Original Article

Post Liver Transplantation Survival and Related Prognostic Factors among Adult Recipients in Tehran Liver Transplant Center; 2002–2019

Elham Madreseh, PhD Candidate[1]; Mahmood Mahmoudi, PhD[1]; Mohssen Nassiri-Toosi, MD[2]; Taban Baghfalaki, PhD[3]; Hojjat Zeraati, PhD[1*]

[1]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[2]Liver Transplantation Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Statistics, Faculty of Mathematics sciences, Tarbiat Modares University, Tehran, Iran

Abstract
Background: Liver transplantation is a standard treatment for patients with end-stage liver disease (ESLD). However, with increasing demand for this treatment and limited resources, it is available only to patients who are more likely to survive. The primary aim was to determine prognostic factors for survival.
Methods: We collected data from 597 adult patients with ESLD, who received a single organ and initial orthotopic liver transplantation (OLT) in our center between 20 March 2008 and 20 March 2018. In this historical cohort study, univariate and multiple Cox model were used to determine prognostic factors of survival after transplantation.
Results: After a median follow-up of 825 (0–3889) days, 111 (19%) patients died. Survival rates were 88%, 85%, 82% and 79% at 90 days, 1 year, 3 years, and 5 years, respectively. Older patients (HR = 1.27; 95% CI: 1.01–1.59), presence of pre-OLT ascites (HR = 2.03; 95% CI: 1.16–3.57), pre-OLT hospitalization (HR = 1.88; 95% CI:1.02–3.46), longer operative time (HR = 1.006; 95% CI: 1.004–1.008), post-OLT dialysis (HR = 3.51; 95% CI: 2.07–5.94), cancer (HR = 2.69; 95% CI: 1.23–5.89) and AID (HR = 2.04; 95% CI: 1.17–3.56) as underlying disease versus hepatitis, and higher pre-OLT creatinine (HR = 1.67; 95% CI: 1.10–2.52) were associated with decreased survival.
Conclusion: In this center, not only are survival outcomes excellent, but also younger patients, cases with better pre-operative health conditions, and those without complications after OLT have superior survival.
Keywords: Ascites, Dialysis, Hepatocellular carcinoma, Tehran Liver Transplant Center
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Introduction

End-stage liver disease (ESLD) is categorized into two main subgroups: acute liver failure (ALF) and chronic liver disease or cirrhosis. The former is a rare and rapidly progressive disorder, whereas the latter is a more common condition, causing damage to liver over time.[1]

ESLD is extremely costly in terms of human suffering, medical visits, and premature loss of productivity. The incidence of ESLD is increasing and in the absence of liver transplantation, it confers a very high fatality rate worldwide every year.[2]

Orthotopic liver transplantation (OLT) using donation after brain death, was initially reported in 1963 by Thomas Starzl.[3] After the discovery of the immunosuppressant cyclosporine in 1971 and the agreement seminar organized by the US National Institute of Health in 1983, liver transplantation (LT) was accepted as a standard treatment for ESLD.[4] LT provides excellent long-term survival, and improves the quality of life and professional activities.[5,6]

In Iran, the national program for LT was commenced in Shiraz in 1993,[7] and in 2002 in Tehran Liver Transplant Center (TLTC). Since 2005, all hospital-based costs are covered by the government for all Iranian patients, but costs related to immunosuppressive drugs after liver transplant are not covered by any health insurance.

In 2016, the annual rate of deceased LT was estimated to be 6.39 per million population worldwide; the United States and China, with the largest number of transplants, i.e. 7496 and 3264, respectively, ranked first and second.[8] Also, Iran's contribution, as the ninth country in the world and the first in the Middle East, was 770 liver transplants.[8] These transplants have been done at eight centers, but most of them had fewer than 100 patients per year.

TLTC is located at the Imam Khomeini Hospital Complex, the first LT center in Tehran (the capital of Iran), and the second largest in Iran; and it operates under the supervision of Tehran University of Medical Sciences. The first liver transplant in TLTC was performed in

*Corresponding Author: Hojjat Zeraati, PhD; Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-21-88989126, Fax: +98-21-88989127, Email: zeraatih@tums.ac.ir

2002. So far, more than 700 consecutive LTs have been carried out by the same retrieval and transplant team with minimal changes in the composition and roles of the team members. The center volume is increasing; 128 transplants were performed in 2016 only and this number has been higher every year since then. According to a published article by Macomber et al, LT programs with more than 75 LTs per year were considered as a high-volume transplant centers, had lower morbidity and mortality rates than lower-volume centers, and were also more cost-efficient.[9] Therefore, TLTC is considered a high-volume transplant center.

According to the data of the International Registry in Organ Donation and Transplantation, in Iran, like most countries, liver is the most common transplant organ after the kidney. In 2017, 33.5% of the deceased donors were assigned to LT – a significant increase compared to 17.1% in 2002. Also, the demand for this organ has increased from 0.7 per million population in 2002 to 11.43 in 2017.[10] Therefore, with increasing demand for LT and limited resources, it is available only to patients who are more likely to survive, given a set of characteristics at the time of transplantation. Some scoring systems have been developed based on such characteristics for creating patient lists for LT.

Transplant success is evaluated through patient survival as the most common outcome. Survival rates range from 79.5% to 84.6% during the first year, and 65% to 79.1% at five years after transplantation.[8] The survival rates for recipients from deceased donors in Shiraz were 74.0% at 1 year and 70.0% at 5 years.[11] Improving the outcomes of transplantation is not only related to graft dysfunction, but also, depends on modifiable factors associated with late mortality.[12,13] According to research findings, several sets of factors affect the survival of LT patients including recipient and organ donor characteristics, transplant center–related factors and sociocultural and economic factors.[14-20]

Despite improvements in surgical techniques and postoperative care, including availability of immunosuppressant drugs, more research is still necessary on the factors associated with short- and long-term outcomes for optimal use of the donated organs in the Iranian population. The current investigation analyzes nearly one decade of experience by the same team in a single center. In this center, the model for End-Stage Liver Disease (MELD) scoring system was used for organ allocation.[21] As a prevailing criterion, it provides donor organs to listed recipients with the highest estimated short-term mortality before LT.[22-24]

In the current study, short- and medium-term outcomes of OLT, and factors affecting survival are analyzed. Also, the incidence and scope of post-OLT complications are determined.

Materials and Methods
Patients
In this single-center historical cohort study, the information of all patients undergoing OLT was collected from their medical records. All recipients younger than 18 years old (n = 27), re-transplantation patients (n = 38), and combined transplant patients (n = 6) were excluded from the study. As the first 6 years of TLTC were considered as an establishment period for the transplant team, the patient information from this period was not included in the analyses (n = 14). In total, 597 adult patients who received a single organ and initial OLT in TLTC between 20 March 2008 and 20 March 2018 were included in the analyses (Figure 1). All patients were followed by regular visits or phone calls until death or the end of the study period (20 January 2019). Right censoring occurs when a subject leaves the study before death occurs, or the study
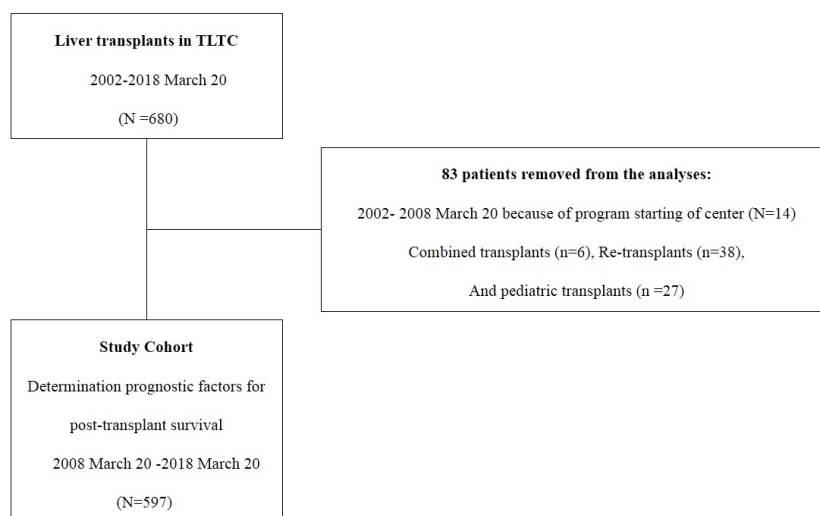

Figure 1. Flow Diagram Showing the Patients in the Study Defined Cohorts. TLTC: Tehran Liver Transplant Center.

ends before the event has occurred. Patients who were lost to follow-up were considered as right censoring at their last visit date (n = 33). Therefore, the starting point of the patient's survival analysis was the time of the LT, while the patient's death, last visit or end of study were considered as the endpoint.

Study Endpoints

Primary endpoints were overall survival after LT and the evaluation of related prognostic factors. Secondary endpoints were to determine the incidence and scope of postoperative complications such as cause of death, recurrence, rejection, renal failure, dialysis, and CMV infection.

Variables

Recipient, donor, laboratory, operative, and postoperative variables that were obtained from our database and had no missing, or <15% missing data, were used. Acute cellular rejection was diagnosed based on histologic criteria. Diabetes mellitus (DM) was defined as a diagnosis that required treatment with insulin or oral hypoglycemic drugs. Renal failure was defined as serum creatinine ≥ 2 mg/dL.[13] The MELD equation used to calculate the severity score was as follows[25]:

$$Meld = 9.6 \times \ln(creatinin(mg/dl)) + 11.2 \times \ln(INR) + 3.8 \times \ln(bilirubin(mg/dl)) + 6.43$$

The Child-Pugh score was evaluated using five parameters: ascites, encephalopathy, bilirubin, prothrombin time and albumin.[26] We adopted an 8-category liver disease classification system and definitions similar to that used by Roberts et al.[27]

Ascites was detected by sensitive imaging studies such as ultrasonography and physical examination. Furthermore, encephalopathy was defined as appearance of signs of occasional forgetfulness, insomnia or distorted sleep pattern.[28] Details about surgical procedures and their related factors in TLTC are provided in previous reports.[29]

According to annual liver data reports,[30] we used the 5-category cause of death among deceased liver donors including: anoxia, cerebrovascular accident, head trauma, central nervous system tumor and other causes.

Statistical Analysis

Categorical variables were summarized as frequencies (percentages). Continuous variables were described as median (range), or mean (±SD). Missing values were imputed by the Markov chain Monte Carlo method, allowing for arbitrary missing data patterns. Reverse Kaplan–Meier method was applied to estimate the median survival time. Kaplan-Meier estimates were used to calculate survival curves.

All considered factors were tested using univariate and multiple Cox proportional hazard (PH) analysis. All variables that were significant in the univariate model (*P* < 0.25) or those clinically important were entered into the multiple model. A stepwise approach based on improvement in Akaike's information criterion (AIC) was used for variable selection.[31]

PH assumption was tested using independence between the scaled Schoenfeld residuals and time. To determine whether any of the continuous variables exhibited non-linearity, the Martingale residuals test was used. According to the results obtained in this test, some variables were log transformed (INR, bilirubin, creatinine) and some were squared (age).[32] The prognostic accuracy of the final model was calculated using time-dependent/dynamic area under receiver operating characteristic curves [AUROC (t)]. Statistical significance was set at 0.05. All statistical analyses were performed using the R3.4.0 statistical software.

Results

Recipients, Donors and Perioperative Characteristics

The mean waiting time for transplant was 318 ± 451 days. The male to female ratio of patients and donors was 1.5:1 and 2.03:1, respectively. The mean ± SD age of recipients and their BMI at transplant was 45 ± 12 years and 25 ± 4 kg/m². Moreover, 24%, 30%, 45%, and 1 % of the patients were 18–34 years, 35–49 years, 50–64 years, and ≥65 years old, respectively. The median donor age for these age groups of recipients was 31 years, 34 years, 36 years, and 37 years, respectively (*P* = 0.079).

Most patients had blood group A (36.2%) and O (35.2%). Overall, 74% of transplanted patients had no comorbidity before LT. Only 12% of patients were hospitalized before LT; however, 76% of them had ascites.

The mean ± SD of MELD scores was 20.5 ± 5.6, and patients were classified into four groups according to their MELD at transplant. Respectively, 6% and 7% of the patients had MELD scores <15 and >30. Categorization of the patients based on the CHILD scoring system showed that 4%, 34%, and 62% of the patients were in class A, B, and C, respectively.

The most common indications for OLT were autoimmune and cryptogenic cirrhosis (AID, 38%), hepatitis B virus (HBV, 11%), hepatitis C virus (HCV, 11%), primary sclerosing cholangitis (PSC, 10%), metabolic liver disease (9%), cancer (7%), ALF (5%), primary biliary cirrhosis (PBC, 3%), and other liver diseases (4%) in adults.

The patients' clinical presentation at the time of transplant was different, and they were mostly not in the hospital at the time of transplant (88%).

Regarding the donors, the most common causes of brain death were head trauma (45%), cerebrovascular accident/stroke (29%), anoxia (6%), central nervous system tumor (3%), others rare causes (6%) and unknown causes (12%).

Most donors were male (69%). The mean ± SD duration of brain death and length of stay in ICU were 4 ± 3 days and 5.5 ± 4 days, respectively.

The mean ± SD duration of operation, cold and warm ischemic times were 230 ± 80, 295 ± 66 and 27 ± 17 minutes, correspondingly. More summaries are shown in Table 1.

In TLTC, the number of LTs increased from 13 in 2008 to 102 in 2017; however, the average waiting time was 470 ± 557 and 350 ± 481 days, respectively (Figure 2). This decrease was not statistically significant ($P = 0.205$). Also, the most common cause of transplantation in 2008 and 2017 was hepatitis and autoimmune/epithelial diseases, respectively

Complications, Survival Outcomes and Related Factors

The mean duration of post-transplant hospitalization was 15 ± 10 days. Moreover, 421 (71%) of the patients showed at least one early or late complication, such as acute cellular rejection [181 (31%)], CMV infection [149 (26%)], diabetes complication [114 (19%)], renal complication [207 (36%)], dialysis [43 (7%)], and recurrence [68 (11%)] after the transplantation, while no complications were found in 176 (29%) patients.

After a median follow-up of 825 (0–3889) days, 111 (19%) patients died due to early or late complications and rejection; of those, 60% were male. The most common causes of death were sepsis (36%), recurrence (14%), bleeding (10%), renal failure (5%), other related causes (21%) and unknown causes (14%).

It should be noted that 69 (62.2%), 16 (14.4%), 15 (13.5%) and 7 (6.3%) of the deaths occurred in 90 days, 1 year, 3 years and 5 years after transplantation, respectively.

In the univariate analysis, donor and recipient age, pre-

Table 1. Patients' Survival Status at the End of Follow-up According to Pre-transplantation Characteristics of Recipient, Donor and Surgical Factors, Tehran Liver Transplant Center (2008-2019)

Variables, Mean ± SD or No. (%)	All OLT n = 597	Survival Status		Unadjusted* HR (95% CI)
		Alive n = 486 (81%)	Died n = 111 (19%)	
Age (y)	44.81±12.5	44.34±12.53	46.88±12.21	**1.02 (1.004- 1.04)**
Sex (male)	356 (60%)	289 (81%)	67 (19%)	1.03 (0.70-1.51)
BMI (kg/m²)	25.12±4.15	24.98±4.01	25.71±4.69	1.03 (0.99- 1.09)
Waiting time (day)	314±448	312±445	319±465	1.001 (0.99-1)
Diseases				
HCV/HBV (reference)	128 (21%)	110 (86%)	18 (14%)	-
ALF	28 (5%)	23 (82%)	5 (18%)	1.87 (0.69- 5.06)
PBC/ PSC	78 (13%)	67 (86%)	11 (14%)	1.07 (0.50- 2.27)
ALD	14 (2%)	11 (79%)	3 (21%)	1.63 (0.48- 5.55)
AID	227 (38%)	181 (80%)	46 (20%)	1.55 (0.89-2.67)
HCC	42 (7%)	32 (76%)	10 (24%)	1.98 (0.91- 4.31)
Metabolic liver disease	54 (9%)	45 (83%)	9 (17%)	1.34 (0.60-2.98)
Other	26 (4%)	17 (65%)	9 (35%)	3.58 (1.60 -8.0)
Precondition (hospitalized)	72 (12%)	48 (67%)	24 (33%)	**2.96 (1.86-4.69)**
Pre-creatinine** (mg/dL)	1.07±1.40	1.03±1.48	1.21±1.00	**1.92 (1.39-2.64)**
Pre-total bilirubin** (mg/dL)	6.55±8.33	6.47±8.42	6.88±8.00	0.97 (0.77-1.23)
Pre-INR**	1.97±0.83	1.95±0.79	2.06±0.96	1.38 (0.77-2.47)
Pre-prothrombin time (s)	18.25±4.6	18.0±4.0	19.19±5.0	**2.98 (1.32-6.72)**
MELD score	21±5	20±5	22±6	**1.06 (1.03-1.09)**
Pre-ascites (yes)	459 (77%)	364 (79%)	95 (21%)	**1.83 (1.07-3.13)**
Cytomegalovirus (yes)	149 (25%)	128 (86%)	21 (14%)	0.68 (0.42-1.11)
Rejection (yes)	181 (30%)	150 (83%)	31 (17%)	0.88 (0.58-1.36)
Diabetes mellitus (yes)	114 (19%)	92 (81%)	22 (19%)	1.06 (0.66-1.69)
Dialysis (yes)	43 (7%)	16 (37%)	27 (63%)	**7.58 (4.82-11.91)**
Donor sex (male)	402 (67%)	326 (81%)	76 (19%)	1.04 (0.68-1.61)
Donor age (year)	35.0±13.0	34.59±12.68	36.58±12.33	**1.01 (0.99-1.03)**
length of stay in ICU (day)	5.5±3.5	5.0±3.0	6.0±3.0	1.03 (0.98-1.09)
Duration of brain death (day)	4.3±3.0	4.0±3.0	5.0±3.0	**1.06 (1.004-1.12)**
CIT (min)	295±66	291±62	313±77	**1.004 (1.001-1.006)**
Operative time (min)	302±80	293±68	344±110	**1.005 (1.003-1.007)**

OLT: orthotopic liver transplantation; HR: hazard ratio; CI: confidence interval; BMI: body mass index; ALF: Acute liver failure; PBC: Primary biliary cirrhosis; PSC: Primary sclerosing cholangitis; ALD: Alcoholic liver disease; AID: Autoimmune and cryptogenic disease; HCV: hepatitis C virus; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; INR: international normalized ratio; MELD: model of end-stage liver disease; CIT: cold ischemic time.
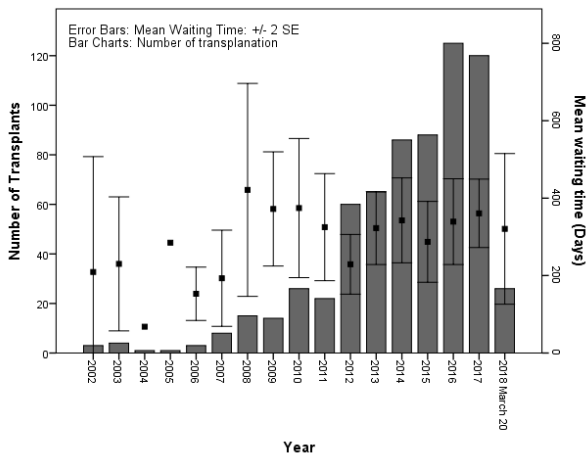* Univariate cox proportional hazard model; ** In natural log scale for modeling.

Figure 2. Bar Chart Showing the Number of Liver Transplantation and Error Bar Showing the Mean Waiting Time in Tehran Liver Transplant Center from 2002 to 2018.

Table 2. Risk Factors for Patient Failure after Liver Transplant by the Results of Multiple Cox PH Regression Model, Tehran Liver Transplant Center; 2008-2019

Variables	Adjusted HR	95% CI	P Value[a]
Age*	1.27	1.01-1.59	0.038
Pre-ascites (yes)	2.03	1.16-3.57	0.014
Pre-condition (hospitalized)	1.88	1.02-3.46	0.042
Pre-prothrombin time**	2.39	0.95-6.04	0.064
Operative time	1.006	1.004-1.008	<0.001
Post-dialysis (yes)	3.51	2.07-5.94	<0.001
Diseases			
HCV/HCV (reference)	-	-	-
ALF	2.18	0.69-6.89	0.185
PBC/ PSC	1.40	0.61-3.19	0.427
ALD	0.77	0.20-3.03	0.712
AID	2.04	1.17-3.56	0.012
HCC	2.69	1.23-5.89	0.013
Metabolic Liver Disease	2.07	0.92-4.69	0.079
Other	4.37	1.84-10.4	<0.001
Alcohol consumption history (yes)	1.79	0.94-3.41	0.075
Pre-creatinine**	1.67	1.10- 2.52	0.016
Pre-comorbidity (yes)	1.51	0.87-2.61	0.142
Waiting time	1.0004	1.00-1.001	0.060
Post-diabetes mellitus (yes)	0.64	0.35-1.17	0.144

HR: hazard ratio; CI: confidence interval; BMI: body mass index; ALF: Acute liver failure; PBC: Primary biliary cirrhosis; PSC: Primary sclerosing cholangitis; ALD: Alcoholic liver disease; AID: Autoimmune and cryptogenic disease; HCV: hepatitis C virus; HBV: hepatitis B virus; HCC: hepatocellular carcinoma.
[a] Final multivariate cox PH model based on stepwise selection variable and AIC criteria; * In square scale; ** In natural log scale.

OLT ascites, pre-OLT condition, pre-prothrombin time, donor brain death duration, cold ischemia time, length of operation, patients' renal problems and MELD score were found to be effective factors on the patients' survival (some results are not represented). These significant variables along with those clinically important, were considered in multiple models.

In the multiple analysis of the 12 prognostic variables selected for the final Cox model, only the recipient's age (in square scale), pre-OLT ascites, pre-OLT condition, length of operation, existence of post-LT dialysis, etiology/ underlying diseases, and pre-OLT creatinine (in log scale) were the significant variables (Table 2).

The hazard of death after LT was two-fold among patients with autoimmune disease (AID) as compared with hepatitis patients (HR = 2.04, 95%CI [1.17-3.56]). Also, the hazard of death increased by 80% when patients had been hospitalized pre-OLT. The hazard ratios of those who had pre-OLT ascites and post-OLT dialysis were 2.01 and 3.51, respectively.

The mortality rate of patients with old age, high creatinine and high operative time was higher than those with lower values. The rest of the results are presented in Table 2. Furthermore, the adjusted survival rates were estimated as: 0.88% at 90 days, 85% at 1 year,82% at 3 years, and 79% at 5 years.

Dynamic AUC versus time under the PH assumption was estimated. Since the AUC values were more than 0.7 until 5 years, our final model is accurate for predicting the risk of mortality until this time. The area under the ROC curves (AUC) for predicting the risk of mortality at 1 year, 3 year and 5 years after LT was 81.08%, 78.48% and 71.98%, respectively (results not shown).

Discussion

In the current shortage of organs for transplant, it is important to identify patients who benefit the most from liver transplantation, and to discover the risk factors associated with poor outcome.

In this study, the effect of recipient and donor characteristics, perioperative factors and some complications on patient survival in TLTC are investigated. According to Figure 2, while the number of LTs has increased over time, the average waiting time in the TLTC has declined. This demonstrates that improvements have been made in the management of organ allocation in recent years in this center, especially after 2005 when liver transplant became free of charge for patients in Iran. Currently, the mean interval between listing and transplantation is under 400 days, which is longer than the European Liver Transplant Registry.[33,34]

TLTC is a well-established center in the Eastern Mediterranean region. According to our findings, short- (1 year) and median-term survivals (5 years) are 89% and 84%, respectively. Thus, survival after liver transplantation in TLTC is excellent, which is similar to some studies.[33,34] The main findings of the final multiple Cox model represented that recipient's age, underlying diseases, pre-OLT ascites, precondition condition and creatinine, length of operation and post-LT dialysis were significantly related to patient survival. According to this model, other factors such as pre-OLT prothrombin time, history of

alcohol consumption, pre-OLT comorbidity status, post-LT diabetes, and waiting time to LT were not associated with survival. As the results revealed, the accuracy of this model was high.

According to similar studies,[12,35,36] and our results in the univariate and multiple analysis (Table 1), recipient's age was identified as a risk factor which affects mortality after transplantation. This may be due to physiological status; therefore, diagnosing and transplanting at younger age are important in improving patient survival. So, one may consider adding age as a variable in the criteria for determining priority of transplantation. The upper age limit for patients undergoing transplantation in TLTC is 70 years; this is similar to other LT centers during the past three decades.[37-40]

Compared with older donors, the younger were more commonly male and traumatized. Advanced donor age was identified as a risk factor only in our univariate analysis. The death risk of patients who received liver from donors in the age group of 50–64 years was 5 times more than those under 18 years old. Therefore, the effect of aging on various organs, such as liver, reduces their functions; but with adjusting in the multiple model, donor age was not significant. This finding is in contrast with numerous previous studies which demonstrated a significantly decreased survival in recipients of older donations within a large study.[15,17,27,35,41-43] Setting an appropriate cut-off point for recipients and donors age could lead to better allocations; more research is required in this regard.

In this center, the etiology of liver disease was mostly AID (38%), while approximately one quarter of LTs performed in Europe and the United States were due to autoimmune liver diseases.[44] Hepatitis (B and C) was the second most common cause of transplantation in this study, while it was considered as the most common cause in some studies.[34] Contrary to the Western world,[45] due to religious beliefs, alcoholic liver cirrhosis was not a common indication for liver transplant in our study. Different classification of disease may have led to these various results. In the present study, the liver disease classification system used by Dawwas et al was employed.[46]

As other studies show, post liver transplant survival was strongly related to underlying diseases.[11,27,42,46,47] In this study, patients with autoimmune-cryptogenic cirrhosis (about 2-fold) and HCC (about 3-fold) had poorer survival compared to those with hepatitis. Since the recurrence of autoimmune liver disease after LT is prevalent and may be asymptomatic early on, biopsies could be used to prevent poor outcomes. However, hereditary background and unknown factors still exist in these individuals even after LT. These results were in contrast with some studies which demonstrated that LT was associated with excellent patient survival in subjects with autoimmune liver diseases.[48]

The MELD score is a controversial matter in patient survival. In most studies, MELD score was only effective on short-term survival, and it was indicated that high MELD score was an independent risk factor for poor outcomes after LT.[11,17,49-51] This finding was confirmed in our univariate analysis; however, after adjusting for the effect of other variables, this score was not significant because the MELD score was valuable for identifying the patients with the worst conditions, and might not be a suitable survival predictor. Furthermore, according to previous studies, it has been shown that patient prognosis is more related to clinical parameters than laboratory data and MELD score.[15,52,53]

However, presence of ascites before transplant was a significant factor for post-OLT survival. Since ascites can cause hyper-fibrinolysis in advanced liver disease,[54,55] and also, severe liver disease is a known risk factor for developing hyper-fibrinolysis,[56] the accuracy of prediction may be increased when ascites is included in the MELD index.

The study by Horvatits et al[57] showed that postoperative dialysis was associated with increased mortality after LT. Also, in our study, dialysis patients had a higher mortality rate (3.5-fold), possibly because they had more medical comorbidities. In addition, similar to other studies, high creatinine levels at the time of transplantation increased the risk of death.[53]

As noted in the results, the risk of death after transplantation increased 0.6% for every hour of operative duration. This may be due to the complexity of the surgery which some studies have also suggested.[11,17,43]

Similar to the study by Roberts et al,[27] in our research, if patients were admitted for hospitalization before surgery, they were 88% more likely to die than others. This could be due to the physical condition of patients, which is more fragile, and this situation usually persists after surgery and reduces patient survival.

The cold ischemic time had a significant effect on survival only in the univariate analysis; this finding was seen in some other studies, as well.[17,35,42,58-60]

Other variables, such as post-LT diabetes, waiting time to LT, Pre-OLT prothrombin time, history of alcohol consumption and pre-OLT comorbidity, existed in the final model but were not statistically significant.

Our study had some limitations. Overall, there are many genetic variables which can affect patient survival, but we did not consider them due to the retrospective nature of the study. Since almost all donors and recipients resided in the same region, often the northern part of Iran, it could be assumed that their genetic information matches, and has little influence on the final results.

Different individual characteristics, various clinical status, and unequal experience of physicians and centers lead to different findings in various studies. Therefore, caution should be taken when extrapolating our results to other LT patient populations.

From the statistical viewpoint, since heavy censoring

existed at the end of the study (plateau form of Kaplan–Meier plots), and also, trend of AUC values decreased over time, our final model was not efficient in estimating the risk of mortality in the long-term. Thus, for estimating long-term survival (10 years and more), it is suggested to use more data or to apply advanced statistical models.

In conclusion, in 2000, TLTC started the LT program. In this study, we presented one of the largest reported single-center experiences with OLT in Iran. Many barriers have been overcome in this center to achieve high survival rates after LT; thus, it is expected that LT survivors can increase over the next decade. In summary, younger patients, cases with better health conditions before surgery and those without complications after OLT have superior post-transplantation survival. Furthermore, there is variability in the survival of patients with different underlying liver diseases.

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