

# Quality of Life and Its Determinants in Liver Transplantation Candidates: A Missed Link in Liver Care Program during the Waiting Time for Liver Transplantation

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## What's Known

- In the patients with a model for end-stage liver disease (MELD) score of less than 15, health-related quality of life (HRQOL) was higher than those with a score higher than 15.
- The physical component of HRQOL did not differ significantly between the patients with normal and high body mass index (BMI) in the pre-transplantation stage.
- The diabetic and non-diabetic patients had comparable HRQOL scores after liver transplantation (LT).

## What's New

- Job status, anemia, weight loss, and diabetes mellitus (DM) are stronger determinants for HRQOL than the MELD score in the LT candidates.
- The physical component of HRQOL had a lower score than its mental component in the LT candidates.
- For the first time, the association between weight loss/drug use with HRQOL in the LT candidates was investigated.

## Abstract

**Background:** The health-related quality of life (HRQOL) in the before liver transplantation (LT) stage has not been studied as much as that after the LT stage. We aimed to assess HRQOL and its determinants before the LT stage.

**Methods:** As a cross-sectional study, HRQOL of all adult patients (n=632) referred to the LT center of Shiraz, Iran in 2018-2019 were assessed. Demographic, socioeconomic, medical, and paraclinical data were requested. Physical (PCS) and mental (MCS) aspects of HRQOL were assessed using the SF36 questionnaire. Univariable, multivariable (linear regression), and confirmatory factor analysis were performed utilizing SPSS 20 and Mplus 6.1 software. P value<0.05 was considered to be significant.

**Results:** The mean age of the patients was 47.6±12.3 years, while 414 (65.6%) were men and the mean score of model for end-stage liver disease (MELD) was 18.36±5.58. The mean score of QOL, PCS, and MCS was 50.01±21.73, 46.23±23.23, and 53.78±23.91 (out of 100), respectively. Vitality had the most association with HRQOL, while role limitations had the lowest. The multivariable analysis revealed that unemployment (P<0.001), anemia (P=0.005), weight loss (P=0.005), diabetes mellitus (DM) (P=0.009), low MELD score (P=0.027), and drug use (P=0.03) were the significant determinants of HRQOL, respectively.

**Conclusion:** The present study showed that HRQOL in the LT candidates was at the intermediate level, while their PCS and MCS are at the low and moderate levels, respectively. Furthermore, physical performance, job status, anemia, weight loss, MELD score, DM, and drug use should be considered as the significant determinants of HRQOL in the LT candidates.

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**Keywords** • Quality of life • Liver • Transplantation • Waiting list

## Introduction

The liver is the second most transplanted organ.<sup>1, 2</sup> Liver transplantation (LT) has become the best treatment for patients with end-stage liver disease (ESLD).<sup>1-3</sup> During a period of 23

years, from 1993 to 2016, 4,485 LTs were performed at six centers (mainly Shiraz) in Iran. In the performed LTs, 4106 of the donors were deceased and 379 were living donors; meanwhile, there were 3553 adult and 932 pediatric recipients.<sup>4</sup> In 2017, 8082 individuals in the United States of America underwent LT, while 13885 people were on the waiting list for LT.<sup>5</sup> On the other hand, due to the increasing prevalence of non-alcoholic fatty liver disease (NAFLD) as the most common etiology of chronic liver disease, the need for LT increased faster than the growing facilities for LT.<sup>6-9</sup> Therefore, the ensued supply-demand imbalance in LT led into a long waiting list in the centers around the world.<sup>10, 11</sup> Consequently, it may cause the death of a considerable proportion of patients while being on the waiting list,<sup>12</sup> or suffering from psychological and mental stress,<sup>13</sup> and a dramatic reduction in the quality of life (QOL).<sup>14, 15</sup>

As a multidimensional concept, health-related quality of life (HRQOL) includes mental assessments of the areas related to the physical, emotional, psychological, and social functioning in the bed of a disease and its treatment.<sup>16</sup> Therefore, with improvements in the patient and the graft survival after LT, QOL of the recipient has become an important focus of patient care and clinical outcomes.<sup>17</sup> Moreover, some evidence revealed that higher HRQOL predicts lower mortality in these patients.<sup>18</sup> Reciprocally, factors, such as severity and the complications of the chronic liver diseases decline HRQOL.<sup>19-22</sup>

Therefore, assessing HRQOL and its determinants in the LT candidates is important, since some of these patients die, while being on the LT waiting list. On the other hand, numerous studies have investigated HRQOL after LT or compared it in the after LT with the before LT to measure the effect of LT on HRQOL while the objective of a few others was to only measure HRQOL in the patients during their waiting time for LT. This study aimed to measure the baseline HRQOL and its determinants in the LT candidates during their waiting time for LT to detect the factors (especially modifiable ones) other than LT, possibly influencing the patients' HRQOL.

## Methods

### Study Design

In this cross-sectional study, all adult patients with ESLD referred to Shiraz University of Medical Sciences (SUMS) affiliated LT center (n=632) in 2018-2019 were included and HRQOL of all of them was assessed once during their first attendance in the LT center when being

registered in the LT waiting list.

Written informed consent was obtained from all the subjects, and voluntary participation in all stages of this study was respected. The privacy of the participants was assured in all the steps of the study, including interview, data gathering, recording, analyzing, and reporting. The protocol of the current study conforms to the ethical guidelines of the 1975 declaration of Helsinki as reflected in a prior approval by the SUMS Ethics Committee with the registered number of IR.SUMS.REC.1399.233.

### Studied Independent Variables

A comprehensive checklist was designed by a team of gastroenterologists, liver transplant experts, and biostatistics experts. This form consisted of demographic and socioeconomic characteristics, medical history, and paraclinical data, such as ultrasonography findings. In order to gather the demographic and socioeconomic information of the patients, in-person interviews were conducted in the LT clinic of SUMS and the rest of the patients' information was extracted from their medical records. The demographic and socioeconomic characteristics are composed of age, gender, marital status, being or not being the head of the family, family dimension (number of family members), level of education, living place (urban versus rural), job status, homeownership status, owning a car, and having complementary insurance. The medical history consisted of body mass index (BMI), tobacco smoking, alcohol consumption, drug use, weight loss, ascites (detected via abdominal ultrasonography), and dialysis. The medical history also comprised being the known cases of cryptogenic cirrhosis, diabetes mellitus (DM), hyperlipidemia, hepatitis C virus (HCV), hepatitis B virus (HBV), autoimmune hepatitis, primary biliary cholangitis (PBC), primary sclerosing cholangitis, Budd-Chiari, Non-alcoholic steatohepatitis, and hepatocellular carcinoma (HCC). The gathered paraclinical data were related to the enrollment of patients for less than one week in the LT waiting list and consisted of the MELD score (used for the allocation of LT, consisting of three components, including bilirubin, creatinine, and the international normalized ratio of prothrombin time (PT), red blood cell (RBC) count, white blood cell (WBC) count, hematocrit (HCT), mean corpuscular hemoglobin concentration, albumin (Alb), alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, serum blood urea nitrogen (BUN), serum potassium, and serum sodium. The findings of the last liver ultrasonography of the patients were also extracted.

### Assessment of QOL

The 36-Item Short Form Health Survey (SF-36) is a popular questionnaire widely applied to measure HRQOL.<sup>23, 24</sup> We utilized the Persian version of this questionnaire, the validity and reliability of which was confirmed in another study.<sup>23</sup> The SF-36 consists of 36 items and eight subscales: physical functioning (PF; 10 items), role limitations due to the physical health problems (RP; four items), pain (P; two items), general health (GH; five items), vitality (V; four items), social functioning (SF; two items), role limitations due to the emotional health problems (RE; three items), and emotional well-being (EW; five items). In addition to the eight subscales, we included one item related to the self-report for overall health status. In this questionnaire, PF, RP, P, and GH subscales measure the physical health component scale (PCS) and V, SF, RE, and EW measure the mental health component scale (MCS). For each scale, the raw score was converted to the transformed scale, while the minimum and maximum achievable scores were 0 and 100, respectively. It must be noted that the higher the score, the higher the level of health status.

### Statistical Analysis

The data were analyzed via IBM SPSS Statistics 20 (SPSS Inc, Chicago, IL) and Mplus 6.1 software. Mean±SD was applied for the description of continuous variables and frequencies (percentages) were calculated for the categorical variables. For univariable analysis, student *t* test (for the comparison of QOL, PCS, and MCS scores among the nominal variables) and Pearson correlation coefficient (for the comparison of QOL, PCS, and MCS scores among the continuous variables) were employed. The variables with  $P \leq 0.2$  were included in the multivariable linear regression analysis, and the forward method of variable selection was applied. The multicollinearity of variables was also checked with the variance inflation factor (VIF), while considering a level of less than five as an indicator of non-important correlation among the studied independent variables entered into the regression model. In the final analysis,  $P < 0.05$  was considered to be of statistical significance. In addition, the confirmatory factor analysis (CFA) was performed to assess the association (amount of factor loading) between each of the subscales of QOL and the overall QOL. The goodness of fit of the overall CFA model was evaluated through a combination of several fit indices, including the root mean square error of approximation (RMSEA), comparative fit index (CFI), and Tucker–Lewis index (TLI).

## Results

### Demographic and Waiting List Characteristics of Patients

The demographic, socioeconomic, medical history and paraclinical characteristics of patients on the liver transplant waiting list are displayed in table 1. The mean age of patients was  $47.6 \pm 12.3$  years. The participants in this study were mainly men 414 (65.6%), and the majority of them lived in the city 551 (87.5%). Among the participants, 519 (82.3%) were married, 492 (78%) had finished high school, and 362 (57.4%) were unemployed.

### Medical History and Paraclinical Characteristics of Patients

The mean MELD score was  $18.36 \pm 5.58$  (ranging from 6 to 36) and the mean adjusted BMI for the ascites was  $24.6 \pm 4.8$  kg/m<sup>2</sup>. While, out of all the participants, 306 (60.4%) patients had ascites, 294 (46.7%) had a history of weight loss, 48 (10.7%) had HCC, and 17 (3.8%) had HCV infection. A total of three (0.5%) patients had a history of dialysis. The frequency of the etiologies of ESLD and the paraclinical characteristics are demonstrated in table 1.

### QOL and Its Subscales

The mean scores of QOL, physical, and mental components of patients were  $50.01 \pm 21.73$ ,  $46.23 \pm 23.23$ , and  $53.78 \pm 23.91$  (out of 100), respectively. The results of the confirmatory factor analysis (CFA) are shown in figure 1, which support the suitability of the eight-factor model for SF36 (RMSEA=0.06, CFI=0.97, TLI=0.95). As shown in figure 1, QOL was most strongly associated with the vitality subscale (factor loading= 0.86,  $P < 0.001$ ) and least associated with role limitations due to physical health (factor loading=0.51,  $P < 0.001$ ).

### QOL and Its Determinants

#### Univariable Analysis

Table 2 shows the results of the univariable analysis of the association between the SF-36 dimensions and the patients' characteristics. In this table, we showed only the 21 variables associated at least with one of the dimensions of QOL at a level of  $P \leq 0.2$ . According to the univariable analysis, the higher scores of QOL belonged to men and the single patients, employed, with complementary insurance, family heads, with a higher level of education, city residents, owners of personal housing or cars, without a history of medical disease (ascites, gastrointestinal disease, DM, weight loss) and the ones, who did not use drugs.

**Table 1:** Demographic, Socioeconomic, Medical, and Paraclinical Data of Liver Transplant Candidates in Shiraz, Iran (n=632)

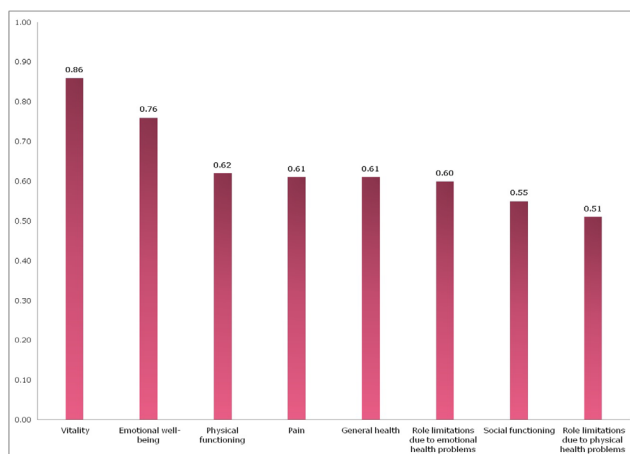
Variable		Mean±SD or N (%)	Variable		Mean±SD or N (%)
Age (year)		47.68±12.65	Alb (g/dL)		3.24±0.63
Adjusted BMI (kg/m <sup>2</sup> )		24.59±4.89	ALT (IU/l)		71.47±85.53
MELD score		18.36±5.58	AST (IU/l)		103.74±183.79
WBC (x10 <sup>9</sup> /L)		6687.15±5897.58	ALP (IU/l)		484.82±431.85
RBC (x10 <sup>12</sup> /L)		3.92±0.79	BUN (mg/dL)		17.53±12.19
Hb (gr/dl)		11.77±2.17	Cr (mg/dL)		1.50±5.70
HCT (%)		35.41±5.74	K (mEq/L)		4.25±0.62
MCHC (gr/dl)		33.14±2.34	Na (mEq/L)		136.93±9.16
Platelet (x10 <sup>9</sup> /L)		9768.68±41636.67	PBC	Yes	12 (2.69)
Sex	Male	414 (65.61)		No	432 (97.31)
	Female	217 (34.39)	AIH	Yes	42 (9.43)
Marital status	Single Life	112 (17.75)		No	403 (90.57)
	Married	519 (82.25)	PSC	Yes	94 (21.12)
Education (year)	≤12	492 (77.97)		No	351 (78.88)
	>12	139 (22.03)	AIH+PSC	Yes	11 (2.47)
Place of living	City	551 (87.46)		No	434 (97.53)
	Village	79 (12.54)	HCC	Yes	48 (10.69)
Occupation status	Having Job	269 (42.63)		No	401 (89.31)
	Jobless	362 (57.37)	Budd Chiari	Yes	19 (4.26)
Family head	Yes	397 (63.01)		No	426 (95.74)
	No	233 (36.99)	Non-alcoholic steatohepatitis	Yes	50 (11.23)
Supplementary insurance	Yes	266 (42.22)		No	395 (88.77)
	No	360 (57.78)	Cryptogenic cirrhosis	Yes	81 (18.20)
Personal house	Yes	457 (72.43)		No	364 (81.80)
	No	174 (27.57)	DM	Yes	110 (17.44)
Personal car	Yes	390 (61.90)		No	521 (82.56)
	No	240 (38.10)	Kidney disease	Yes	77 (12.18)
Cigarette smoking	Yes	157 (24.84)		No	555 (87.82)
	No	475 (75.16)	Gastrointestinal disease	Yes	149 (23.61)
Hookah smoking	Yes	66 (10.47)		No	482 (76.39)
	No	564 (89.53)	Hyperlipidemia	Yes	49 (7.76)
Alcohol drinking	Yes	98 (15.50)		No	582 (92.24)
	No	534 (84.50)	Weight Loss	Yes	294 (46.66)
Drug use	Yes	64 (10.12)		No	336 (53.34)
	No	568 (89.88)	Ascities	Yes	306 (60.35)
HCV	Yes	17 (3.82)		No	201 (39.65)
	No	428 (96.18)	Liver Size in Sonography	Small	266 (65.84)
HBV	Yes	66 (14.83)		Normal	108 (26.73)
	No	379 (85.17)		Large	27 (7.43)

SD: Standard deviation; BMI: Body mass index; MELD: Model for end-stage liver disease; WBC: White blood cell; RBC: Red blood Cell; Hb: Hemoglobin; HCT: Hematocrit; MCHC: Mean corpuscular hemoglobin concentration; HCV: Hepatitis C virus; HBV: Hepatitis B virus; Alb: Albumin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALKP: Alkaline phosphatase; BUN: Blood urea nitrogen; Cr: Creatinine; K: Potassium; Na: Sodium; PBC: Primary biliary cholangitis; AIH: Autoimmune hepatitis; PSC: Primary sclerosing cholangitis; HCC: Hepatocellular carcinoma; DM: Diabetes mellitus

The patients with a low MELD score, a low adjusted BMI, or a low BUN, and those without a low count of RBC, Hb, HCT, or Alb were reported to have

higher QOL scores. The associations between each of the variables with the physical and mental dimensional of SF-36 are presented in table 2.





**Figure 1:** This figure represents the association between health-related quality of life and its subscales (Numbers indicate factor loading).

**Table 2:** Univariate Analysis of Variables Association with Health-Related Quality of Life and its Sub Scales in the Liver Transplantation Candidates.

Variable		HRQOL Mean±SD	P value	Physical Health Mean±SD	P value	Mental Health Mean±SD	P value
MELD score		-0.15	<0.001	-0.18	<0.001	-0.09	0.016
Adjusted BMI (kg/m2)		-0.06	0.135	-0.06	0.129	-0.04	0.214
RBC (x10 <sup>12</sup> /L)		0.15	<0.001	0.18	<0.001	0.11	0.006
Hb (gr/dl)		0.12	0.002	0.12	0.002	0.10	0.012
HCT (%)		0.13	<0.001	0.14	<0.001	0.11	0.005
Alb (g/dL)		0.08	0.044	0.11	0.003	0.03	0.430
BUN (mg/dL)		-0.05	0.165	-0.07	0.079	-0.03	0.413
K (mEq/L)		0.05	0.215	0.02	0.507	0.06	0.107
Sex	Male	51.77±21.99	0.004	47.96±23.34	0.008	55.58±23.82	0.008
	Female (Ref)	46.58±20.88		42.87±22.75		50.29±23.78	
Marital status	Married	49.62±21.39	0.368	45.49±22.76	0.096	53.75±23.61	0.986
	Single Life (Ref)	51.68±23.29		49.55±25.19		53.82±25.41	
Family head	Yes	51.07±21.71	0.098	47.26±23.09	0.135	54.88±23.56	0.121
	No (Ref)	48.14±21.76		44.44±23.50		51.85±24.51	
Education (year)	≤12	53.99±21.17	0.014	49.37±23.36	0.071	58.61±23.17	0.007
	>12 (Ref)	48.85±21.78		45.32±23.16		52.39±23.98	
Place of living	City	50.55±21.78	0.121	46.78±23.45	0.141	54.32±23.82	0.164
	Village (Ref)	46.45±21.01		42.63±21.41		50.27±24.30	
Personal House	Yes	51.14±22.03	0.029	46.93±23.94	0.203	55.35±23.73	0.006
	No (Ref)	46.95±20.70		44.32±21.25		49.58±23.99	
Personal car	Yes	51.08±21.80	0.105	47.04±23.86	0.252	55.12±23.47	0.066
	No (Ref)	48.21±21.61		44.88±22.25		51.55±24.57	
Supplementary insurance	Yes	51.79±21.22	0.068	47.45±23.52	0.260	56.14±22.97	0.026
	No (Ref)	48.60±22.10		45.25±23.12		51.96±24.51	
Occupation status	Having Job	54.98±21.37	<0.001	51.83±23.24	<0.001	58.12±22.84	<0.001
	Jobless (Ref)	46.28±21.28		42.04±22.38		50.52±24.22	
Weight Loss	Yes	47.63±21.61	0.013	44.34±23.00	0.063	50.91±23.94	0.007
	No (Ref)	51.96±21.67		47.79±23.39		56.14±23.63	
DM	Yes	45.73±21.64	0.023	40.51±22.68	0.004	50.94±24.27	0.171
	No (Ref)	50.82±21.59		47.35±23.12		54.30±23.77	
Gastrointestinal disease	Yes	43.79±21.28	<0.001	41.13±22.61	0.002	46.45±23.20	<0.001
	No (Ref)	51.88±21.52		47.78±23.23		55.97±23.68	
Drug Use	Yes	45.91±20.89	0.112	42.78±21.18	0.210	49.05±24.34	0.095
	No (Ref)	50.47±21.79		46.62±23.44		54.31±23.82	
Ascites	Yes	48.79±21.01	0.001	43.61±22.82	<0.001	53.97±23.33	0.050
	No (Ref)	55.23±21.28		52.60±22.51		57.86±23.65	

In Pearson correlation coefficient (r) and independent samples t test, a difference P<0.2 was considered to be significant. HRQOL: Health related quality of life; MELD: Model for end-stage liver disease; BMI: Body mass index; RBC: Red blood cell; Hb: Hemoglobin; HCT: Hematocrit; Alb: Albumin, BUN: Blood urea nitrogen; K: Potassium; DM: Diabetes mellitus

**Table 3:** Multivariable Analysis of Variables Association with Health-Related Quality of Life and its Sub Scales in the Liver Transplantation Candidates

Dependent Variable	Independent Variable	Standard $\beta$	Un standard $\beta$	95% CI	P value
HRQOL	Having Job	0.20	8.81	(5.46,12.16)	<0.001
	Normal RBC count ( $\times 10^{12}/L$ )	0.11	3.90	(1.18,6.62)	0.005
	Having DM	-0.10	-5.83	(-10.21,-1.45)	0.009
	Having weight loss	-0.10	-4.76	(-8.05,-1.48)	0.005
	Low MELD score	-0.09	-0.42	(-0.80,-0.50)	0.027
	Being Drug User	-0.08	-6.00	(-11.40,-0.59)	0.030
Physical health	Having Job	0.21	10.01	(6.45,13.57)	<0.001
	Low MELD score	-0.10	-0.51	(-0.92,-0.11)	0.012
	Normal RBC count ( $\times 10^{12}/L$ )	0.11	4.16	(1.25,7.07)	0.005
	Having DM	-0.10	-6.16	(-10.82,-1.50)	0.010
	Being Married	-0.08	-5.09	(-9.68,-0.51)	0.029
	Having Weight loss	-0.08	-4.05	(-7.52,-0.58)	0.022
Mental health	Having Ascites	-0.08	-4.02	(-7.83,-0.21)	0.039
	Having Job	0.15	7.26	(3.55,10.96)	<0.001
	Having weight loss	-0.11	-5.40	(-9.06,-1.74)	0.004
	Normal RBC count ( $\times 10^{12}/L$ )	0.09	3.45	(0.56,6.34)	0.019
	Having personal house	0.09	4.87	(0.78,8.97)	0.020

Multivariate Analysis of Variables (forward method) where a difference of  $P < 0.05$  is considered significant.

CI: Confidence interval; HRQOL: Health related quality of life; RBC: Red blood cell; DM: Diabetes mellitus; MELD: Model for end-stage liver disease

### Multivariable Analysis

The results of multivariable linear regressions are depicted in table 3. The multivariable analysis implied that six variables were statistically associated with QOL. The unemployed patients had a 20% lower HRQOL score compared to the employed ones. The participants with a low RBC count experienced a 0.11 decrease in their HRQOL score by each  $10^{12}/L$  decrease in their RBC count. Several other significant determinants of QOL in the LT candidates are the MELD score (with a 0.09 decrease in HRQOL score by increasing one MELD score), a history of weight loss (10% decrease in the HRQOL score in patients with a history of weight loss compared to the ones without such a history), a history of DM (a 10% lower HRQOL score in the diabetic patients compared to non-diabetic one), and a history of drug use (with an 8% decrease in the HRQOL score compared to the non-drug users). Thus, seven variables in the multivariable model revealed statistically significant associations with PCS, including job status, history of DM, marital status (married patients had an 8% lower HRQOL score than the singles), RBC count, a history of weight loss, ascites (patients with ascites had an 8% lower HRQOL score than the ones without), and the MELD score. The MCS dimension was also associated with job status, ownership of house (house owner had a 9% higher HRQOL score), RBC count, and a history of weight loss. These findings indicated that job status, RBC count, and a history of weight loss influenced all the three subscales of HRQOL.

### Discussion

This study implied that the HRQOL in the LT candidates was at the intermediate level. The physical and mental components of patients were at low and moderate levels, respectively. Moreover, the patients, who were jobless, anemic, or non-drug users along with the patients with a lower MELD score, a history of weight loss, or a history of DM and experienced a lower level of HRQOL. Among the QOL subscales, vitality had the most association, while the role limitations due to physical health had the lowest association with HRQOL of patients.

One study has shown that the HRQOL in the male LT candidates was higher than in women.<sup>25</sup> However, we did not find any significant association between gender and HRQOL in the multivariable analysis of variables in this study. In line with our findings, another study has revealed that the employment is an indicator of HRQOL in these patients;<sup>26</sup> and being employed is associated with the increased HRQOL before and after transplantation.<sup>26-29</sup> Self-confidence, self-efficacy, psychosocial adjustment, financial stability, balance in the family system, and the ability to afford treatment are observed more in the employed patients.<sup>27-29</sup> One study has stated that the patients with a lower BMI had a higher level of HRQOL;<sup>24</sup> however, we did not find such an association. Zaydfudim and others concluded that PCS did not differ significantly between the two groups of people with normal and high BMI in the pre-transplantation stage, but after one year of LT, those with normal BMI

developed a higher level of PCS than those with high BMI, irrespective of no comparable changing in MCS between these groups.<sup>24</sup> We found a lower HRQOL in patients with a history of weight loss. HRQOL may be disrupted by underlying diseases. Several studies have revealed that patients' HRQOL increases dramatically with the improvement of anemia.<sup>30,31</sup> Herein, the low count of RBC was associated with the lower level of HRQOL. Regarding DM, the patients with diabetes seemed to have worse HRQOL early after LT; however, the diabetic and non-diabetic patients had comparable HRQOL scores after LTx.<sup>32</sup> The pain and opioid use is frequent in chronic liver disease, and while the disease variables contribute to pain, psychological symptoms were most strongly associated with pain and opioid use in these patients.<sup>33</sup> As a result, opioid dependence is a problem frequently encountered in the LT programs,<sup>34</sup> and as we found in the current work, it may influence inversely on HRQOL of the LT candidates. Bownik and colleagues revealed that in contrast to post-transplantation, HRQOL is affected via the etiology of liver cirrhosis in the pre-transplantation stage with the hepatocellular and cholestatic etiologies comprising higher HRQOL scores than alcohol or viral hepatitis etiologies.<sup>35</sup> On the other hand, in this study, we did not find any significant association between the etiologies of ESLD and HRQOL in the LT candidates. In the study by Sabb and others, it was shown that the MELD score had a weak relationship with the individual's physical performance, and there was no association between this score and mental health.<sup>36</sup> Kanwal and colleagues found that the association of HRQOL with the outcome of cirrhotic patients was independent of MELD.<sup>18</sup> A longitudinal study on forty patients indicated no association between the MELD score and HRQOL after LT.<sup>37</sup> The liver status assessed with the MELD and CPT scores pre-transplant had a minor effect on HRQOL after LTx and exerted no significant effect in patients being evaluated for more than 12 months after LTx, as reported in a study by Kotarska and others.<sup>32</sup> However, in accordance with our results, Mabrouk and colleagues stated that in people with a MELD score of less than 15, HRQOL was higher in those with a score higher than 15.<sup>38</sup> In terms of the strengths of this study, it was among the scarce studies that have been conducted yet to assess HRQOL and both its physical and mental components only in the pre-liver transplantation period and with a nearly large sample size of LT candidates, while other studies focused more on HRQOL in the post-transplantation era. Moreover, this

work studied the demographic, social, economic (except income), clinical, and paraclinical factors simultaneously with the subscales of HRQOL. One of the limitations of this study was that we could not investigate the HRQOL of patients as a cohort follow-up study and over time, due to the logistics and difficulties confronted for the repeated access to the patients. Despite the possible importance of income in HRQOL of patients, we could not test this variable due to the possibility of participants' unpleasant feelings or the false report of their real income; however, we considered other factors, such as job, personal house, and private car as the indirect indices of financial status.

## Conclusion

This study found that the HRQOL in the LT candidates was at the intermediate level. PCS and MCS were at low and moderate levels, respectively. Furthermore, physical performance, job status, anemia, weight loss, MELD score, DM, and drug use should be considered as the significant determinants of HRQOL in the LT candidates. It is recommended to conduct a multi-center, longitudinal, and comprehensive study to measure HRQOL of patients from pre-transplantation to post-transplantation stages and to achieve more generalizability of results. Moreover, designing and using an LT-specific checklist for the assessment of HRQOL in both the before and after LT is recommended.

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