function tests were closely monitored. If any abnormalities were noted, patients were admitted for investigation. The follow-up visits became less frequent and at one year post transplant, the blood work was performed on a monthly basis, with a clinic visit every two to three months. The survival rate was calculated by Kaplan-Meier product limit estimates.

Results

The follow-up period ranged from two months to 4½ years. None of the patients in the series was lost in the follow-up period. Perioperative mortality (within one month) occurred in 11 patients. Another five died between the first and third months, making a three-month actuarial survival rate of 98%. The rest (67 patients) were discharged home. A further three patients died after three

months, resulting in an overall long-term survival rate (i.e., one year actuarial survival rate) of 89%. The causes of early mortality are shown in Table 2, and those of late mortality, i.e., after three months, are shown in Table 3.

Out of 22 deaths, six were directly attributed to technical complications (27%). Four of these were directly related to hepatic artery thrombosis. Table 4 details the technical complications related directly to the liver transplant procedure.

Discussion

The survival rates of patients following liver transplant in this series were 98% at three months and 89% at one year, with a long-term survival rate of 67% at more than three years. These figures are comparable to international statistics in North America and Europe. The overall success rate had been close to 80%, which is above the average of North American standards based on the data of the United Network of Organ Sharing in the United States.⁸ Deaths directly attributed to technical complications occurred in six patients. These were mainly related to hepatic artery thrombosis. Generally, the only treatment for patients with hepatic artery thrombosis is re-transplant, with excellent outcome predicted if surgery is performed in a timely manner.⁹ In our patients, it was invariably the case that either no organ was available for re-transplant, or if an organ became available, it was too late and at the stage where the patient was already in a septic condition, which produces inferior transplant results if the retransplant did occur. The other cause of death which could have been prevented if timely retransplant had occurred was primary non-function. In our series, two patients presented with this complication following transplant, and in both patients retransplant was performed. However, because of the delay in obtaining organs, neither of these patients was saved with re-transplant. It is clear from the above that if organs became

TABLE 1. Etiology of liver disease in 83 patients.

Type of disease	Number of cases
Hepatitis C	44
Hepatitis C and HCC	10
HBV cirrhosis	4
Primary sclerosing cholangitis	4
Autoimmune hepatitis	3
Primary biliary cirrhosis	2
Wilson's Disease	5
Hemochromatosis and HCC	1
Familial cholestasis	2
Schistosomiasis	2
Alcoholic cirrhosis	1
Cryptogenic cirrhosis	5
Total	83

HCC=hepatocellular carcinoma.

TABLE 2. Causes of mortality in 16 patients within the first three months.

Complication	Number of cases
Sepsis	5
Vascular	4
Primary non-function	2
Intraoperative bleeding	1
Hemorrhage post-liver biopsy	1
Pulmonary hypertension	1
Mediastinitis	1
Cardiovascular accident	1
Total	16

TABLE 3. Causes of late death (after three months) in six patients.

Cause of death	Number of cases
Chronic rejection (recurrent hepatitis C)	3
Myocardial infarction	1
Cardiovascular accident	1
Post-transplant lymphoproliferative disease	1
Total	6

available in a timely fashion for the retransplants, at least 25% of the deaths which occurred could have been prevented. The availability of an average of two donors every month makes timely retransplant, as well as urgent transplant for cases such as fulminant hepatic failure, a remote possibility. Certainly, if the donor situation improves in the Kingdom, then significant reduction in mortality would be achieved by timely retransplant.

The other common cause of death in our series is sepsis, which occurred in six patients. A significant number of these were related to pulmonary sepsis in the form of overwhelming pneumonia. These cases presented early on in the program, when our patients were cared for in a mixed surgical medical unit, where septic techniques were not strictly followed. After the first year of the program, our patients were nursed in an isolated unit with compliance to septic techniques observed while in the intensive care unit. This dramatically decreased the number of pneumonia cases and, therefore, the number of deaths related to pulmonary sepsis.

Liver transplantation is a technically demanding procedure. Patients are usually very morbid to start with. The combination of portal hypertension and coagulopathy makes the procedure challenging, requiring precise surgical techniques to avoid severe hemorrhage. Following the hepatectomy, precise anastomotic techniques are required to construct the vascular and biliary anastomoses. Technical error may lead to devastating results in such

an immunocompromised patient. Technical complications in our series have been below the reported average, however, they led to mortality in cases of hepatic artery thrombosis. Such cases might have been salvaged if timely re-transplant had been performed.

The majority of our patients are transplanted for end-stage liver disease secondary to hepatitis C. Although this had no effect on the short-term survival following liver transplantation, the recurrence of hepatitis C is universal, resulting in graft loss after the first year in a small percentage of patients with hepatitis C. This occurred in three patients out of the 54 (6%) who were transplanted for hepatitis C, also a similar outcome to other reported cases.¹⁰

The experience we have had with liver transplantation in the Kingdom in just over four years indicates that the procedure can be performed with an excellent survival and accepted complication rate. The main obstacle to the growth of liver transplant programs in Saudi Arabia is organ shortage, which not only limits the number of deserving patients, but also contributes to the increasing mortality due to delay in obtaining organs for the re-transplants. With the proven success of liver transplantation in the Kingdom demonstrated so far, it is essential for the authorities involved in the field of transplantation to devise strategies to increase the donor pool.

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