Outcome and Characteristics of Patients on the Liver Transplant Waiting List: Shiraz Experience

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ABSTRACT

BACKGROUND

The only curative therapy for end-stage liver disease is transplantation but due to a shortage of available donor livers the waiting list mortality is high. This study aimed to evaluate the outcome and characteristics of patients on the waiting list for liver transplantation in Shiraz, southern Iran during the period from April 2004 to March 2007.

METHODS

Medical records of all chronic liver disease patients ≥14 years that were on the waiting list for liver transplantation at the Nemazee Hospital Organ Transplant Center during April 2004 to March 2007 were reviewed. Hospital records were used to retrieve demographic, clinical and laboratory data. Records of the referring gastroenterologists provided information about the etiology and complications of liver disease. The patients were followed at the end of the study period by clinic visits or telephone contact.

RESULTS

There were 646 patients on the waiting list for liver transplant during April 2004 to March 2007. Hepatitis B was the most common etiology of liver disease (31.2%). Of those on the waiting list, 144 patients 22.3%) underwent liver transplant and 166 (25.7%) died while waiting for a transplant. The mean waiting period for transplant was 6.6 months. Receiving a transplant was correlated with the etiology of liver disease and Rh blood group ($p<0.05$) but had no significant association with gender or ABO blood type. Among non-transplanted patients, survival was lower in those who had a history of encephalopathy, SBP or uncontrolled ascites and in patients with a Child-Turcotte-Puph (CTP) class C and/or a Model of End-stage Liver Disease (MELD) score ≥15.

CONCLUSION

Hepatitis B virus is the most common cause of end-stage chronic liver disease amongst patients on the waiting list for liver transplant in Shiraz, southern Iran. Patients with a MELD score ≥15 particularly those with a history of SBP, hepatic encephalopathy or uncontrolled ascites are recommended for waiting list enrollment.

KEYWORDS

Liver transplant; Waiting list; Iran

INTRODUCTION

Liver transplantation is the only curative therapy for patients with end-stage liver disease. It gives excellent long-term survival and improves the quality of life including resumption of active social and professional activities as well as reproductive capacity.[1,2]

Before the era of liver transplantation, patients with end-stage liver disease had poor prognoses and low long-term survival rates.[3] The Model of End-Stage Liver Disease (MELD) scoring system is now the prevailing criterion for donor liver allocation.

It provides donor organs to listed patients with the highest estimated short-term mortality.[4,5] The numbers of referrals for liver transplantation have increased over the years but a shortage of available donor livers has led to a low overall rate of transplantation and high waiting list mortality.[6,7]

Most patients awaiting liver transplant are those with cirrhosis of the liver, who in our center, are referrals from different parts of the country. These patients may be considered as a representative of end-stage liver disease in our region and analysis of etiologic agents, presentation and outcome is helpful for planning of health system management, research and educational programs in our country. Nemazee Hospital, affiliated to Shiraz University of Medical Sciences in southern Iran, is the first hospital in the country to offer liver transplantation, which began in 1991.[8] It is currently the major liver transplantation center in the Islamic Republic of Iran.

In this study we aimed to evaluate the outcome and characteristics of those patients listed for liver transplantation in Shiraz, southern Iran during the period of April 2004 to March 2007.

MATERIALS AND METHODS

The medical records of all chronic liver disease patients aged 14 years or older who were listed for liver transplantation in Shiraz Organ Transplant Center at Nemazee Hospital between April 2004 and March 2007 were retrospectively reviewed. The criteria for listing included a MELD score of ≥15, a Child-Turcotte-Puph (CTP) score of 7 or more and/or documented variceal bleeding, hepatic encephalopathy, SBP, ascites, uncontrolled itching related to liver disease, recurrent cholangitis or growth retardation uncontrolled by the usual medical or non-medical measures.

Clinical judgment was also an important factor for establishing transplantation priority which was determined by committee members of the transplant team. Hospital records were used to retrieve demographic, clinical and laboratory data.

Records of the referring gastroenterologists provided information on the etiology and complications of liver disease. While the referring physicians continued to manage their patients, a simultaneous follow-up process was done at the transplant clinic. The follow-up was undertaken through clinical visits or by telephone contact at the end of the study period. Statistical analysis was performed using the SPSS computer software package (Version 11.5, Chicago, IL).

A *P*-value of 0.05 or less was considered to be statistically significant. Student t-test was used to analyze continuous variables and Chi-Square test was used to evaluate the correlation between different factors. Survival rates were calculated using the Kaplan-Meier method and were compared by the log-rank test.

RESULTS

There were 646 patients listed for liver transplant at our center between April 2004 and March 2007 [455 men (70.4%), mean age=40.3±12.7 years]. The most common etiology of liver disease was hepatitis B (31.2%) followed by cryptogenic cirrhosis (26.9%; Table 1). CTP scores were as follows: 95 patients (14.7%) were in class A (CTP score <7), 277 patients (42.9%) were in class B (CTP score=7-9) and 274 patients (42.4%) were in class C (CTP score ≥10).
Of the 646 patients on the waiting list, 144 (22.3%) underwent liver transplant (three cases with living donor liver transplantation) and 166 (25.7%) died while waiting for transplant. The waiting period for transplant, defined as the time from listing to transplantation, ranged from 0.03 month (21.6 hr) to 48.5 months with a mean of 6.6 months. As demonstrated in Table 2, liver transplants were performed

Table 1: Etiologies of liver disease among patients on liver transplant waiting list in Shiraz from April 2004 to March 2007.

Etiology	Number	%
Hepatitis B	201	31.2
Cryptogenic	174	26.9
Autoimmune hepatitis	86	13.4
Cholestatic liver disease (PBC or PSC*)	74	11.5
Hepatitis C	54	8.4
Wilson disease	26	4.0
Alcoholic	13	2.0
Buddchiari syndrome	9	1.4
Caroli's disease	4	0.62
Hemochromatosis	3	0.46
Hyperlipidemia	2	0.31

* PBC: Primary biliary cirrhosis, PSC: Primary sclerosing cholangitis

for 22.0% of the males and 23.0% of the females on the waiting list. There was no difference between the two groups (p=0.768).

Similarly, transplantation had no significant correlation with ABO blood groups (p=0.085).

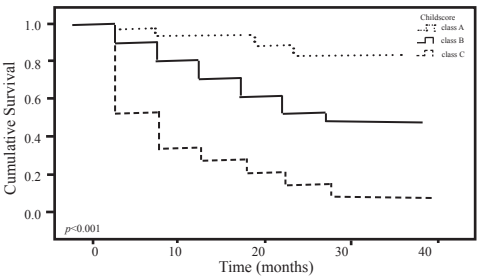

Fig. 1: Survival in non-transplanted patients on the liver transplant waiting list according to CTP class.

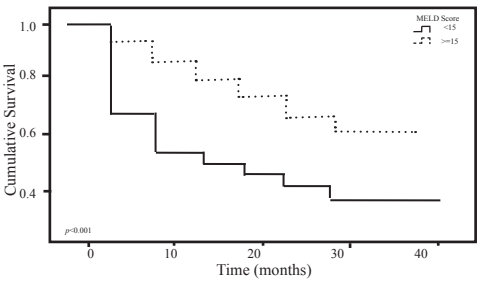

Fig. 2: Survival in non-transplanted patients on the liver transplant waiting list according to MELD score.

Table 2: Correlation between liver transplant and gender, blood group and Rh type.

		Transplanted N (%)	Not transplanted N (%)	Total N (%)	*p*-value
Gender	Male	100 (22.0)	355 (78.0)	455 (100.0)	0.768
	Female	44 (23.0)	147 (77.0)	191 (100.0)	
Blood Group	O	66 (27.7)	172 (72.3)	238 (100.0)	0.085
	A	38 (19.9)	153 (80.1)	191 (100.0)	
	B	31 (18.8)	134 (81.2)	165 (100.0)	
	AB	9 (17.3)	43 (82.7)	52 (100.0)	
Rh	Positive	138 (23.6)	446 (76.4)	584 (100.0)	0.012
	Negative	6 (9.7)	56 (90.3)	62 (100.0)	

On the other hand, a larger proportion of Rh-positive patients underwent liver transplantation when compared with the Rh-negative patients, and the difference was statistically significant (p=0.012).The mean survival time for patients who were not transplanted was 22.8 months. Among non-transplanted patients, cumulative survival decreased in those who had encephalopathy, SBP or ascites (p<0.001).

On the other hand, variceal bleeding had no effect on survival (p=0.62). Cumulative survival also varied significantly according to CTP class (p<0.001) and was lowest in class C (Figure 1). When non-transplanted patients were divided on the basis of MELD score, we observed that those with a MELD score of <15 survived longer, and the difference was highly significant (p<0.001, Figure 2).

DISCUSSION

Among the 646 patients who were listed for liver transplantation at our center from April 2004 until March 2007, the most common etiology of liver disease was hepatitis B (31.2%). This was in contrast with a Sumskiene et al. study in Lithuania where alcoholic liver cirrhosis was the most prevalent (28.9%) followed by viral hepatitis (17.8%).[9]

Due to the prohibition of alcohol by Islamic rules, alcoholic liver cirrhosis is not common in Iran. In another study, the majority of patients (72.1%) were listed for liver cirrhosis secondary to hepatitis C, hepatitis B or hepatitis B-hepatitis D viral infections.[10] The distribution of our patients according to CTP score was 14.7% in class A, 42.9% in class B and 42.4% in class C. Although only chronic liver disease patients with CTP class B or C should be listed for liver transplantation, some patients on the waiting list in our center were class A. These included class A cirrhotic patients with uncontrolled complications such as bleeding, severe pruritis or recurrent cholangitis, as well as non-cirrhotic patients with metabolic etiologies.

A total of 144 patients underwent liver transplants at the Shiraz Organ Transplant Center from April 2004 to March 2007 which showed a four-fold increase in the rate of transplants as compared with the April 1993 to November 2004 period when 140 liver transplants were performed in the same center.[11]

A number of factors could have contributed to this increase including an increase in the number of transplant team members and their experience, improvement in facilities, and more support from the university and the Ministry of Health.

The mean waiting time for transplant at our center was 6.6 months which was considerably shorter than the 23.1±7.5 months reported by Gheorghe et al. in Romania.[10] In the latter study, only 5.3% of the patients on the waiting list were transplanted and 20.2% died while waiting for transplants. In contrast, 22.3% of our patients underwent liver transplants and 25.7% expired while waiting.

Overall, it appears that the waiting period for a liver transplant at our center is acceptable but needs to be shortened.

Although it has been said that waiting time to transplant depends on patient's blood type,[12] we found no significant correlation between transplantation and ABO blood groups. Rh-positive patients, however, had a higher chance of undergoing transplants which is due to the availability of more donors for this group.

We found that the mean survival time was 22.8 months in patients who were not transplanted. According to Sumskiene et al., correct timing of liver transplantation could reduce waiting list mortality and improve post-transplant survival.[9] Disease severity at the time of listing is another important predictor of waiting list mortality.[13]

We observed that among non-transplanted patients, cumulative survival was lower in patients with encephalopathy, SBP or ascites but was not different in those with variceal bleeding.

Therefore, when allocating donor livers to patients on the waiting list, higher priority should be given to encephalopathy, SBP and ascites as compared to bleeding. Nowadays, the treatment for esophageal variceal bleeding has improved dramatically by endoscopic modalities such as rubber band ligation and Histoacryl injection sclerotherapy which are performed routinely in this country.

Comparison of survival functions among non-transplanted patients shows that survival decreases from class A to B to C (Figure 1).

Similarly, cumulative survival was significantly higher in patients with MELD scores <15 when compared to the group with MELD scores ≥15 (Figure 2). Other authors have also reported the significant influence of both CTP scale and MELD score evaluation for prediction of patients' mortality.

MELD score showed discriminate ability among patients who survived and those who died.[9] The lower survival among the non-transplanted patients with MELD score ≥15 in our study confirms the "MELD score ≥15" as a criterion for liver transplantation at our center. Still, patients

with MELD score<15 should be considered on an individual basis for selection for the waiting list.

CONFLICT OF INTEREST

None declared.

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