Result of Orthotopic Liver Transplantation at King Chulalongkorn Memorial Hospital : The First Series From Thailand

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Abstract

Liver transplantation is one of the best treatments for advanced liver disease since it can prolong the patient's survival. In Thailand, the first liver transplantation was performed in 1987 at King Chulalongkorn Memorial Hospital. Up till now the authors have transplanted the most in Thailand, having done more than 30 cases.

From 1997 to 2002, there were 20 cases of liver transplantation and this is the result is presented. The authors classified the patients into 2 groups, according to primary indications for transplantation. Patients with cirrhosis were included in group I and patients with hepatocellular carcinoma were included in group II. The one year survival in group I and II was 64 per cent and 29 per cent respectively. Mortality rate in the cirrhotic group was high during the first 3 months post transplant. The reason for a high mortality rate in the hepatocellular carcinoma group may be secondary to the advanced stage of cancer and the poor condition of the patients. However, the acute rejection rate in the present series of 25 per cent is relatively low compared to other series and this may need further study.

The one year survival rate in patients who received a new liver from 1997 to 1999 compared to 2000-2002 was 33 per cent and 54 per cent respectively. This showed an improvement in the result of liver transplantation in Thailand.

In conclusion, this report showed a satisfactory result of liver transplantation. The main problem with liver transplantation in Thailand is that potential donors do not understand the problems which leads to few donors. There is also a shortage of skilled personnel, budget, and the appropriate instruments.

Key word : Liver Transplantation, Thailand, Survival

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Liver transplantation has revolutionized the care of patients with end-stage liver disease. It is indicated for acute or chronic liver failure from any cause. Before transplantation, these patients were doomed to die within months or years. They now have the opportunity to extended survival with an excellent quality of life after transplantation[1]. The increase in the transplantation rate appears to have improved the mortality rate of liver failure in the United States [2]. In Thailand, there are many liver diseases that can lead to liver failure. Chronic viral hepatitis is one of the commonest diseases that ultimately turns to the end stage but less than one per cent of them underwent liver transplantation. So far, there is no report from Thailand regarding liver transplantation. The possible explanation for such a small volume of liver transplantation in the past is the lack of specialists in this field, inadequate funding, and poor public awareness of organ donation. Fortunately, over the last two years, these problems have received more public attention.

Chulalongkorn University Hospital is the hospital with the best liver transplant program in Thailand. It is the first hospital in Thailand to perform liver transplantation and now more than 30 cases of liver transplantation have been performed since 1987.

METHOD

The authors retrospectively reviewed data of patients who underwent liver transplantation between 1997 and 2002. Cases prior to 1997 were not reviewed in detail because this data was incomplete due to missing records. The survival time was analysed according to the primary indication for transplantation by classifying these patients into 2 groups according to period of transplantation, before, and after the year 2000.

Table 1. Demographic data of liver transplant patients.

	1997-1999	2000-2002
N	9	11
One year survival time (N)	33%	54%(72%*)
Still alive	3 cases	8 cases
Recipient age (Mean)(Yr)	41.9	50.7
Recipient sex (M : F)	4 : 4	8 : 3
Malignancy	3	4
Cirrhosis	5	6
FHF	1	1
Donor sex (M : F)	6 : 3	6 : 5
Donor age (Mean)(Yr)	30.22	27.06

* If the last 2 cases, who had a liver transplant 4, 8 months ago and now being followed-up, were included.

RESULTS

Table 1 demonstrates all the demographic data of these 2 groups which are classified according to the time of transplantation. From 1997 to 1999 the survival rate of patients who underwent liver transplantion was 33 per cent. Since then the survival rate has improved to 54 per cent (2000-2002) as demonstrated in Table 2 and Table 3.

Since 1997, there were 11 cases of cirrhosis, 7 cases of malignancy, 2 cases of fulminant hepatic failure who underwent liver transplantation at our hospital as shown in Fig. 1. Their survival time, classified according to the primary indication for liver transplantation, is demonstrated in Fig. 2. Patients

Table 2. Detail of cases between 1997-1999.

No	Group	Age (years)	Sex	Indication	Survival time (months)
3	Cirrhosis	21	Female	HBV cirrhosis	46.00
5	Cirrhosis	25	Female	AMA negative PBC	48.00
6	Malignant	50	Male	HBV cirrhosis, HCC with portal vein invasion	5.00
7	Malignant	50	Female	HBV cirrhosis, HCC with portal vein invasion	4.00
8	FHF	50	Male	FHF	0.00
9	Cirrhosis	45	Male	Alcoholic cirrhosis, post portalcaval shunt	0.00
12	Cirrhosis	26	Female	Cirrhosis from wilson's disease.	48.00
27	Malignant	59	Male	HCV Cirrhosis with HCC	0.10
28	Cirrhosis	51	Female	Alcoholic cirrhosis	1

FHF = fulminat hepatic failure, HBV = hepatitis B virus, AMA = antimitochrondrial antibody,
PBC = primary biliary cirrhosis, HCC = hepatocellular carcinoma

Table 3. Detail of cases between 2000-2002.

No	Group	Age (years)	Sex	Indication	Duration of survival (months)
1	Cirrhosis	56	Female	HCV Cirrhosis with hepatic hydrothorax	16.00
2	Malignant	61	Female	Hepatoma with cirrhosis post chemoembolization	14.00
4	Cirrhosis	17	Male	Biliary atresia with cirrhosis	27.00
10	Cirrhosis	59	Female	HCV Cirrhosis	36.00
11	FHF	45	Male	Cirrhosis and toxic hepatitis, HBV carrier	2.00
13	Malignant	60	Male	HCV cirrhosis with recurrent HCC (Post hepatectomy and chemoembolization)	0.1
14	Cirrhosis	55	Male	Alcoholic cirrhosis with HBV positive, post-portacaval shunt	2.00
15	Malignant	54	Male	Ruptured angiosarcoma	14.00
16	Cirrhosis	26	Male	Budd chiari syndrome with cirrhosis	4.00*
29	Cirrhosis	70	Male	HCV cirrhosis	13.00
30	Malignant	55	Male	Alcoholic cirrhosis with HCC	8.00*

FHF = fulminat hepatic failure, HCV = hepatitis C virus, HBV = hepatitis B virus, HCC = hepatocellular carcinoma,
* OLT was done on last 4 and 8 months and now they were in process of follow-up.

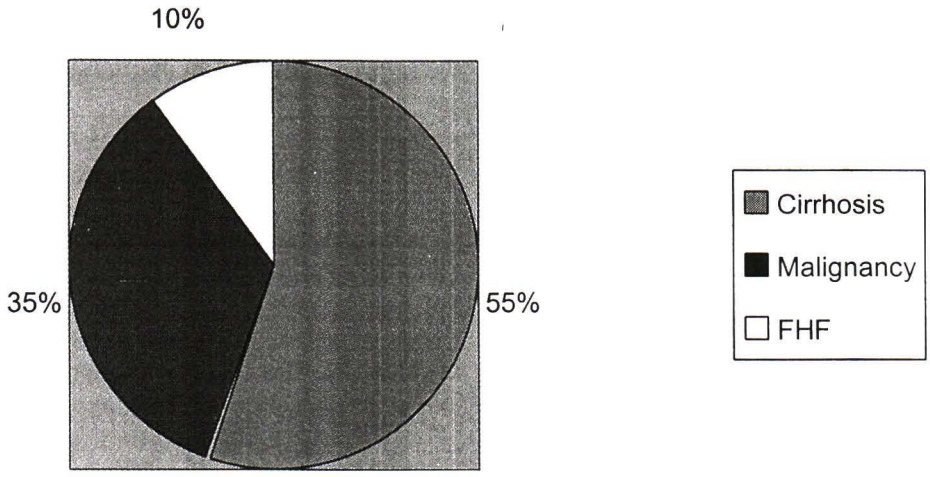

Fig. 1. Primary indications for liver transplantation (1997-2002).

with cirrhosis were included in group I and patients with hepatocellular carcinoma were included in group II. The one year survival in group I and II was 64 per cent and 29 per cent respectively. Another two cases of drug induced fulminant hepatic failure died within 2 months after transplantation because of very poor pre-operative liver function.

Only two of seven patients (29%) who underwent liver transplantation due to primary hepatic malignancy were still alive after 1 year. Of those who died early, two had portal vein thrombosis in the explants. Seven of thirteen patients who underwent liver transplantation due to cirrhosis were alive after 1 year. Of these patients, there was one from each group who underwent transplantation within a year and is still alive.

Four cases developed acute rejection after liver transplantation but all of them did not require

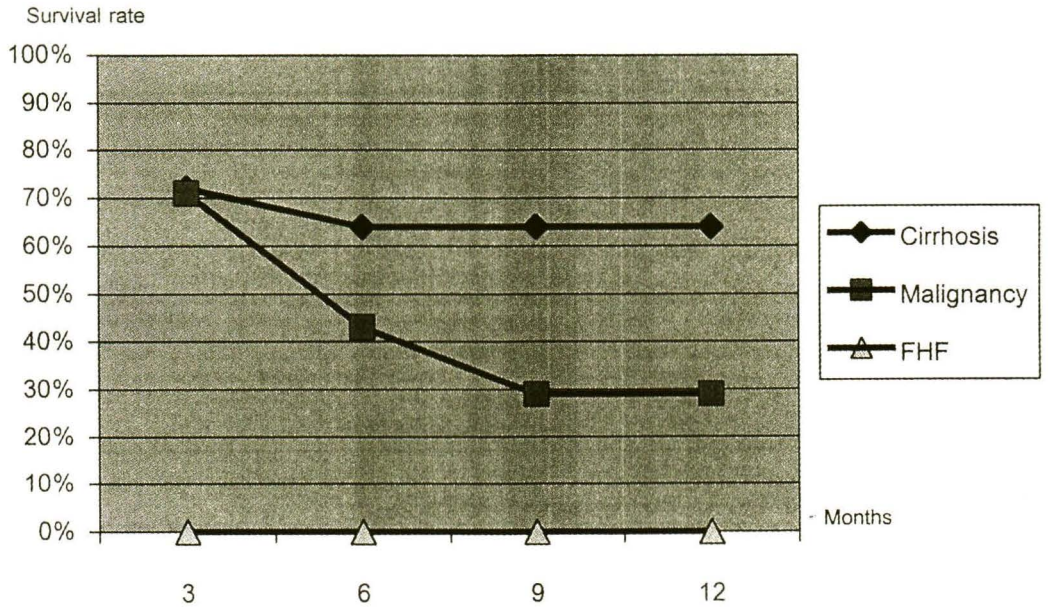

Fig. 2. Patient survival according to primary indications for liver transplantation.

re-transplantation and were controlled with medication. Another developed late rejection after the first 3 months because of poor compliance to immunosuppressive agents but the rejection disappeared after adjusting the dose of medication.

DISCUSSION

Liver transplantation is indicated for acute or chronic liver failure from any cause. The most frequent indication for liver transplantation in the present series was cirrhosis and the most common cause of cirrhosis was chronic viral hepatitis.

In the present series the survival rate after the year 2000 seems to have improved compared to previous data. This may be because of the improved surgical technique, equipment, and advance in immunosuppressive agents. This data is comparable to others[3]. A recent review demonstrated the 1 year survival of the patients to be around 85-90 per cent[3]. Moreover, patients with cirrhosis appeared to have longer survival (83% to 91%) than patients with cancer (72%)[3].

Acute cellular rejection develops in 25 to 70 per cent of liver transplant recipients treated with cyclosporine or tacrolimus-based immunosuppression [4,5]. In the present series the acute rejection rate was only 25 per cent (5 of 20 cases). This seems to be low when compared to other series[4]. One reason that may explain such a low rate of rejection is the the age of the donors and recipients (mean donor age 28.5 years, recipient 46.3 years). According to the study published in Hepatology 1998, donor age more than 30 years and lower recipient age are factors associated with an increased risk of acute rejection[4]. Approximately 5 to 10 per cent of liver transplant recipients who develop acute cellular rejection within 42 days of transplantation progress to severe ductopenic rejection despite antirejection therapy[6]. These patients may require retransplantation. Fortunately, in the present series no patient required retransplantation.

Tacrolimus or cyclosporin was used as the immunosuppressive drug similar to other series[7] and only one case developed late cellular rejection. This case was also associated with a low level of immunosuppressive drug due to poor compliance which is the most common cause of late rejection

Biliary complications following liver transplantations are bile leaks and bile duct strictures. The incidence of bile leak was 4 per cent in Sheng's series

(8). Bile leaks tend to present early after transplantation, most often arising from the T-tube insertion site or occurring after T-tube removal(9). Leakage can also occur at the site of the anastomosis, which may indicate ischemia of the bile duct since the hepatic artery is the sole blood supply to the donor biliary system. In the present series there was one patient with biliary leak at the anastomotic site that occurred within the first 3 months and she developed biloma, cholangitis, hepatic artery thrombosis, and finally died because of intracerebral hemorrhage.

Two cases in the present series developed anastomotic stricture of the common bile duct. Normally, biliary strictures develop in approximately 9 to 15 per cent of liver transplant recipients(10-12). They usually occur two to six months after transplantation, and can affect the common or intrahepatic bile duct. Strictures of the common bile duct frequently involve the anastomosis and result from technical factors occurring during surgery; strictures involving the anastomosis or the donor common bile duct can also arise from ischemia(13).

Interestingly there was one patient who underwent liver transplantation because of HCV cirrhosis and hepatic hydrothorax. She presented with dyspnea for 1 year and radiological studies demonstrated hydrothorax as the cause of dyspnea, she was treated by intermittent large volume paracentesis of the pleura as supportive treatment for 1 year but she still suffered from hepatic hydrothorax. Initially, she had a mild degree of ascites which was detected only by abdominal ultrasonography and her ascites proved to be connected to the pleural cavity by radionuclear study. Finally, she underwent transjugular intrahepatic portosystemic shunt (TIPS). One week after TIPS, she underwent liver transplantation. This patient stayed in the ICU for 16 days and no further hydrothorax was seen after liver transplantation. A previous study, demonstrating TIPS as a choice of treatment for hepatic hydrothorax, included 24 patients with refractory hepatic hydrothorax ; 14 had complete relief of symptoms after TIPS, five patients improved but still required periodic thoracocentesis, whereas 5 others developed worsening liver function and died within 45 days(14). According to that study, TIPS is an alternative treatment but not for everyone with hepatic hydrothorax. In the present series liver transplantation was used as treatment for refractory hepatic hydrothorax.

In conclusion, the liver transplantation program in Thailand has been established for more than 15 years but the number of patients who undergo this procedure is still low due to lack of all resources. The outcome of liver transplantation in the present series is comparable to data from other international centers. The rate of rejection seems to be very low but the long-term survival of patients is still suboptimum. This may be secondary to poor selection of the candidates in the early period of the present study.

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รายงานผลการผ่าตัดเปลี่ยนตับในโรงพยาบาลจุฬาลงกรณ์

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การเปลี่ยนตับเป็นวิธีการรักษาที่ดีที่สุดสำหรับผู้ป่วยตับวายขั้นสุดท้าย โดยสามารถเพิ่มอัตราการรอดชีวิตได้ ในระยะ 10 ปีที่ผ่านมาประเทศไทยมีการผ่าตัดเปลี่ยนตับแต่ก็ยังไม่มากนัก โรงพยาบาลจุฬาลงกรณ์นับว่าเป็นโรงพยาบาลที่ทำการผ่าตัดเปลี่ยนตับเป็นแห่งแรกในประเทศไทยตั้งแต่ปี พ.ศ 2530 จนถึงปัจจุบันมีผู้ป่วยได้รับการผ่าตัดเปลี่ยนตับมากกว่า 30 ราย ซึ่งนับว่ามากที่สุดในประเทศไทย โดยในช่วงก่อนปี พ.ศ 2530 ทำไม่มากนัก แต่ในช่วงปี พ.ศ 2540–2545 นั้นทำไปทั้งหมด 20 ราย

เราได้ทำการวิเคราะห์ข้อมูลของผู้ป่วย 20 รายหลัง โดยแบ่งเป็น 2 กลุ่มตามข้อบ่งชี้ที่ใช้ในการเปลี่ยนตับ คือตับแข็งและมะเร็งตับ พบว่าอัตราการรอดชีวิตที่ 1 ปีต่างกัน คือ 64% และ 29% ตามลำดับ โดยพบว่าผู้ป่วยที่เสียชีวิตใน 1 ปีแรกในกลุ่มที่เป็นตับแข็งนั้น ส่วนใหญ่จะเสียชีวิตใน 3 เดือนแรก ส่วนอัตราการรอดชีวิตของผู้ป่วยโรคมะเร็งที่เปลี่ยนตับน้อยกว่าต่างประเทศนั้นอาจมีสาเหตุส่วนหนึ่งมาจากสถานภาพของผู้ป่วยในขณะก่อนผ่าตัดที่เป็นมาก และอยู่ในสภาพที่ยังไม่พร้อมนัก อย่างไรก็ตามในผู้ป่วยที่รอดชีวิตนั้น เราพบว่ามีอัตราการปฏิเสธตับแบบเฉียบพลันนั้นค่อนข้างต่ำคือ 25% ซึ่งเป็นข้อสังเกตที่น่าสนใจซึ่งต้องติดตามต่อไป

อัตราการรอดชีวิตที่ 1 ปี ในผู้ป่วยที่เปลี่ยนตับในช่วง พ.ศ. 2540–2542 เปรียบเทียบกับ พ.ศ. 2543–2545 คือ 33% และ 54% ตามลำดับ ซึ่งแสดงให้เห็นถึงพัฒนาการของผลการเปลี่ยนตับในประเทศไทยที่น่าพอใจ

โดยสรุปผลของการผ่าตัดเปลี่ยนตับในประเทศไทยนั้นอยู่ในเกณฑ์ที่น่าพอใจ ปัญหาที่สำคัญของการผ่าตัดเปลี่ยนตับในประเทศไทยก็คือ ความไม่เข้าใจของผู้บริจาคอวัยวะ ซึ่งทำให้อัตราการบริจาคค่อนข้างน้อย, การขาดแคลนบุคลากรที่มีความรู้ด้านนี้, การขาดเงินทุนและเครื่องมือที่เหมาะสม

คำสำคัญ : การผ่าตัดเปลี่ยนตับ, ประเทศไทย, อัตรารอดชีวิต

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