

Biopsychosocial functioning among cirrhotic patients in various stages of transplant process in comparison to liver transplant recipients

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Título: Funcionamiento biopsicosocial entre pacientes cirróticos en distintas etapas del proceso de trasplante y su comparación con trasplantados hepáticos.

Resumen: *Antecedentes:* Si bien la evaluación de la calidad de vida en fases previas y posteriores al trasplante es un objetivo científico de actualidad; ésta aún no ha sido abordada a lo largo de todo el proceso de trasplante. *Objetivos:* 1) Comparar la salud mental y calidad de vida en las tres siguientes fases del proceso de trasplante: en el estudio previo a la lista de espera, en lista de espera y en fase post-trasplante; 2) analizar la correlación entre estas variables afectivas y de calidad de vida y las puntuaciones en Model for End-Stage Liver Disease (MELD). *Métodos:* Se seleccionaron dos grupos de pacientes hepáticos: 51 pacientes cirróticos evaluados en dos etapas (en el estudio previo a la lista de espera y en lista de espera), y 51 pacientes con trasplante hepático procedente de un donante cadáver; ambos grupos igualados en género y edad mediante apareo. Se emplearon como instrumentos el HADS y el Cuestionario de Salud SF-36. *Resultados:* Los pacientes en estudio pre-lista de espera percibieron su estatus global de salud mucho peor que los pacientes trasplantados. Los pacientes en lista de espera presentaron mucha mayor ansiedad, más limitaciones funcionales por problemas físicos, peor funcionamiento físico, y percibieron su estatus global de salud mucho peor que los pacientes trasplantados. Correlaciones estadísticamente significativas fueron únicamente observadas en los pacientes en lista de espera entre MELD y las subescalas de Ansiedad y Funcionamiento Social. *Conclusiones:* Los pacientes en lista de espera presentaron el peor estatus de bienestar biopsicosocial; por el contrario, los trasplantados hepáticos gozaron del mejor nivel en estas dimensiones.

Palabras clave: Sintomatología ansioso-depresiva; calidad de vida; estudio pre-lista de espera; fase lista de espera; trasplante hepático.

Abstract: *Background:* Although assessment of pre- and post-transplant quality of life is a current scientific target; it has not yet been carried out throughout the entire transplant process. *Aims:* 1) To analyze differences in mental health and quality of life at pre-waiting-list-study, waiting-list, and post-transplant phases; 2) to analyze correlation between these quality-of-life and affective variables and Model for End-Stage Liver Disease (MELD) scores. *Methods:* Two liver patient groups were recruited: 51 cirrhotic patients, who were assessed at two different stages (at pre-waiting-list-study and waiting-list phases), and 51 cadaveric liver transplant recipients; groups were homogeneous in gender and age variables by matching. Anxiety-depressive symptomatology and quality of life were assessed by HADS and SF-36 Health Survey, respectively. *Results:* Pre-waiting-list-study patients self-perceived their global health status much worse than transplant recipients. Waiting-list patients displayed much higher anxiety, more role limitations due to physical problems, worse physical functioning, as well as perceiving their global health status much worse than transplant recipients. Statistically significant correlations were only found in waiting-list patients between MELD-Anxiety and MELD-Social Functioning subscales. *Conclusions:* Waiting-list patients displayed the worst biopsychosocial well-being status; liver transplant recipients enjoyed the best status instead. **Key words:** Anxiety-depressive symptomatology; quality of life; pre-waiting-list study; waiting-list phase; liver transplant.

Introduction

Currently, liver transplant is the treatment of choice for patients with severe hepatopathy with poor short-term prognosis. For the past decades, this intervention has shown relevant advances, with very satisfactory results in terms of survival and quality of life (Forsberg, Bäckman, & Svensson, 2002; Karam et al., 2003; Ripoll & Bañares, 2008). However, most investigations of quality of life among transplant recipients conclude that these patients' quality of life does not reach the levels of the general population (Sumskiene, Sumskas, Petrauskas, & Kupcinskis, 2006; Taylor, Franck, Gibson, & Dhawan, 2005), not even 15 years after the surgical intervention (Kousoulas et al., 2008).

Therefore, this is a process that involves several complications since the moment the patients undergo a medical study in order to consider the possibility of their inclusion

on the waiting list, followed by their admission on the waiting list, until they are finally transplanted.

However, although the survival of severe hepatopathic patients has been studied during several phases of this hospital process, the functional state of the patients during all three stages has received much less attention (Gutteling, de Man, Busschbach, & Darlington, 2007; Perkins, 2009), and the results about whether or not quality of life improves after transplant are controversial (Braun et al., 2009; Karam et al., 2003; Ratcliffe et al., 2002; Sainz-Barriga et al., 2005; Telles-Correia, Barbosa, Mega, Mateus, & Monteiro, 2009). Consequently, in this study, we aimed to offer more empirical evidence about the quality of life and mental health of these patients, as well as to analyze the relationship of these variables with liver disease severity during this entire hospital process. Most studies regarding biopsychosocial outcomes during the transplant process do not usually include patients who are hospitalized in order to undergo a pre-waiting-list study because of their severe liver disease. Therefore, it is really important to identify the psychological complications suffered by these patients during all stages of this medical process and the differences among them.

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During the pre-waiting-list study, the patients and their relatives both suffer the medical assessment with a mixture of conflictive feelings, distress, and ambivalence. This state may encompass the hope of attaining a healthy future and a normal life, combined with fear of the risks of surgical intervention, particularly graft rejection. Most patients express willingness to carry on with the assessment, but they also display high anxiety levels due to possibility of being included on the waiting list (Rainer, Thompson, & Lambros, 2010).

When the need for a transplant has already been decided -because other therapeutic procedures have been dismissed- waiting-list patients continue to experience ambivalent feelings. On the one hand, transplant intervention represents the possibility of recovering health and quality of life; however, it is also a source of fear and uncertainty in view of possible medical complications after transplant. Overall, this stage has been identified as the most distressful period of the entire transplant process, where anxiety is the most frequent reaction, which could negatively affect the post-operative phase (Jiménez-Torres, Martínez, Miró, & Sánchez, 2012; Rainer et al., 2010; Scott, 2004).

On the other hand, although research concludes that transplant improves physical and social functioning, as well as promoting a return to daily activities, there are some controversial results regarding mental health (Rainer et al., 2010). In this sense, some of the following psychological difficulties are displayed after transplant: mood disorders, anxiety disorders, sexual dysfunctions, fantasies about the donor, and body image dissatisfaction (Dew et al., 1994, 2005; Pérez-San-Gregorio, Martín-Rodríguez, & Galán-Rodríguez, 2005). Nevertheless, many investigations show that liver transplant recipients enjoy significantly better quality of life than cirrhotic patients, particularly than patients with advanced hepatopathy (O'Carroll, Turner, Flatley, McGregor, & Hayes, 2008; Pantiga et al., 2005; Pérez-San-Gregorio et al., 2012). Cirrhotic patients' quality of life is impaired due to the characteristic symptoms of liver disease, especially if it is decompensated. Subsequently, this aspect varies after transplant because most patients report significant improvement.

The Model for End-Stage Liver Disease (MELD) has been established as a measure of hepatic disease severity, replacing the Child-Turcotte-Pugh (CTP) for liver allocation, because the MELD scores predict short-term survival better than the CTP scores (Wiesner et al., 2003). However, in view of the fact that current liver transplantation research does not only focus on survival but also on quality of life, there is increasing scientific interest in analyzing the relationship between the MELD and quality-of-life dimensions. To date, the results about this relationship are controversial, ranging from an absence of correlation (Ortega et al., 2009; Saab et al., 2005) to negative correlations (Kanwal, Hays, Kilbourne, Dulai, & Gralnek, 2004; Rodrigue, Lisson, Wiak, Nelson, & Reed, 2006), or even positive correlations (the higher the MELD scores, the better quality of life), but only in cases of very severe hepatopathy (Castaldo, Feurer, Russell, & Pinson, 2009).

Therefore, in view of the relevance of this topic and taking various phases of the transplant process into account, in the current investigation, we aimed to study the following specific goals. Firstly, to compare quality of life and anxiety-depressive symptomatology between: 1) cirrhotic patients at two phases of transplant process, that is, pre-waiting-list study and waiting-list stages; 2) cirrhotic patients from the pre-waiting-list study and liver transplant recipients; and 3) cirrhotic patients on the waiting list and liver transplant recipients. Lastly, we aimed to analyze the correlations between these patients' quality of life, affective variables, and MELD scores.

Method

Participants

To carry out this investigation, we formed two liver patient groups: 51 cirrhotic patients and 51 liver transplant recipients. The former patients were assessed at two time points: a) firstly, when they were admitted to the Digestive Diseases Unit for a medical study in order to determine their inclusion on the waiting list (pre-waiting-list study); b) secondly, when they had been admitted on the waiting list for subsequent liver transplant. This cirrhotic patient group was made up of 44 men and 7 women, mean age 55.16 years ($SD = 8.09$ years). Regarding etiology of liver cirrhosis, it was frequently alcoholic cirrhosis ($n = 24$) and hepatitis C virus (HCV) ($n = 17$), followed by others ($n = 7$) and hepatitis B virus (HBV) ($n = 3$). Their mean MELD score during the pre-waiting-list study was 15.81 ($SD = 4.13$) and, at the waiting-list stage, 16.88 ($SD = 3.96$).

The transplant recipient group was made up of 44 men and 7 women, mean age 54.98 years ($SD = 7.74$ years). They had all received a first liver transplant five years ago, on average, proceeding from a deceased donor. With regard to the clinical variables, the etiology of the disease leading to transplant was mainly alcoholic cirrhosis ($n = 20$), followed by hepatocarcinoma ($n = 11$), HCV ($n = 10$), HBV ($n = 5$), and others ($n = 5$). Their mean MELD score was 17.17 ($SD = 4.01$).

Instruments

Psychosocial survey

This was created by the authors for the current investigation and included several sociodemographic and clinical variables: gender, age, etiology of cirrhosis, and MELD scores.

Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983)

This instrument has 14 items, 7 of depression and 7 of anxiety, on which patients rate how they felt during the past week, selecting one out of four responses. The test provides

two scores, one for each subscale; in both cases, the scores are classified as: normal (0-7 points), doubtful (8-10 points), and clinical problem (≥ 11 points). In Spanish studies, Cronbach's alpha values range between .80 and .90. We used the Spanish version developed by Caro and Ibáñez (Caro & Ibáñez, 1992).

SF-36 Health Survey (Alonso, Prieto, & Antó, 1995)

This is made up of 36 items, each one with various response alternatives that provide a health status profile. The test explores eight dimensions: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and general mental health. In each dimension, a score ranging from 0 (worse health status) to 100 (better health status) is obtained. Alonso et al. (1995) studied the psychometric properties of this test in Spanish population and found that internal consistency (Cronbach's alpha) of the diverse dimensions ranged between .45 and .94, with a mean value of .78, and always above the value of .70, except for the dimension Social Functioning, which did not exceed .45. For test-retest reliability, the correlation coefficients ranged between .51 and .85.

Procedure

In the two groups (cirrhotic patients and liver transplant recipients), the following inclusion criteria were taken into account: being over 18 years of age, having a reading/writing level that allowed them to complete the diverse scales employed, not being currently in psychiatric or psychological treatment, not presenting any severe or incapacitating pathology at the moment of assessment, and giving their written informed consent to participate in the investigation.

Aside from these general requirements, there were other specific inclusion criteria depending on the patient group. Regarding the cirrhotic patients: either being admitted to the Digestive Diseases Unit for a medical study to determine their inclusion on the waiting list; or else the Transplant Commission had already decided their inclusion on the waiting list for subsequent liver transplant, taking the following criteria into account: suffering from a hepatic pathology; other therapeutic interventions were not possible or had failed; and survival about one year later was less than survival that would be achieved by means of liver transplant. With regard to transplant recipients, the specific inclusion criterion was having received a first liver transplant proceeding from a deceased donor; retransplant recipients and possible recipients of a combined liver-kidney transplant were excluded.

Both groups of patients were selected from the University Hospital Virgen del Rocío of Seville, taking into account that the Ethics and Health Research Commission had previously approved the adequacy and implementation of this investigation. Once we had received approval, the medical data

of the patients were obtained through the Hepatic-Biliary-Pancreatic Surgery and Liver Transplant Unit and from the Digestive Diseases Unit.

To select the group of cirrhotic patients, we started with all the patients who, during a 2-year interval (2009 and 2010), had been scheduled for admittance in the Digestive Diseases Unit in order to undergo a pre-liver transplant study due to the advanced state of their hepatic pathology. During this time interval, 83 patients were admitted; we excluded 8 of them because they did not meet the inclusion criteria: 3 could not read or write, 4 did not wish to participate, and 1 was under study for a liver-kidney transplant. Therefore, we assessed 75 patients in the pre-waiting-list study, taking into account that 24 cirrhotic patients were not included on the waiting list because of not meeting above-mentioned specific inclusion criteria. Finally, these 51 cirrhotic patients were assessed twice during the medical protocol for a liver transplant.

To select the group of transplant recipients, we started with a clinical population made up of all the patients in Seville who had received a liver transplant from a deceased person during the 1990-2007 interval. During this time interval, 662 liver transplants were carried out in adults, of whom 236 died. Of the 426 living transplant recipients, 28 could not be located, and 230 did not meet the inclusion criteria: 44 could not read or write, 36 were in psychiatric and/or psychological treatment, 140 did not wish to participate, and 10 had been retransplanted. We finally assessed 168 patients.

As we aimed to have two homogeneous patient groups (cirrhotic patients and liver transplant recipients), we selected 51 liver transplant recipients from the 168 assessed previously. To carry out this goal, we formed the groups by matching gender and age. When there were several patients meeting the same conditions, random selection was used.

Statistical Analysis

Data were analyzed with the SPSS 19.0 statistical package. To compare continuous variables between pre-waiting-list and waiting-list groups, we used Student's *t*-test for paired samples (first goal). To compare pre-waiting-list and waiting-list groups with transplant recipients, we used Student's *t*-test for unpaired samples (second and third goal). To analyze the relationship between MELD scores and quality of life and affective variables, we computed Pearson's correlations for these three intergroup comparisons (fourth goal). When homocedasticity was not achieved, we took Welch's *t* into account instead of Student's *t*-tests. We used Cohen's *d* as effect size indexes (Cohen, 1992), computing them from the means and standard deviations, instead of *t*-tests in order to avoid the overestimating associated with paired *t*-test values (Dunlap, Cortina, Vaslow, & Burke, 1996). Likewise, we performed item analysis by means of *t*-tests for those items of the subscales whose previous pairwise comparisons had obtained large effect sizes.

Results

Firstly, we aimed to ensure that post-transplant time - number of months passed from transplantation to assessment- ($M = 56.71$ months, $SD = 40.04$) did not influence any quality of life and affective variables. Therefore, we computed Pearson's correlations and no statistically significant correlations were found in most dimensions, excepting in bodily pain ($r = .286$, $p = .42$), although reaching a small-to-moderate effect size. Overall, since simple linear regression is based on Pearson's correlations, we can conclude that post-transplantation time did not predict changes in quality of life and affective variables.

Pre-transplant phase: psychological differences between cirrhotic patients at the pre-waiting-list study and on the waiting list.

Regarding variables that assess affective status (anxiety and depression by means of HADS), no statistically significant differences were found in any subscale: Anxiety ($p = .344$) and Depression ($p = .305$) (Table 1).

With regard to quality of life, statistically significant differences were only found in the Physical-Role ($p = .017$) and General Health ($p = .015$) subscales (Table 1). In both dimensions, patients displayed better scores when they were at the pre-waiting-list study than on the waiting-list phase for transplant (Figure 1).

After computing effect sizes, null and small effect sizes were obtained in all variables.

Table 1. Comparisons in Mental Health (HADS) and Quality of Life (SF-36).

Psychological variables	Intergroup comparisons					
	Pre-waiting and waiting list patients ($n = 51$)	Cohen's d	Pre-waiting list and transplant recipients ($n = 51$)	Cohen's d	Waiting List and transplant recipients ($n = 51$)	Cohen's d
HADS¹:						
- Anxiety	$t(50) = -.955$ $p = .344$	-0.10 –	$t(91.27) = -3.251$ $p = .002^{**}$	0.64 M	$t(95.10) = -4.008$ $p = .000^{**}$	0.80 L
- Depression	$t(50) = -1.037$ $p = .305$	-0.13 –	$t(100) = -2.894$ $p = .005^{**}$	0.57 M	$t(90.68) = -3.601$ $p = .001^{**}$	0.71 M
SF-36²:						
- Bodily pain	$t(50) = -.811$ $p = .421$	-0.13 –	$t(100) = 1.200$ $p = .233$	-0.24 S	$t(100) = 0.495$ $p = .622$	-0.10 –
- Physical-role	$t(50) = 2.467$ $p = .017^{**}$	0.30 S	$t(100) = 2.921$ $p = .004^{**}$	-0.58 M	$t(100) = 4.631$ $p = .000^{**}$	-0.92 L
- Mental health	$t(50) = 1.602$ $p = .116$	0.20 S	$t(100) = 1.898$ $p = .061$	-0.38 S	$t(100) = 2.854$ $p = .005^{**}$	-0.57 M
- General health	$t(50) = 2.512$ $p = .015^{**}$	0.27 S	$t(100) = 6.157$ $p = .000^{**}$	-1.22 L	$t(100) = 7.474$ $p = .000^{**}$	-1.48 L
- Vitality	$t(50) = 1.258$ $p = .214$	0.17 –	$t(100) = 2.785$ $p = .006^{**}$	-0.55 M	$t(100) = 3.678$ $p = .000^{**}$	-0.73 M
- Social functioning	$t(50) = 1.238$ $p = .221$	0.19 –	$t(100) = 1.652$ $p = .102$	-0.33 S	$t(96.57) = 2.589$ $p = .011^*$	-0.51 M
- Emocional-role	$t(50) = 1.861$ $p = .069$	0.24 S	$t(100) = 0.760$ $p = .449$	-0.15 –	$t(94.22) = 2.007$ $p = .048^*$	-0.40 S
- Physical functioning	$t(50) = 1.506$ $p = .138$	0.19 –	$t(100) = 3.733$ $p = .000^{**}$	-0.74 M	$t(100) = 4.733$ $p = .000^{**}$	-0.94 L

¹The higher score, the worse mental health. ²The lower score, the worse quality of life. * $p < 0.05$, ** $p < 0.01$
Effect sizes, Cohen's d –, null; S, small; M, medium; L, large.

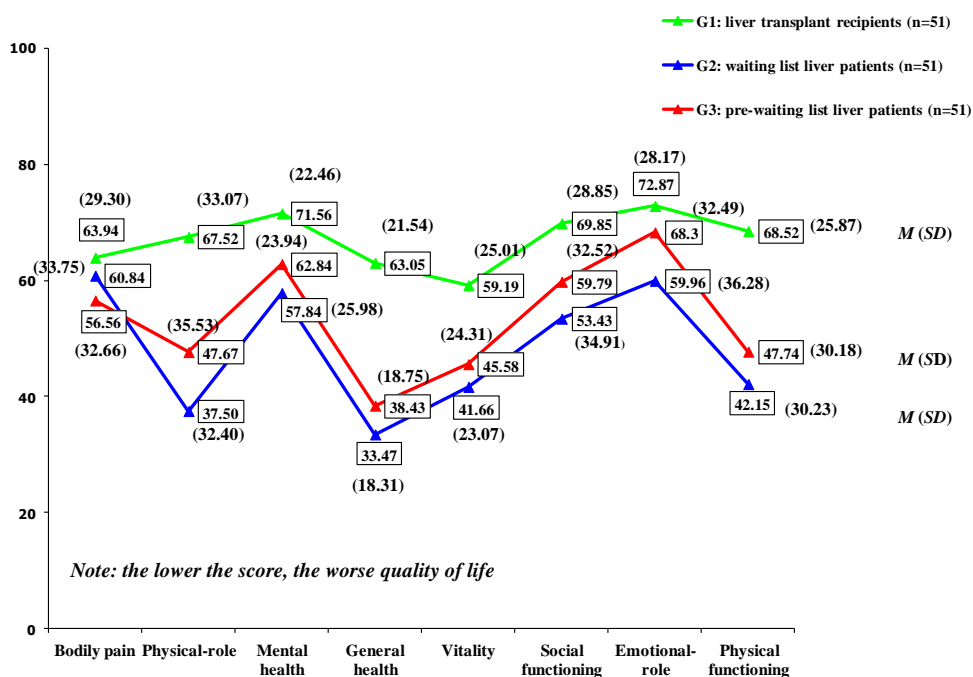


Figure 1. SF-36 comparisons between cirrhotic patients and liver transplant recipients.

Pre- and post-transplant phase: psychological differences between cirrhotic patients at the pre-waiting-list study and transplant recipients.

and Depression ($p \leq .005$) subscales and medium effect sizes were reached. As observed in Table 1 and Figure 2, pre-waiting-list patients reached higher scores than transplant recipients in both variables.

Regarding affective status variables, statistically significant differences were found both in the Anxiety ($p = .002$)

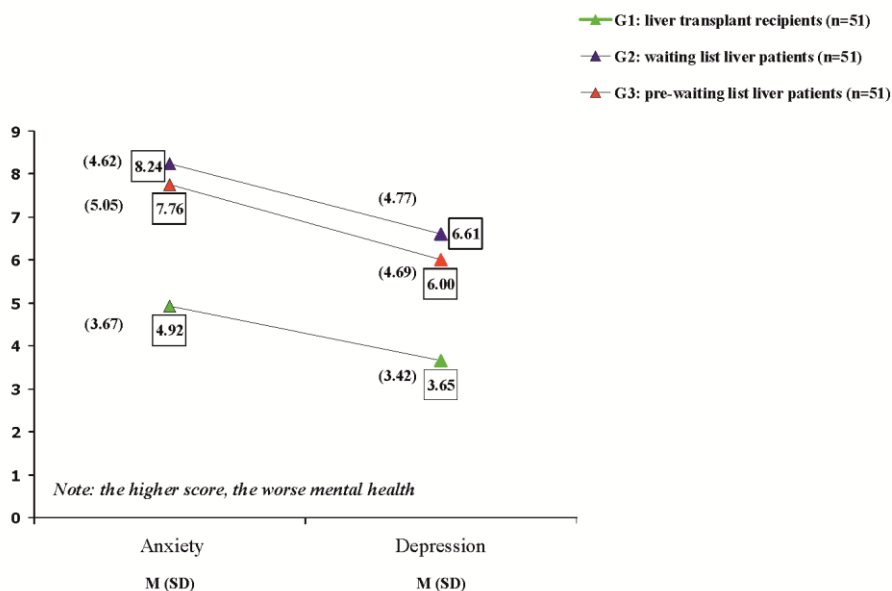


Figure 2. HADS comparisons between cirrhotic patients and liver transplant recipients.

With regard to quality of life, statistically significant differences were found in four dimensions: Physical-Role ($p = .004$, medium effect size), Vitality ($p = .006$, medium effect size), Physical Functioning ($p \leq .000$, medium effect size), and General Health ($p \leq .000$). Particularly, transplant patients reached higher scores in all these subscales in compari-

son to cirrhotic patients at the pre-waiting-list study; that is, the transplant recipients enjoyed better quality of life (Table 1 and Figure 1). Only one subscale achieved a large effect size, General Health, where three items presented the highest group differences (Table 2).

Table 2. Comparisons between liver transplant recipients and patients on pre-waiting list regarding SF-36 dimensions with a large (L) effect size. Items Analysis.

SF-36 ITEMS	Liver transplant recipients ($n = 51$) M (SD)	Pre-waiting list patients ($n = 51$) M (SD)	t -test (p)	Cohen's d
<i>General health</i>				
- In general, would you say your health is... ¹	57.84 (26.21)	20.10 (20.01)	$t(100) = 8.173$ (.000**)	1.619 L
How true or false is each of the following statements for you:				
- I am as healthy as anybody I know ²	60.78 (32.88)	31.86 (25.04)	$t(93.39) = 4.997$ (.000**)	0.990 L
- My health is excellent ²	63.24 (32.15)	27.45 (27.50)	$t(100) = 6.040$ (.000**)	1.196 L

The answers range: ¹ excellent (100)-poor (0), ² definitely true (100)-definitely false (0); the lower the score, the worse quality of life; ** $p < 0.01$ Effect size, Cohen's d : L, large.

Pre- and post-transplant phase: psychological differences between cirrhotic patients on the waiting list and transplant recipients.

With regard to affective status, statistically significant differences were observed in the Anxiety ($p \leq .000$) and Depression subscales ($p \leq .001$, medium effect size). As observed in Table 1 and Figure 2, waiting-list patients displayed higher levels of anxiety-depressive symptomatology in comparison to liver transplant recipients. Likewise, differences in the Anxiety subscale were very relevant (large effect size) and an item showed the greatest group differences ("I get a sort of frightened feeling as if something awful is about to happen") (Table 3).

Regarding quality of life, statistically significant differences were found in all SF-36 dimensions, except for Bodily Pain: Physical-Role ($p \leq .000$), Mental Health ($p = .005$), General Health ($p \leq .000$), Vitality ($p \leq .000$), Social Functioning ($p = .011$), Emotional-Role ($p = .048$), and Physical Functioning ($p \leq .000$). Among these variables, the following had medium effect sizes: Mental Health, Social Functioning, and Vitality. And the remaining variables (except for Emotional-Role) reached large effect sizes (Table 1). Particularly, in the Physical-Role dimension, the item which most emphasized group differences was, "How long have you had difficulty performing work or other activities (for example, it took extra effort), as a result of your physical health?" (See Table 3). In the General Health dimension, there were very relevant differences in three items. And regarding the Physi-

cal Functioning dimension, two items showed the greatest differences.

In all these dimensions, transplant patients reached higher scores than waiting-list patients. Therefore, the former showed better quality of life (Table 1 and Figure 1).

Correlations between MELD scores and affective and quality of life dimensions as a function of type of phase

Firstly, we compared scores on MELD scale among the three groups: pre-waiting-list cirrhotic patients ($M_1 = 15.81$, $SD = 4.139$), waiting-list cirrhotic patients ($M_2 = 16.75$, $SD = 3.938$), and transplant patients ($M_3 = 17.17$, $SD = 4.018$). In view of fact there were missing values, we performed these analyses by means of a different sample size: 48 cirrhotic patients and 42 transplant recipients. No statistically significant differences were found in any comparison ($t(47)_{1-2} = -1.929$, $p = .060$; $t(88)_{1-3} = 1.570$, $p = .120$; $t(88)_{2-3} = .496$, $p = .621$), and the magnitude of these differences was small (null and small effect sizes: $d_{1-2} = -0.23$; $d_{1-3} = -0.33$; $d_{2-3} = -0.11$).

Likewise, we computed Pearson's correlations between MELD scores and affective and quality-of-life dimensions as a function of type of phase (pre-waiting-list study, waiting list, and transplant). No statistically significant correlations were found in any group, excepting for waiting-list patients between MELD and Anxiety subscale ($r = .306$, $p = .029$), and between MELD and SF-36 Social Functioning ($r = -.286$, $p = .042$); the correlations were moderate and small-to-moderate, respectively.

Table 3. Comparisons between liver transplant recipients and patients on waiting list regarding HADS and SF-36 dimensions with a large (L) effect size. Items Analysis.

HADS ITEM	Liver transplant recipients (<i>n</i> = 51) <i>M</i> (<i>SD</i>)	Waiting list patients (<i>n</i> = 51) <i>M</i> (<i>SD</i>)	<i>t</i> -test (<i>p</i>)	Cohen's <i>d</i>
Anxiety				
- I get a sort of frightened feeling as if something awful is about to happen ¹	0.61 (0.72)	1.33 (0.95)	<i>t</i> (93.29) = -4.333 (.000**)	-0.854 L
SF-36 ITEMS				
Physical-role				
During the past 4 weeks:				
- How long have you had difficulty performing the work or other activities (for example, it took extra effort), as a result of your physical health? ²	66.18 (34.21)	35.78 (31.72)	<i>t</i> (100) = 4.652 (.000**)	0.922 L
General health				
- In general, would you say your health is... ³	57.84 (26.22)	20.10 (18.04)	<i>t</i> (88.68) = 8.470 (.000**)	1.677 L
How true or false is each of the following statements for you:				
- I am as healthy as anybody I know ⁴	60.78 (32.88)	25.49 (26.22)	<i>t</i> (95.27) = 5.993 (.000**)	1.187 L
- My health is excellent ⁴	63.24 (32.15)	22.06 (25.81)	<i>t</i> (95.53) = 7.132 (.000**)	1.413 L
Physical functioning				
Does your current health limit you in...:				
- vigorous activities, such as running, lifting heavy objects, participating in strenuous sports? ⁵	35.29 (35.06)	10.78 (20.77)	<i>t</i> (81.24) = 4.295 (.000**)	0.851 L
- moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or walking more than a hour? ⁵	67.65 (37.18)	30.39 (38.83)	<i>t</i> (100) = 4.949 (.000**)	0.980 L

The answers range: ¹ Very definitely and quite badly (3)-Not at all (0), ² always (0)-never (100), ³ excellent (100)-poor (0), ⁴ definitely true (100)-definitely false (0), ⁵ Yes, limited a lot (0)-No, not limited at all (100); the lower the score, the worse quality of life; ***p* < 0.01

Effect sizes, Cohen's *d*: L, large.

Discussion

In this study, we aimed to analyze the quality of life and affective status among three liver patient groups, from the following comparisons: 1) cirrhotic patients in the pre-waiting-list study with patients on the waiting list for a liver transplant; 2) cirrhotic patients from the pre-waiting-list study and liver transplant recipients; 3) cirrhotic patients on the waiting list and liver transplant recipients. Lastly, we aimed to analyze the correlations between these quality of life and affective variables and MELD scores.

Regarding the first goal, no relevant differences were found either in anxiety-depressive symptomatology or in quality of life between cirrhotic patients at the two assessment phases: when they were in the pre-waiting-list study and on waiting list for transplant. Thus, although patients at the waiting-list phase displayed statistically significant higher impairment on the Physical-Role and General Health subscales, these discrepancies were of a minimal magnitude (small effect sizes). In this sense, patients on the waiting list were slightly more impaired in their daily activities due to their physical condition, in comparison to those who were at a previous phase; the waiting-list patients also perceived themselves as slightly worse in terms of global health status.

With regard to the second goal, transplant recipients enjoyed better outcomes than pre-waiting-list patients, both in anxiety-depressive symptomatology (medium effect sizes) and quality of life, mainly in the physical dimensions. The differences obtained were of moderate magnitude (medium effect sizes) in the Physical Functioning, role limitations due to physical problems (Physical-Role), and Vitality subscales. On the one hand, to explain results in the affective area (anxiety-depressive symptomatology), we should take into account that cirrhotic patients in the pre-waiting-list study were hospitalized and had to undergo several medical tests that would decide their inclusion on the waiting list for subsequent liver transplant. Hospitalization generates loss of control over one's own life and involves several identified stressful factors, such as isolation, loss of intimacy, depersonalization, interruption of daily roles, etc. Likewise, while they are hospitalized, the patients receive a large amount of information that must be assimilated, which -along with the uncertainty due to the results of the medical tests- can produce high levels of anxiety in view of the possibility of a liver transplant. On the other hand, quality of life was more impaired among the pre-waiting-list patients, because cirrhosis involves several medical complications, particularly related to the physical domain (fatigue, ascites, encephalopathy, variceal bleeding, etc.) (Díaz-Domínguez, Pérez-Bernal, Pérez-

San-Gregorio, & Martín-Rodríguez, 2006; Molina-Jiménez, Gutiérrez-García, Hernández-Domínguez, & Contreras, 2008). Consequently, both groups displayed very relevant differences (large effect size) in the General Health scale. Hence, the pre-waiting-list patients perceived their global health status as much worse than the liver transplant recipients. In this sense, it was highlighted that they were not as healthy as people they knew, and that their health was not excellent.

Regarding the third goal, except for the Bodily Pain and the Emotional-Role dimensions, transplant patients enjoyed higher physical, psychological, and social well-being, in terms of statistical significance and of effect sizes (both large and medium ones) in all the remaining variables studied, in comparison to patients at the waiting-list stage. This negative affective status and worse quality of life among cirrhotic patients may be attributed to the fact that they were at a phase that was full of uncertainty due to poor information about diagnosis, complex decisions about future transplant, ignorance about organ availability, unclear expectations about medical procedures and results, etc. Likewise, waiting-list patients experience feelings of loss of freedom because of having to be localized 24 hours a day, as well as they suffer high levels of anxiety due to having to be admitted to an operating theater in order to undergo a high risk intervention (Brown, Sorrell, McClaren, & Creswel, 2006; Dudley, Chaplin, Clifford & Mutimer, 2007; Jurado et al., 2011; López-Navas et al., 2011; Martín, Stone, Scott, & Brashers, 2010). In this same vein, the waiting-list patients of this investigation commented much more frequently than transplant recipients that they felt frightened, as if something awful was about to happen. However, although quality of life is better among transplant recipients, risk of rejection and side effects from immunosuppressive drugs are always present (Morales, Varo, & Lázaro, 2012; Sargent & Wainwright, 2006). On the other hand, impairment in the physical dimensions was much higher in waiting-list patients than in pre-waiting-list patients in comparison to liver transplant recipients; large effect sizes were obtained in the Physical Functioning and role limitations due to physical problems (Physical-Role) scales. Thus, the waiting-list patients indicated that they had difficulty performing their activities as a result of their physical health more frequently than the transplant recipients. They also suffered more limitations performing vigorous activities (e.g., running, lifting heavy objects) or moderate activities (e.g., moving a table, pushing a vacuum cleaner, walking more than an hour). Therefore, the slightly higher impairment in the Physical-Role subscale in waiting-list patients in comparison to pre-waiting-list patients was more notable when compared to transplant recipients.

These differences cannot be attributed to hepatic disease severity as measured by MELD scores, because neither statistically significant group differences nor relevant effect sizes were found in this clinical scale, nor were statistically significant correlations found between the SF-36 physical dimensions and MELD. Along the same line as other investi-

gation, MELD scores only were weakly correlated with the SF-36 physical subscales, or did not predict scores in SF-36 dimensions (Saab et al., 2005). Therefore, as these and other authors conclude, physical quality of life impairment in pre-transplant patients may be explained by hepatopathy indicators such as ascites and encephalopathy (Les et al., 2010), which are not included in the MELD score. However, other authors (Rodríguez et al., 2006) state that these signs of decompensated cirrhosis do not predict post-transplantation quality of life.

On the other hand, in view of this higher physical impairment, waiting-list patients also perceived their global health status as much worse than transplant recipients, as was also the case with the pre-waiting-list patients. Likewise, they also commented they were not as healthy as people they knew, and their health was not excellent in comparison to the transplant recipients.

Moreover, regarding the last goal, no statistically significant correlations were found between quality of life, affective status, and MELD in any group, except for the waiting-list patients. In this group, not even significant weak correlations were found between SF-36 physical dimensions and MELD, as could be expected from other investigations about patients on the waiting list for liver transplant; although the correlation between MELD scores and mental health (measured by the HADS Anxiety subscale in our study) was corroborated by a higher effect size (Saab et al., 2005). On the contrary, another statistically significant correlation found between MELD and the variables studied was in the SF-36 Social Functioning dimension. Thus, this indicator of liver disease severity was weakly to moderately related to impairment of daily social relationships (with friends, family and neighbors) among patients awaiting for liver transplant. This result was found in another investigation, although the hepatopathy severity measure was the pre-transplant Child-Turcotte-Pugh score, and social functioning was a post-transplant outcome (Karam et al., 2003).

In conclusion, waiting-list patients displayed the worst biopsychosocial health status, followed by pre-waiting-list patients and liver transplant recipients; the latter enjoyed the best quality of life and affective status (Ortiz & Alós, 2011). Moreover, the MELD score is not sufficient to explain the differences between these groups, because relevant contrasts regarding quality of life and affective domains were found between patients in pre-transplant phases and liver transplant recipients, although the MELD scores were similar among them. Likewise, the MELD was only related to affective and social dimensions among the waiting-list patients and not to physical quality-of-life domains.

Lastly, although our results confirm the benefits derived from liver transplant as the intervention of choice in order to improve severe cirrhotic patients' quality of life and affective functioning, psychological treatments are also necessary during the entire medical transplant protocol to achieve better biopsychosocial adjustment. On the one hand, particularly in the pre-transplant phase, because worse mental health pre-

dicts negative post-transplant outcomes (Kelly et al., 2006; Zipfel et al., 2002). On the other hand, even in the post-transplant phase, because these patients do not achieve the well-being levels of the general population (Estraviz et al., 2007; Kousoulas et al., 2008) and mental health impairment predicts worse daily functioning -by means of fatigue- (Van Ginneken et al., 2010) and mortality after transplant (Pérez-San-Gregorio, Martín-Rodríguez, Galán-Rodríguez, & Bor-

da-Más, 2009). Likewise, if the psychological complications at the pre-waiting-list-study phase are identified and treated, future disorders will be prevented in next stages such as at the waiting-list and post-transplant phases.

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