



## Quality of life and psychiatric disorders before and one year after liver transplantation

Liver transplantation and quality of life

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### Abstract

**Aim:** Liver transplantation (LT) is a challenging operation with a burden affecting patients, families, and donors. The aim of the study was to compare the prevalence of psychiatric disorders and symptoms, and the quality of life of patients waiting for LT, with patients one year after transplantation. **Material and Method:** The patients in the LT waiting list (n: 68), and the outpatients evaluated for routine controls twelve months after LT (n: 53) were included in the study. Thus, patients were evaluated cross-sectionally in two groups: the pretransplantation group (PrTG) and the post-transplantation group (PsTG). The patients were administered the Receiver Sociodemographic Data Form, Short Form-36 Health Survey (SF-36), Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-1), and the Hospital Anxiety and Depression Scale (HADS). **Results:** There was no difference by means of the sociodemographic and clinical variables between the two groups. The PrTG showed significantly lower levels in all of the SF-36 scores except the mental health subscale when compared to the PsTG. Current psychiatric disorder was found in 29.4% of the PrTG while in 20.8% of the PsTG. There was no significant difference in the prevalences of psychiatric disorders between the groups. **Discussion:** Liver transplantation provides improvement in most of the domains of the quality of life of patients except the mental health domain. After LT, patients continue to be under risk of psychiatric disorders even later in the follow-up.

### Keywords

Liver Transplantation; Quality of Life; Psychiatric Disorders

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## Introduction

The first encouraging liver transplantation (LT) in humans was performed by Thomas Starzl in the United States in 1967 [1]. Liver transplantation has now been acknowledged as the approved therapy for all types of acute and chronic liver failures. According to a recent European registry report, rates of patient survival have increased considerably in the last 25 years, around 96% at one year after LT and around 71% at 10 years [2].

Despite significant improvements in surgery techniques, immunosuppression, and the evaluation and selection criteria of patients and donors, LT is still a challenging operation affecting both the patients, donors, and their families. Thus, the evaluation of the quality of life (QOL) of patients before and after LT is increasingly important.

Most of the studies concerning the QOL of LT patients in the literature show short-term results within months before and after LT and with inconsistent follow-ups lacking standardized clinical evaluations. On the other hand, there are studies, some cross-sectional and others prospective, providing long-term and consistent results [3-5]. Most of these studies report improvements in most dimensions of QOL after LT.

Chronic liver failure, along with other comorbid diseases such as diabetes mellitus, viral infections, and the complications before and after LT, makes patients prone to psychiatric disorders. Although transplantation surgery has particularly focused on the medical aspect of the challenge until today, the consideration of the psychiatric aspect is acknowledged to be affecting the treatment success directly. In a recent meta-analysis among patients with depression, a 65% increased risk of post-transplant mortality was found [6].

In one study approximately half of the patients who were candidates for heart or liver transplantation had at least one psychiatric disorder, and candidates for liver transplantation were found to have the highest psychiatric comorbidity prevalence [7]. Rocca et al. [8] reported that 43% of their LT candidates had a current psychiatric diagnosis and Child-Pugh score and previous psychiatric diagnosis were found as significant independent predictors of depressive disorders. Among psychiatric disorders in their LT candidates, adjustment disorder was found particularly prevalent. The prevalence of depression in LT candidates is reported between 2% and 80% when self-administered questionnaires were used. However, with diagnostic and standardized tools a smaller but still important range of prevalence (4.5-43%) is found [9]. On the other hand in the post-liver-transplantation period, the prevalence of psychiatric disorders is reported in a range from 30% to 70%, depending on the time of the study after transplantation and the diagnostic tools used [10].

In the literature, there are numerous studies investigating the QOL of liver transplanted patients depending on the etiology and severity of the failure, donor type, sociodemographic features, and the psychiatric symptoms and conditions of patients. In these studies the parameters affecting the QOL are usually cross-sectional and to a lesser extent comparative and prospective [4,11,12]. It is proposed that the investigation of the QOL of this patient group in more prospective designs and within different cultures is still needed.

The purpose of this single-centre, cross-sectional, and comparative study was to evaluate the impact of LT on the QOL and the prevalence of psychiatric symptoms and disorders at one year in recipients with chronic liver disease. It also aims to document the prevalence of psychiatric disorders before and one year after LT by using a standardized diagnostic tool in a group of Turkish patients.

## Material and Method

Adult patients with chronic liver disease who were enrolled on the waiting list for LT and evaluated for pretransplantation examinations (n:68) and outpatients evaluated for routine controls at the General Surgery Department twelve months after liver transplantation (n:53) were included in the study between 15.11.2008 and 31.07.2010. Thus, patients were evaluated cross-sectionally in two groups: the patients on the waiting list for LT as the pretransplantation group (PrTG) and the patients one year after LT as the posttransplantation group (PsTG). Patients with severe hepatic encephalopathy and those who do not speak Turkish were excluded from this study. The Recipient-Sociodemographic Data Form was filled out for all patients and the sociodemographic properties (age, sex, marital status, total education time, job), and information about the liver disease (etiology, severity, treatment history) were documented. All patients were given Short Form-36 (SF-36) for QOL assessment and Hospital Anxiety and Depression Scale (HADS) for evaluating the psychiatric symptoms. SCID-1/CV (Structured Clinical Interview for DSM-IV Axis I Disorders/Clinical Version) was applied to all patients by a psychiatrist to document the current psychiatric disorders before and after LT. The results of the groups were compared with each other. The Ethics Committee of Dokuz Eylul University Medical School approved this study, and verbal and written informed consents of all patients enrolled in the study were obtained.

In the pretransplantation group (PrTG) a total of 102 patients were evaluated; 34 of them were excluded from the study and 68 of them who met the inclusion criteria were included in the study. Among the excluded patients from PrTG, 5 had  $\geq$  Grade 2 hepatoencephalopathy, 12 were illiterate, 8 had severe comorbid disease (acute/chronical kidney insufficiency, complicated diabetes mellitus) or were evaluated for other indications (acute toxic hepatitis/carcinoid tumor), one had active delirium, one refused to participate in the study, and one didn't speak Turkish. Another six patients were also excluded after it was learned that they were taken out of the transplantation waiting list (because they had better-preserved liver reserves or transplantation was highly risky for them).

In the posttransplantation group (PsTG) a total of 65 patients were evaluated; 12 of them were excluded from the study and 53 of them who met the inclusion criteria were included in the study. Among the excluded patients from PsTG, nine were illiterate, one had a recent acute myocardial infarction, one was reoperated due to the complication, and one was pregnant.

## Scales

SF-36 is the most common generic scale used to evaluate the QOL of patients, especially with physical disorders but also successfully used for patients with psychiatric disorders. As a

self-report form with 36 items, it evaluates eight dimensions of health as physical functioning, physical role functioning, emotional role functioning, social functioning, mental health, vitality, bodily pain, and general health perceptions. It is easy to apply as it is short and comprehensible and filled in by patients themselves [13]. The scale was developed by Ware and Sherbourne (1992) [14]. The validity and reliability of the Turkish form were studied by Koçyiğit et al. (1999) [15].

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-1/CV) is a clinical diagnostic tool applied by the interviewer and developed by First et al. (1997). Turkish validity and reliability studies were carried out by Özkürkçügil et al. (1999) [16].

HADS is a self-report scale, developed by Zigmond and Snaith (1983), to detect levels of depression and anxiety, including measuring the severity of emotional disorder [17]. It includes 14 items, and seven of these (odd numbers) evaluate for anxiety and the other seven (even numbers) for depression. It provides quartile Likert type measurement. The validity and reliability of the Turkish form were studied by Aydemir et al. (1997) [18]. The cut-off point for the anxiety subscale was found as 10 and for the depression subscale as 7. Patients with scores above these points are regarded as at risk.

#### Statistical analysis:

All statistical analysis was performed by using SPSS 15.0 program. To compare the PrTG and PsTG groups parametric statistical analysis methods were used. In comparing categorical demographic and clinical data *Chi-square test* was used. *Fisher's Exact Test* was used for 2x2 cross-tabulations. In two independent samples (PrTG and PsTG), to compare the differences of means (e.g., Scales) *t-test* was applied. The statistical significance was accepted as  $p < 0.05$ .

#### Results

Regarding the sociodemographic variables, no statistically significant difference was found between PrTG and PsTG (Table 1). Regarding clinical variables, such as the etiology and severity of liver disease, history of hepatocellular malignancy before transplantation, and the presence of diabetes mellitus, no significant quantitative difference were found between PrTG and PsTG. We also found no significant difference in terms of psy-

chiatric history, alcohol use disorders history (alcohol abuse or alcohol dependence), or the history of psychiatric medication usage between the groups. The two groups were comparable to each other as there were no differences in means of sociodemographic or clinical characteristics.

According to t-test measures in independent groups, the subscales of physical functioning, physical role functioning, bodily pain, general health perception, vitality, social role functioning, and emotional role functioning of SF-36 in PrTG showed statistically significant and lower scores compared to PsTG ( $p < 0.05$ ). We found significant improvements in many dimensions of quality of life in recipients one year after LT. On the other hand, we found no significant difference in mental health subscale scores between the groups (Table 2).

In PrTG, 29.4% of patients on the waiting list had current psychiatric disorder according to SCID-1 interview. In PsTG, the percentage of current psychiatric disorder using the same diagnostic tool at twelve months post-transplant was 20.8% (Table 3). We found no statistically significant difference in the prevalences of psychiatric disorders between the groups.

According to t-test measures in independent groups, HADS Depression subscale mean scores in PrTG were found significantly higher compared to PsTG ( $p < 0.05$ ). Regarding the anxiety subscale mean scores, no significant difference was found between the groups.

According to scale significance levels; the number of patients having scores above the anxiety subscale cutoff point (HADS

Table 1. The comparison of the sociodemographic characteristics of the pretransplantation group (PrTG) and posttransplantation group (PsTG)

	PrTG (n=68)		PsTG (n=53)		p
Age (year±SD)	50.0±10.7		47.6±11.1		0.240
Total education time (year±SD)	7.5±3.5		7.1±3.1		0.526
Marital status	n	%	n	%	0.385
Married	55	80.9	46	86.8	
Other	13	19.1	7	13.2	
Sex					0.383
Female	10	14.7	11	20.8	
Male	58	85.3	42	79.2	
Job					0.482
Working	29	42.6	26	49.1	
Not working	39	7.4	27	50.9	

SD: standard deviation, PrTG: Pretransplantation group, PsTG: Posttransplantation group

Table 2. The comparison of the mean scores of the SF-36 subscales between PrTG and PsTG

	PrTG (n=68)	PsTG (n=53)	p
Physical Functioning (score±SD)	18.5±5.1	24.7±3.7	0.001
Physical Role Functioning (score±SD)	4.5±1.0	6.3±1.7	0.001
Bodily Pain (score±SD)	8.1±2.5	9.5±2.4	0.002
General Health Perception (score±SD)	11.5±3.3	17.8±4.7	0.001
Vitality (score±SD)	14.1±3.7	17.7±4.6	0.001
Social Functioning (score±SD)	6.2±2.0	8.0±1.8	0.001
Emotional Role Functioning (score±SD)	3.9±1.0	5.0±1.2	0.001
Mental Health (score±SD)	21.5±4.5	23.1±5.4	0.090

SD: standard deviation, SF-36: Short Form-36, PrTG: Pretransplantation group, PsTG: Posttransplantation group

Table 3. Current Psychiatric disorders in PrTG and PsTG

PrTG (n:68)	Number (n)	Percentage(%)
Adjustment Disorder	10	14.7
Major Depression	1	1.5
Alcohol Use Disorders	6	8.8
Sleep Disorder	2	2.9
Dysthymia	1	1.5
Total	20	29.4
PsTG (n:53)	Number (n)	Percentage(%)
Adjustment Disorder	3	5.7
Major depression	4	7.5
More than one disorder	1	1.9
Sleep disorder	3	5.7
Total	11	20.8

PrTG: Pretransplantation group, PsTG: Posttransplantation group

anxiety score > 10) showed no statistically significant difference between the groups. On the other hand, in PrTG the number of patients who had high scores in the depression subscale (HADS depression score > 7) were found statistically higher compared to PsTG ( $p < 0.05$ ) (Table 4).

Table 4. Evaluations concerning scale significance levels

	PrTG (n=68)		PsTG (n=53)		P
	n	%	n	%	
Patients showing significant anxiety levels (HAD-anxiety score > 10)					
Yes	5	7.5	3	5.7	1.000
No	62	92.5	50	94.3	
Patients showing significant depression levels (HAD-depression score > 7)					
Yes	27	39.7	9	17.0	0.007
No	41	60.3	44	83.0	

PrTG: Pretransplantation group, PsTG: Posttransplantation group

## Discussion

In our study, we found that one year after Liver Transplantation the quality of life of patients is increased in most dimensions except for their mental health. Ratcliffe et al. [3] reported similar results in their prospective multicenter study where they compared QOL of patients pretransplantation and 3, 6, 12, and 24 months posttransplantation. They found that with the exception of Role-emotional and Mental Health dimensions of the SF-36, the other dimensions indicated significant improvement over the 12-month and-24 month measurement period. On the other hand, Karam et al. [12], using a different QOL assessment tool, reported in their prospective study that one year after LT, patients showed dramatic improvements in five domains of QOL including psychological status and the overall psychological score which became identical to the general population score. In a recent cross-sectional study Braun et al. [19] compared recipients who underwent transplantation in a period of 15 years with a healthy cohort group of individuals and patients in the waiting list. Although neither finding was statistically significant, they reported that QOL of liver transplanted patients was decreased when compared with the control group, and increased when compared with the waiting list patients. Compared to our study, the recipients in their study were recruited in different year intervals after LT. They also reported that recipients treated with cyclosporine showed superior QOL results when compared with recipients treated with tacrolimus. Immunosuppressants play a vital role in graft survival after transplantation with possible morbid or mortal complications in the course of time for transplant recipients. Both cyclosporine and tacrolimus are known as calcineurin-inhibitors (CNI). On the other hand, calcineurin-inhibitor-free protocols including agents like steroids or azathioprine are also present. Moreover, when new immunosuppressive agents like rapamycin or mycophenolate mofetil are used as monotherapies or in combination, they are known to decrease the common side effects. Kousoulas et al. [20] evaluated the quality of life of adult LT recipients who survived for more than 15 years. They indicated no statistically significant finding when comparisons just after LT or in the long term were carried out regarding any of the

SF-36 subscales between recipients taking CNI-associated or non CNI-associated immunosuppression. Thus they concluded that immunosuppressive protocols did not appear to have as much impact on the QOL, especially in the long-term survivors. Therefore the use of immunosuppressive regimens in the post-transplantation group may not be seen as a confounding factor. In the same study, Kousoulas et al. compared QOL of recipients more than 15 years after LT with a healthy-reference population and they concluded that with the exceptions of bodily pain and mental-health subscales the recipients showed lower scores in all the other subscales of SF-36. Their long-term LT recipients showed similar scores when compared to the reference population by means of bodily pain and mental health subscales. Compared to our study we can translate these findings and conclude that although there may not be an increase in the mental health scores of recipients one year after LT, in the long term, they may show mental QOL scores similar to the control population. This needs further verification in different cultures. Long-term survivors may have better mental health scores due to better coping with their disease and complications. Van der Plas et al. [21] concluded similar results as they noted that liver transplanted patients scored similarly on the bodily pain and mental health subscales as the healthy controls did. In their study, they also emphasized the importance of social support as a ground for overcoming chronic illness provided by family or medical staff because it influences the post-transplantation survival and QOL.

In our study, we found adjustment disorder as the most common psychiatric disorder among pretransplantation patients. In a larger sample of LT candidates, Rocca et al. [8] similarly pointed out that 33% of their patients waiting for LT had adjustment disorder as the most common psychiatric disorder. They also found the prevalence of psychiatric disorders in their LT candidates as 43%. In our pretransplantation sample we found the prevalence of psychiatric disorders as 29% and when we compared this with the prevalence of psychiatric disorders in the one-year after transplantation group (20.8%) no statistically significant difference was found. Our findings provide further information regarding the impact of LT one year after LT showing that the improvements especially in the mental health dimension after LT may not be as good as expected. This outcome may be due to the slowly progressing rehabilitation after a major surgery, the ongoing psychiatric stress factors associated with drug side effects, or comorbid disorders, poor social support systems of the patients, or the enduring role of being ill for the patient. Additionally, in a recent meta-analysis, among patients with depression an increased risk of mortality after transplantation was found as 65%, showing the vital importance of diagnosing and treating depression promptly for patients in the LT process [6].

Rothenhausler et al. [22] evaluated 281 candidates for liver transplantation with a semi-structured psychiatric interview and found a prevalence rate of psychiatric disorders of 65.8%; alcohol abuse (27.8%) and alcohol dependence (11.7%) were the most common psychiatric disorders in their study group. In our study, we found a smaller percentage of alcohol use disorders. This difference may be due to the higher frequency of alcohol use disorders as an etiology for chronic liver disease

in Western societies compared to infections as an etiology elsewhere. Gledhill J. et al. [23] compared social and psychological results and the QOL of transplanted alcoholic cirrhosis patients with patients transplanted for other chronic etiologies. They found that although QOL was impaired when compared to the general population and there was worse physical mobility among alcoholics, but the results otherwise were similar for the two groups. The psychosocial outcome was found similar for the two groups as well. They concluded that for alcoholic recipients, difficulties in physical mobility might be because of the chronic alcohol consumption related complications, like peripheral neuropathy or myopathy. They also emphasized that after transplantation, recipients transplanted for alcoholic liver disease do not carry a bigger risk for psychiatric outcomes than recipients transplanted for other etiologies.

We found that our candidates for liver transplantation showed higher depressive scores compared to the one-year post-transplantation group. On the other hand, there was no significant difference in means of anxiety scores for the two groups. O'Carroll et al. [24] evaluated the data of 70 patients both pretransplantation and one-year post-transplantation in a prospective fashion. They found that both depression and anxiety scores improved significantly in the post-transplantation group. They concluded that elevated levels of anxiety and neuroticism at pretransplantation assessment were associated with worse psychosocial outcome at one year posttransplantation. They also found no differential effect of immunosuppressant (cyclosporine versus tacrolimus) on QOL or affective status at one-year follow-up. These findings indicate the importance of psychiatric evaluations before and after LT as prompt interventions for the treatment of psychiatric disorders might yield major benefits for treatment compliance, QOL, and survival of transplanted patients.

In our study, the most important limiting factors might be the lack of comparisons with healthy individuals and having mainly cross-sectional rather than completely prospective evaluations. On the other hand, the aim of our study was to focus on the effects of LT, in recipients' psychiatric well-being and QOL in one year. The two groups in our study were comparable to each other as there were no significant differences in the mean sociodemographic and clinical characteristics. Similar results as in prospective studies were found, discussed, and compared with other prospective and cross-sectional studies. When evaluating studies, we must keep in mind the cultural, economic factors, and social support systems of patients which might directly affect the outcome. These factors might be overlooked in studies, and this may result in the overestimation of the outcomes regarding the QOL. On the other hand, unlike many studies in the literature, there was consistency in the evaluation time in our study: LT recipients were evaluated at one year after the transplant. As the strong points of our study, the data was not collected in a questionnaire or postlike fashion; instead, valid and reliable scales and a structured clinical and diagnostic interview by a psychiatrist were applied.

### Conclusion

Our study adds valuable information regarding the prevalence of psychiatric disorders in recipients before and after LT. It also

evaluates and gives comparable data on the effects of LT on the QOL and psychiatric parameters of patients in a one-year period. The inevitable exclusion of high-grade or comatose patients or patients who have died during follow-ups might cause the QOL outcomes in the literature to be over-estimated. Therefore data in studies in the literature should be examined carefully. Future studies evaluating the social support perception and systems of patients together with the QOL may add holistic and valuable information to the literature. Placing psychiatric evaluation units into transplantation centres might help to preserve a multidisciplinary approach to detecting and treating psychiatric symptoms and disorders in a timely way. Also, it may result in providing better cooperation with patients and their relatives, thus decreasing the difficulties encountered in the transplantation process.

### Scientific Responsibility Statement

*The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.*

### Animal and human rights statement

*All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

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### Conflict of interest

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