



Mental health and quality of life in liver transplant and cirrhotic patients with various etiologies¹

María Ángeles Pérez-San-Gregorio² (*Universidad de Sevilla, Spain*),
Agustín Martín-Rodríguez (*Universidad de Sevilla, Spain*),
Elisabeth Domínguez-Cabello (*Universidad de Sevilla, Spain*),
Eduardo Fernández-Jiménez (*Universidad de Sevilla, Spain*),
Mercedes Borda-Más (*Universidad de Sevilla, Spain*), and
Ángel Bernardos-Rodríguez (*Hospital Universitario Virgen del Rocío, Spain*)

ABSTRACT. In this study we aimed to: 1) examine whether there were differences in mental health and quality of life of liver transplant recipients according to etiology that led to transplantation (alcoholic cirrhosis, Hepatitis B/C Virus, hepatocellular carcinoma and others); and 2) to compare mental health and quality of life between liver transplant and cirrhotic patients, according to etiologies that most often lead to liver transplantation (alcoholic and Hepatitis C Virus). Two patient groups participated: 168 transplant recipients and 63 cirrhotic patients. Mental health was assessed by the Hospital Anxiety and Depression Scale and quality of life by the SF-36 Health Survey. We found the following results: 1) statistically significant differences were found in anxiety, depression, general health, and vitality; in all of them, transplant patients due to Hepatitis C Virus showed the highest impairment and transplant patients due to alcoholic cirrhosis showed the lowest deterioration; 2) cirrhotic patients, compared to transplanted, and patients with Hepatitis C Virus, compared to alcoholic liver patients, were the groups with greater biopsychosocial impairment. In the absence of interactive effects between factors groups and etiology, Hepatitis C Virus patients had higher biopsychosocial impairment than alcoholic liver patients, regardless of whether or not they underwent transplant.

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² Correspondence: Departamento de Personalidad, Evaluación y Tratamiento Psicológicos. Facultad de Psicología. Universidad de Sevilla. C/ Camilo José Cela, s/n. 41018 Sevilla (Spain). E-mail: anperez@us.es

KEYWORDS. Biopsychosocial well-being. Liver transplantation. Liver cirrhosis. Etiologies leading to transplant. *Ex post facto* study.

RESUMEN. En este estudio se plantea: 1) analizar diferencias en salud mental y calidad de vida entre trasplantados hepáticos en función de la etiología desencadenante del trasplante (etílica, Virus de la Hepatitis B/C, hepatocarcinoma y otras), y 2) comparar la salud mental y la calidad de vida entre trasplantados hepáticos y enfermos cirróticos en función de las etiologías que con más frecuencia desencadenan el trasplante hepático (etílica y Virus de la Hepatitis C). Se seleccionaron dos grupos: 168 trasplantados y 63 cirróticos. Se empleó la Escala Hospitalaria de Ansiedad y Depresión y el Cuestionario de Salud SF-36. Los resultados indicaron: 1) diferencias significativas en las variables ansiedad, depresión, salud general y vitalidad; en todas ellas el mayor deterioro correspondió a trasplantados con el Virus de la Hepatitis C y el menor a etílicos, 2) enfermos cirróticos *versus* trasplantados hepáticos, y enfermos con el Virus de la Hepatitis C *versus* etílicos, fueron los grupos con mayor deterioro biopsicosocial. Ante la inexistencia de efectos interactivos entre los factores grupo y etiología, se concluye que los pacientes con Virus de la Hepatitis C presentan mayor deterioro biopsicosocial en comparación con pacientes etílicos, independientemente de que hubieran sido o no trasplantados.

PALABRAS CLAVE. Bienestar biopsicosocial. Trasplante hepático. Cirrosis hepática. Etiologías desencadenantes del trasplante. Estudio *ex post facto*.

Liver transplantation is a completely consolidated therapy that improves patients' quality of life, although they do not achieve the same levels as the general population (Karam *et al.*, 2003; Sumskiene, Sumskas, Petrauskas, and Kupcinskas, 2006; Taylor, Franck, Gibson, and Dhawan, 2005). Thus, for example, in a study that analyzed health-related quality of life in three groups (cirrhotic patients who presented diverse levels of severity -mild, moderate, and severe-, liver transplant patients, and healthy population), it was found that the quality of life of the transplant recipients did not reach the levels of the healthy population, although it was significantly better than that of the cirrhotic patients, especially compared to those who were in advanced stages of the liver disease (Pantiga *et al.*, 2005). Similarly, another study that compared the same groups also found that the best functioning corresponded to the healthy people and the worst to the transplant candidates. In comparison to the last group, the liver transplant recipients had fewer limitations in their psychosocial functioning, but in comparison to the control group, some aspects of their functioning were worse, especially the physical and social dimensions (O'Carroll, Turner, Flatley, McGregor, and Hayes, 2008).

The quality of life of liver transplant recipients may be conditioned by the diverse etiologies that lead to transplantation, with alcoholic cirrhosis and cirrhosis associated with Hepatitis C Virus (HCV) being the main indications. In the same vein, most of the investigations report that the quality of life of HCV transplant recipients is worse than that of other transplant recipients: poorer physical functioning (Feurer *et al.*, 2002; Paterson *et al.*, 2000), higher presence of anxious-depressive symptomatology (De Bona

et al., 2000; Dwight *et al.*, 2000; Paterson *et al.*, 2000), fibromyalgia (Goulding, O'Connell, and Murray, 2001) and fatigue (Kallman *et al.*, 2007). In general, the studies conclude that alcoholic cirrhotic patients have better quality of life than cirrhotic patients with HCV, both before and after the transplant (Burra *et al.*, 2005). Nevertheless, other studies reach different, and even contradictory, conclusions: transplant recipients with alcoholic cirrhosis or cryptogenic cirrhosis have worse quality of life than patients with autoimmune hepatitis or viral hepatitis (Aadahl, Hansen, Kirkegaard, and Groenvold, 2002); HCV transplant recipients have worse quality of life than patients with hepatocellular carcinoma or primary biliary cirrhosis (Estraviz *et al.*, 2007); and alcoholic cirrhotic patients display worse psychological functioning in comparison to HCV-infected patients (Minazzato *et al.*, 2009).

Likewise, regarding the studies focused on analyzing the influence of the etiology of cirrhosis on the biopsychosocial well-being of patients who are candidates for a liver transplant, the conclusions are also contradictory: cirrhotic patients with Hepatitis B Virus (HBV) have better quality of life than cirrhotic HCV patients or than patients with primary biliary cirrhosis (Bondini *et al.*, 2007); patients with autoimmune hepatitis display higher levels of clinical anxiety in comparison to patients who suffer alcoholic cirrhosis or hepatocellular carcinoma (Santos *et al.*, 2010), and the etiology of the cirrhosis does not determine the quality of life (Jurado *et al.*, 2011).

In view of the relevance of this topic in clinical practice, the scarcity of this topic in Spain, and of the controversial results of previous investigations, we aimed to continue to analyze the differences between pre- and post- transplant liver patients as a function of etiology of liver disease in the Spanish population. Therefore, in the present *ex post facto* study (Montero and León, 2007), we proposed two main goals: 1) firstly, to determine whether there are any differences in mental health and quality of life of liver transplant recipients as a function of the etiology of the disease that led to the transplant (alcoholic, HBV, HCV, hepatocellular carcinoma, and others), and 2) secondly, to compare the mental health and quality of life between liver transplant recipients and cirrhotic patients who are potential transplant candidates as a function of the etiologies that most frequently lead to liver transplant (alcoholic and HCV). Likewise, we aimed to control demographic and clinical parameters as covariables, in order to highlight in the analysis the influence of factors *groups* (liver transplant recipients and cirrhotic patients) and *etiology* (alcoholic and HCV).

Method

Participants

To carry out this study, two groups of patients were selected: 168 liver transplant recipients and 63 patients with hepatic cirrhosis. The group of transplant recipients was made up of 126 men and 42 women, mean age 50.42 years ($SD = 10.57$ years). They all had received a first liver transplant five years ago, on average, proceeding from a donor who had died from the following causes: cerebrovascular accidents (60.5%), craneoencephalic traumas (34.1%), and others (5.4%). This group was divided into five

subgroups as a function of the etiology of the disease that led to the transplant: alcoholic ($n = 59$), HCV ($n = 40$) hepatocellular carcinoma ($n = 28$), HBV ($n = 14$), and others ($n = 27$). The group of cirrhotic patients was made up of 58 men and 5 women, mean age 56.16 years ($SD = 7.72$ years). This group was divided into two subgroups depending on the etiology of the disease: alcoholic cirrhosis ($n = 38$) and HCV ($n = 25$).

Instruments

- Clinical variables. In the case of the transplant recipients, we collected the following clinical data related to the diverse stages of the transplant: a) preoperative: etiology of the disease that led to transplant (alcoholism, HBV, HCV, hepatocellular carcinoma, and others), scores on the Child-Pugh scale (mild, moderate, and severe) and on the Model for End-stage Liver Disease (MELD) scale; b) perioperative: quality of the graft implanted (optimal or suboptimal); and c) postoperative: complications of the function of the graft (rejection), complications of the depressed immune system (Epstein Barr Virus -EBV- and cytomegalovirus -CMV), hospital admissions due to medical problems after transplant, and type of immunosuppressive medication prescribed (cyclosporine, tacrolimus, micophelionate, cyclosporine + micophelionate, and tacrolimus + micophelionate). In the case of the cirrhotic patients, we collected the same data as for the transplant recipients in the preoperative stage: etiology of the liver pathology and scores on the Child-Pugh and MELD scales.
- Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983). This instrument has 14 items, 7 of depression and 7 of anxiety, in which patients indicate how they felt during the past week, selecting one of four response options. The test provides two scores, one for anxiety and the other for depression. According to Herrero *et al.* (2003), the optimal cut-off point for the screening of depressive disorders is 5 and is 8 for the screening of anxiety disorders in several clinical populations in Spain. In Spanish studies, Cronbach's alpha values range between .80 and .90. We used the version developed by Caro and Ibáñez (1992). This questionnaire has been described as one of the most commonly used in liver transplantation, as well as, has shown suitable psychometric properties in this clinical population (Jay, Butt, Ladner, Skaro, and Abecassis, 2009).
- SF-36 Health Survey (Alonso, Prieto, and 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 (physical-role), bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems (emotional-role), 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.* 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

Before beginning the psychological assessment of the participants of the study, they were informed about the study, their doubts were clarified, and written informed consent was obtained, emphasizing that their participation was voluntary and they could leave the study at any time, without having to offer any explanation and without this having any negative effects on their medical care.

In the two groups (liver transplant recipients and cirrhotic patients), we took the following inclusion criteria into account: being over 18 years of age, having a reading/writing level that allowed them to complete the diverse scales employed, not presenting any incapacitating state (severe encephalopathy, coma, etc.) to understand items of questionnaires at the moment of assessment, and giving their written informed consent to participate in the investigation. Other specific inclusion criteria were: in the transplanted group, having received a first liver transplant (retransplant recipients were excluded) proceeding from a deceased donor; and in the group of cirrhotic patients, being admitted in the Digestive Diseases Unit with alcoholic cirrhosis or cirrhosis associated with HCV, for a medical study to determine their inclusion on the waiting list for subsequent liver transplant (possible recipients of a combined liver-kidney transplant were excluded) proceeding from a deceased donor.

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 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 following inclusion criteria: not being able to read or write, not wishing to participate, and having been retransplanted. We finally assessed 168 patients.

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 admission 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 20 of them because they did not meet the following inclusion criteria: not being able to read or write, not wishing to participate, suffering very uncommon etiologies -HBV, autoimmune and cryptogenic- and being under study for a liver-kidney transplant. We finally assessed 63 patients.

Data analyses

All the analyses were performed with the SPSS 19.0 statistical package. To compare the categorical variables in the diverse groups, we used Pearson's chi-square statistic, and to compare the continuous variables among the five subgroups of transplant

recipients with different etiologies, we used the Kruskal-Wallis statistic (with *post hoc* analysis by means of the Mann-Whitney *U* statistic). We also applied Analysis of Covariance (ANCOVA), to analyze the influence of two independent variables with two levels in each variable: *groups* (liver transplant recipients and cirrhotic patients) and *etiology* (alcoholic and HCV). This analysis allowed us to control the possible influence of clinical (MELD and Child-Pugh scores) and demographic variables (age and gender).

Results

Firstly, we compared the clinical data of the liver transplant recipients taking into account the five types of etiologies that determined the transplant (see Table 1). We found no statistically significant differences in variables such as MELD scores ($p = .07$), quality of the graft ($p = .26$), rejection of the graft ($p = .52$), presence of EBV ($p = .44$), and hospital admissions due to medical complications after the transplant ($p = .07$). Other clinical variables (Child-Pugh, CMV, and type of immunosuppressive medication) could not be compared because there was a very small number of patients in some levels.

TABLE 1. Comparisons in clinical data among liver transplant patients.

<i>Etiology leading to transplant</i>	<i>MELD Mean (SD)</i>	<i>Graft quality (%)</i>	<i>Graft rejection (%)</i>	<i>Presence of EBV (%)</i>	<i>Hospital Admissions (%)</i>
Alcohol ($n = 59$)	17.24 (3.96)	Optimal: 69.5 Suboptimal: 30.5	Yes: 22 No: 78	Yes: 67.8 No: 32.2	Yes: 10.2 No: 89.8
HCV ($n = 40$)	17.69 (3.84)	Optimal: 80 Suboptimal: 20	Yes: 25 No: 75	Yes: 65 No: 35	Yes: 25 No: 75
Hepatocarcinoma ($n = 28$)	16 (3.51)	Optimal: 57.1 Suboptimal: 42.9	Yes: 21.4 No: 78.6	Yes: 78.6 No: 21.4	Yes: 14.3 No: 85.7
HBV ($n = 14$)	18.69 (2.68)	Optimal: 78.6 Suboptimal: 21.4	Yes: 35.7 No: 64.3	Yes: 50 No: 50	Yes: 35.7 No: 64.3
Others ($n = 27$)	17.52 (4.82)	Optimal: 77.8 Suboptimal: 22.2	Yes: 37 No: 63	Yes: 70.4 No: 29.6	Yes: 29.6 No: 70.4
Intergroup comparisons	$H(4,168) = 8.61$ ($p = .07$)	$\chi^2 = 0.56$ ($p = .26$)	$\chi^2 = 3.18$ ($p = .52$)	$\chi^2 = 3.74$ ($p = .44$)	$\chi^2 = 8.58$ ($p = .07$)

Upon comparing mental health and quality of life among the five subgroups of liver transplant recipients of various etiologies, we found statistically significant differences in the variables anxiety ($p = .05$), depression ($p = .04$), general health ($p = .004$), and vitality ($p = .03$; see Table 2). In all of these variables, we found the same results, that is, the subgroup of HCV transplant recipients showed greater impairment, and the subgroup of alcoholic transplant recipients enjoyed greater well-being.

TABLE 2. Comparisons in mental health (HADS) and quality of life (SF-36) among liver transplant patients with various etiologies.

Psychological variables	Etiology leading to transplant					Contrast statistic	p
	Alcohol (n = 59) M (SD)	HCV (n = 40) M (SD)	Cancer ¹ (n = 28) M (SD)	HBV (n = 14) M (SD)	Others (n = 27) M (SD)		
HADS²							
Anxiety	3.76 (3.05)	6.48 (4.77)	5.54 (4.18)	5.71 (4.26)	6.11 (4.96)	9.505	.05*
Depression	3.42 (3.05)	5.40 (4.14)	3.93 (4.24)	4.43 (3.10)	3.56 (4.19)	9.659	.04*
SF-36³							
Bodily pain	74.84 (26.66)	62.07 (31.69)	62.39 (33.10)	65.35 (29.49)	72.29 (27.72)	6.898	.14
Physical-role	77.54 (24.43)	68.59 (32.87)	58.03 (36.35)	66.96 (28.84)	75.46 (26.34)	7.176	.12
Mental health	77.11 (19.01)	62.87 (26.30)	76.07 (20.69)	70.71 (17.19)	72.22 (21.36)	8.811	.06
General health	73.77 (17.81)	56.00 (24.94)	62.85 (24.33)	57.21 (19.64)	65.07 (26.22)	15.619	.004**
Vitality	72.19 (21.49)	57.81 (24.86)	64.73 (23.94)	59.82 (24.35)	65.41 (22.96)	10.459	.03*
Social functioning	77.96 (23.36)	68.75 (31.52)	69.19 (28.76)	69.63 (31.65)	75.00 (29.41)	2.777	.59
Emotional-role	80.08 (22.37)	63.95 (34.56)	69.34 (30.76)	79.16 (25.89)	78.08 (24.80)	5.954	.20
Physical functioning	72.71 (25.19)	64.12 (28.30)	66.42 (26.27)	76.78 (22.32)	79.25 (24.12)	8.274	.08

Note: ¹Hepatocarcinoma; ²the higher score, the worse mental health; ³the lower score, the worse quality of life; * $p \leq .05$, ** $p < .01$

From the *post hoc* analyses with these four variables, statistically significant differences were found among the following subgroups: alcoholic transplant recipients and HCV transplant recipients, in the variables anxiety ($p = .006$), depression ($p = .009$), general health ($p < .001$), and vitality ($p = .002$). Significant differences were found between the HCV transplant recipients and those who suffered from other etiologies in the variable depression ($p = .013$); and between the alcoholic transplant recipients and the HBV transplant recipients, in the dimension general health ($p = .007$). In the latter two comparisons, the transplant recipients with chronic viral hepatitis (B and C) suffered greater impairment too (see Table 3).

TABLE 3. Intergroup comparisons between liver transplant patients with various etiologies.

Variables	Alcohol and HCV	Alcohol and cancer ¹	Alcohol and HBV	Alcohol and others	HCV and cancer ¹	HCV and HBV	HCV and others	cancer ¹ and HBV	cancer ¹ and others	HBV and others
Contrast statistic (p)										
HADS:										
Anxiety	-2.73 (.006**)	-1.89 (.05)	-1.54 (.12)	-1.90 (.05)	-0.62 (.53)	-0.56 (.57)	-0.35 (.72)	-0.18 (.85)	-0.29 (.76)	-0.16 (.86)
Depression	-2.59 (.009**)	-0.03 (.97)	-1.22 (.22)	-0.70 (.48)	-1.94 (.05)	-0.37 (.70)	-2.47 (.01*)	-0.98 (.32)	-0.48 (.62)	-1.29 (.19)
SF-36:										
General health	-3.61 ($< .001$ ***)	-1.78 (.07)	-2.70 (.007**)	-1.48 (.13)	-0.98 (.32)	-0.35 (.72)	-1.58 (.11)	-0.96 (.33)	-0.43 (.66)	-1.06 (.28)
Vitality	-3.04 (.002**)	-1.36 (.17)	-1.87 (.06)	-1.53 (.12)	-0.98 (.32)	-0.37 (.73)	-1.29 (.19)	-0.55 (.58)	-0.26 (.79)	-0.77 (.43)

Note: ¹Hepatocarcinoma; * $p \leq .05$, ** $p < .01$.

In the Analysis of Covariance (ANCOVA), we used two factors (*groups* and *etiology*) with two levels in each factor: liver transplant versus cirrhotic patients (*groups*), and alcohol versus HCV (*etiology*). The scores in the MELD and Child-Pugh scales, age, and gender were defined as covariates (see Table 4).

TABLE 4. Comparisons in clinical and demographic data among the groups under study.

Groups	MELD <i>Mean (SD)</i>	Child-Pugh (%)	Age <i>Mean (SD)</i>	Gender (%)
Liver transplant patients (<i>n</i> = 99)	17.44 (3.89)	Mild: 4.2 Moderate: 44.2 Severe: 51.6	53.24 (7.58)	Men: 76.8 Women: 23.2
Cirrhotic patients (<i>n</i> = 63)	15.53 (5.02)	Mild: 19 Moderate: 46 Severe: 35	56.16 (7.72)	Men: 92.1 Women: 7.9
Intergroup comparisons	$F(1,160) = 7.28$ ($p = .008^{**}$)	$\chi^2 = 16.60$ ($p = .005^{**}$)	$F(1,160) = 5.39$ ($p = .02^*$)	$\chi^2 = 5.27$ ($p = .02^*$)
Etiology	MELD <i>Mean (SD)</i>	Child-Pugh (%)	Age <i>Mean (SD)</i>	Gender (%)
Alcohol (<i>n</i> = 97)	16.77 (4.72)	Mild: 8.4 Moderate: 44.2 Severe: 47.4	55.06 (6.93)	Men: 91.8 Women: 8.2
HCV (<i>n</i> = 65)	16.46 (4.19)	Mild: 12.7 Moderate: 46 Severe: 41.3	53.35 (8.77)	Men: 69.1 Women: 30.9
Intergroup comparisons	$F(1,160) = 0.44$ ($p = .50$)	$\chi^2 = 1.02$ ($p = .59$)	$F(1,160) = 1.76$ ($p = .18$)	$\chi^2 = 12.27$ ($p < .001^{**}$)

* $p < .05$, ** $p < .01$.

Regarding the interactive effects analyzed with the ANCOVA between the factors *groups* and *etiology*, no statistically significant relationships were found in any of the variables studied (see Table 5). These results indicate that the effects that exert each one of these factors (*groups* and *etiology*) on the variables related to mental health and quality of life are independent of each other. It could be said that the HCV patients presented greater biopsychosocial impairment than the alcoholic liver patients, independently of whether or not they had been transplanted (see Figures 1 and 2).

TABLE 5. Comparisons in mental health (HADS) and quality of life (SF-36) between liver transplant and cirrhotic patients as a function of etiology.

Variables	Groups		Etiology		Main Effects		Interactive effects <i>F</i> (1,160) (<i>p</i>)
	Liver transplant (<i>n</i> = 99) <i>M</i> (<i>SD</i>)	Cirrhotic patients (<i>n</i> = 63) <i>M</i> (<i>SD</i>)	Alcohol (<i>n</i> = 97) <i>M</i> (<i>SD</i>)	HCV (<i>n</i> = 65) <i>M</i> (<i>SD</i>)	Groups <i>F</i> (1,160) (<i>p</i>)	Etiology <i>F</i> (1,160) (<i>p</i>)	
HADS¹:							
Anxiety	4.86 (4.04)	8.40 (4.90)	5.49 (4.40)	7.34 (4.96)	21.23 (<i><.001**</i>)	4.73 (.03*)	1.39 (.24)
Depression	4.22 (3.64)	6.87 (4.61)	4.64 (3.83)	6.17 (4.66)	10.82 (.001**)	6.24 (.01*)	0.87 (.35)
SF-36²:							
Bodily pain	69.68 (29.33)	59.87 (32.88)	70.80 (29.43)	58.50 (32.12)	4.62 (.03*)	3.29 (.07)	0.04 (.82)
Physical-role	73.92 (28.33)	45.83 (35.33)	67.26 (33.08)	56.63 (34.69)	28.03 (<i><.001**</i>)	3.43 (.06)	0.36 (.54)
Mental health	71.36 (23.20)	58.96 (23.57)	71.54 (20.55)	59.07 (26.96)	10.49 (.002**)	7.59 (.007**)	0.34 (.55)
General health	66.59 (22.63)	37.06 (18.16)	61.46 (23.38)	45.63 (25.61)	74.36 (<i><.001**</i>)	20.54 (<i><.001**</i>)	0.35 (.55)
Vitality	66.32 (23.89)	43.94 (24.64)	63.15 (24.87)	49.32 (26.81)	35.07 (<i><.001**</i>)	10.40 (.002**)	0.003 (.96)
Social functioning	74.24 (27.18)	57.33 (30.49)	72.67 (25.59)	60.19 (33.57)	13.67 (<i><.001**</i>)	9.64 (.002**)	0.09 (.76)
Emotional-role	73.56 (28.89)	62.83 (32.98)	75.60 (26.92)	60.12 (34.18)	3.33 (.07)	7.79 (.006**)	0.002 (.96)
Physical functioning	69.24 (26.69)	47.38 (30.91)	64.69 (28.68)	54.84 (31.79)	26.95 (<i><.001**</i>)	5.00 (.02*)	0.19 (.66)

Note: ¹The higher score, the worse mental health; ²the lower score, the worse quality of life; * *p* < .05, ** *p* < .01.

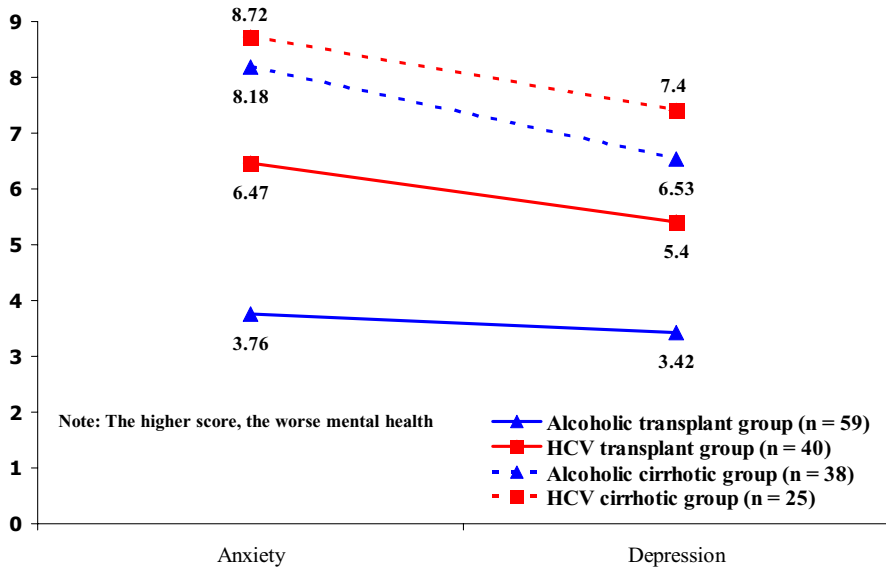


FIGURE 1. Mean scores on mental health (HADS) in liver transplant and cirrhotic groups as a function of HCV and alcoholic etiologies.

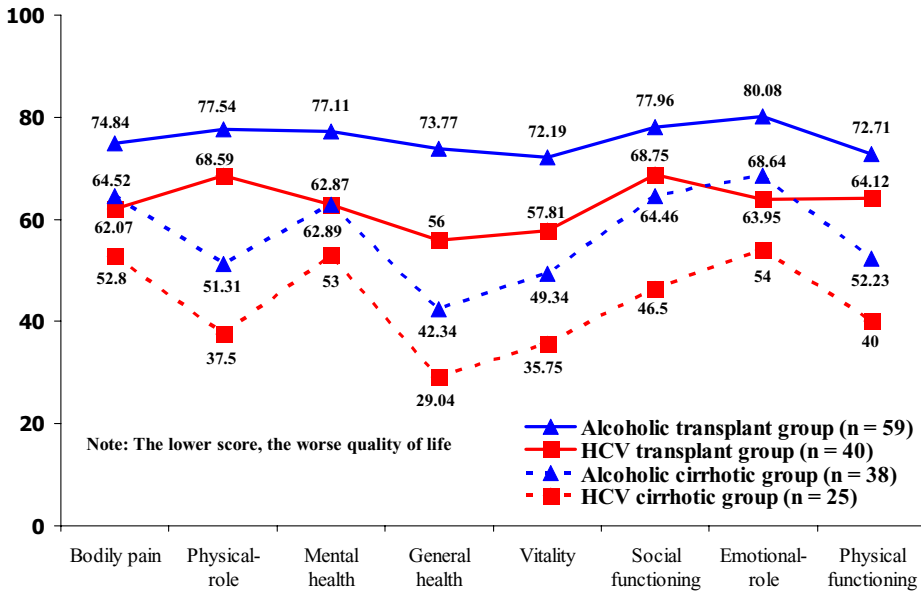


FIGURE 2. Mean scores on quality of life (SF-36) in liver transplant and cirrhotic groups as a function of HCV and alcoholic etiologies.

With regard to the main effects (see Table 5), we found statistically significant differences among the groups of transplant recipients and cirrhotic patients in the variables anxiety ($p < .001$), depression ($p = .001$), bodily pain ($p = .03$), physical-role ($p < .001$), mental health ($p = .002$), general health ($p < .001$), vitality ($p < .001$), social functioning ($p < .001$), and physical functioning ($p < .001$). In all these variables, the cirrhotic patients, in comparison to the liver transplant recipients, displayed greater biopsychosocial impairment. We also found statistically significant differences among the groups as a function of the etiology of the disease in the variables anxiety ($p = .03$), depression ($p = .01$), mental health ($p = .007$), general health ($p < .001$), vitality ($p = .002$), social functioning ($p = .002$), emotional-role ($p = .006$), and physical functioning ($p = .02$). In all of them, the viral patients had poorer well-being in comparison to the alcoholic liver patients.

Discussion

This research continues to study quality of life among various populations, which still remains a focus of scientific interest in Health Psychology, as can be observed from the development of new questionnaires about this construct (Verdugo, Arias, Gómez, and Schalock, 2010). As well as, this is also observed in the study of the psychometric properties of known tools of quality of life in other clinical populations (Van Esch, Den Oudsten, and De Vries, 2011).

With regard to the first goal we had posed, after verifying that the five subgroups of transplant recipients were homogeneous in the main medical variables, we found that the most important differences were concentrated among the groups of alcoholic liver patients and the HCV patients; the latter presented poorer well-being, specifically, more anxious-depressive symptomatology, worse perception of their general health, and less vitality. Likewise, among the HCV patients, the levels of depressive symptomatology are above clinical threshold, according to Herrero *et al.* (2003). As well as, they show worse scores than Spanish nonclinical population in general health and vitality dimensions (Alonso *et al.*, 1998). These results are in the same vein as other studies that confirm a higher incidence of anxious-depressive symptomatology, phobias, and paranoid ideation in these transplant recipients; all of this is conditioned by the fear of HCV recurrence (Burra *et al.*, 2005; De Bona *et al.*, 2000; Dwight *et al.*, 2000; Paterson *et al.*, 2000), despite no physical complications of liver disease are present (Bownik and Saab, 2010). In this sense, although the majority of the transplant recipients perceive an uncertain future regarding the survival of the graft, in the case of the HCV transplant patients, the degree of uncertainty is higher because they are aware of the nonexistence of any effective prophylaxis against a relapse of this virus. This could generate a state of helplessness with negative consequences on the psychological and physical well-being of these patients, especially if it is taken into account that, if there is a relapse of HCV after the transplant, it would advance to a new cirrhosis in 20-30% of the cases after five years. In contrast, the HBV transplant recipients were only different from the alcoholic liver patients in their perception of their general health, with the viral patients displaying greater impairment. In this area, it should be taken into account that there

is also some risk of relapse in HBV but, in contrast to HCV, there is a preventive treatment during and after the transplant. This might explain why other mood-related areas -which were assessed with the HADS, because it detects the presence of negative expectations about the future (hopelessness, pessimism, catastrophic thoughts)- were less affected in these patients.

With regard to the second goal, after controlling the clinical and demographic variables by means of ANCOVA, important differences in mental health were found. Specifically, the patients with cirrhosis presented more anxiety-depressive symptomatology (HADS), which exceeds clinical threshold in both subscales (Herrero *et al.*, 2003), and worse general mental health (SF-36) than the liver transplant recipients. Moreover, in both groups, the HCV patients, in comparison to the alcoholic liver patients, showed more emotional distress and clinical significance was reached in depression subscale (Herrero *et al.*, 2003). To explain these results, we emphasize the situation that the cirrhotic patients were undergoing; they were all hospitalized for a medical assessment that would determine their inclusion on the waiting list. Consequently, for the patients, it was an interval charged with uncertainty, which has negative repercussions on their emotional state. To this must be added the negative anticipations these patients usually have and which disappear after the transplant; which are caused by the following factors: ignorance about the benefits of the surgery versus the associated risks, the impossibility of estimating the time they would have to wait to be transplanted due to the scarcity of organs, and loss of freedom because they must be located 24 hours a day if they are included on the waiting list (Díaz-Domínguez, Pérez-Bernal, Pérez-San-Gregorio, and Martín-Rodríguez, 2006; Martin, Stone, Scott, and Brashers, 2010). These negative anticipations could be the basis of the affective impairment found between cirrhotic and HCV patients, because fear is a nonspecific emotion related to both depressive and anxiety disorders (Watson, Clark, and Stasik, 2011). In both groups (transplant recipients and cirrhotic patients) and in the same vein as other investigations (De Bona *et al.*, 2000; Dwight *et al.*, 2000; Paterson *et al.*, 2000), the HCV patients, in comparison to the alcoholic liver patients, presented greater emotional impairment (more anxiety-depressive symptomatology -HADS- and worse general mental health -SF-36). This can be explained by the habitually worse clinical conditions of these patients, because, on the one hand, in the pre-transplant phase, if the organ does not arrive on time, this could mean their exclusion from the waiting list, thereby increasing their negative expectations about their imminent death, and on the other hand, in the post-transplant phase, they could suffer a relapse of the virus (Burra *et al.*, 2005). All the above could also explain why the dimension referring to the emotional-role is more affected in the viral patients than in the alcoholic liver group.

Likewise, when focusing on the quality of life from a perspective more closely related to the physical aspects, we also found greater impairment in the cirrhotic patients than in the liver transplant recipients in the following dimensions: bodily pain, physical-role, vitality, and physical functioning. Moreover, these scores among cirrhotic patients are very different from Spanish general population's mean levels, above all in vitality, physical-role and physical functioning dimensions (Alonso *et al.*, 1998). This finding is explained because the cirrhotic patients were in an advanced stage of their

hepatopathy, which implied a threat to their quality of life because of the symptoms of decompensated cirrhosis: esophageal varices, ascites, encephalopathy, etc. Along the same lines as other investigations (Feurer *et al.*, 2002; Paterson *et al.*, 2000), the greatest impairment in the dimensions of vitality and physical functioning corresponded to the HCV patients, both in cirrhotic patients and transplant recipients, and these scores are also very different to Spanish general population's mean levels (Alonso *et al.* 1998). In this sense, it should be taken into account that patients with alcoholic cirrhosis can exert some control over their disease through absolute abstinence from alcohol and the practice of healthy habits, whereas patients with HCV cannot exert any control because this virus persists in the organism, which could explain a greater physical impairment of these patients both before and after the transplant.

From a social perspective, the viral patients, in comparison to the alcoholic liver patients, presented a higher degree of impairment in the social functioning dimension regardless of whether or not they had been transplanted. Moreover, this deterioration in social domain was very relevant in comparison to Spanish general population's social functioning (Alonso *et al.*, 1998). A possible explanation is that HCV patients, independently of the stage of the disease they are undergoing, fear the possibility of transmitting the virus to their friends and relatives, which could hinder their social and family activities. With regard to this, the feeling of guilt and shame provoked by the disease has been described by HCV transplant recipients as one of the determinant factors of their quality of life after the transplant (Dudley, Chaplin, Clifford, and Mutimer, 2007; Strauss and Teixeira, 2006).

Lastly, as reflected in the dimension of general health, the HCV patients, in comparison to the alcoholic liver patients, perceive themselves as less healthy, independently of whether or not they were transplanted. Likewise, their self-perception of health is much worse than that of Spanish nonclinical population (Alonso *et al.*, 1998). This could be due to the fact that the viral patients have to undergo more medical controls because, before the transplant, they have a high risk of developing hepatocellular carcinoma, and after the transplant, they could be reinfected with the same virus. In fact, long-term graft survival is notably lower in liver transplant recipients due to HCV than in people whose transplant was due to other etiologies (Forman, Lewis, Berlin, Feldman, and Lucey, 2002).

On the other hand, among the limitations of this study, the following ones are highlighted. First, this research has a cross-sectional design, therefore, no conclusions could be reached about the results in terms of evolution (changes from pre- to post-transplant phase). On the other hand, some subgroups had very few participants (*i.e.*, HBV patients), therefore, this fact limits external validity of results with regard to this clinical condition.

In conclusion, psychological intervention is essential during the entire process of liver transplant, but particularly for HCV patients. In addition, specific psychological interventions would improve the psychosocial well-being of these patients, and likewise, this would improve their therapeutic adherence, in view of worse quality of life before treatment for HCV among imperfect adherent patients (Marcellin *et al.*, 2011). Moreover, psychological treatment is relevant to diminish the mortality rates in this population,

because mental health impairment predicts mortality after transplant (Pérez-San-Gregorio, Martín-Rodríguez, Galán-Rodríguez, and Borda-Más, 2009).

References

- Aadahl, M., Hansen, B.A., Kirkegaard, P., and Groenvold, M. (2002). Fatigue and physical function after orthotopic liver transplantation. *Liver Transplantation*, 8, 251-259.
- Alonso, J., Prieto, L., and Antó, J.M. (1995). La versión española del SF-36 Health Survey (Cuestionario de Salud SF-36): Un instrumento para la medida de los resultados clínicos. *Medicina Clínica*, 104, 771-776.
- Alonso, J., Regidor, E., Barrio, G., Prieto, L., Rodríguez, C., and De La Fuente, L. (1998). Valores poblacionales de referencia de la versión española del Cuestionario de Salud SF-36. *Medicina Clínica*, 111, 410-416.
- Bondini, S., Kallman, J., Dan, A., Younoszai, Z., Ramsey, L., Nader, F., and Younoszi, Z.M. (2007). Health-related quality of life in patients with chronic hepatitis B. *Liver International*, 27, 1119-1125.
- Bownik, H. and Saab, S. (2010). The effects of hepatitis C recurrence on health-related quality of life in liver transplant recipients. *Liver International*, 30, 19-30.
- Burra, P., De Bona, M., Canova, D., Feltrin, A., Ponton, A., Ermani, M., Brolese, A., Rupolo, G., and Naccarato, R. (2005). Longitudinal prospective study on quality of life and psychological distress before and one year after liver transplantation. *Acta Gastro-Enterologica Belgica*, 68, 19-25.
- Caro, I. and Ibáñez, E. (1992). La Escala Hospitalaria de Ansiedad y Depresión. Su utilidad práctica en Psicología de la Salud. *Boletín de Psicología*, 36, 43-69.
- De Bona, M., Ponton, P., Ermani, M., Iemmolo, R.M., Feltrin, A., Boccagni, P., Gerunda, G., Naccarato, R., Rupolo, G., and Burra, P. (2000). The impact of liver disease and medical complications on quality of life and psychological distress before and after liver transplantation. *Journal of Hepatology*, 33, 609-615.
- Díaz-Domínguez, R., Pérez-Bernal, J., Pérez-San-Gregorio, M.A., and Martín-Rodríguez, A. (2006). Quality of life in patients with kidney, liver or heart failure during the waiting list period. *Transplantation Proceedings*, 38, 2459-2461.
- Dudley, T., Chaplin, D., Clifford, C., and Mutimer, D.J. (2007). Quality of life after liver transplantation for hepatitis C infection. *Quality of Life Research*, 16, 1299-1308.
- Dwight, M.M., Kowdley, K.V., Russo, J.E., Ciechanowski, P.S., Larson, A.M., and Katon, W.J. (2000). Depression, fatigue, and functional disability in patients with chronic hepatitis C. *Journal of Psychosomatic Research*, 49, 311-317.
- Estraviz, B., Quintana, J.M., Valdivieso, A., Bilbao, A., Padierna, A., de Urbina, J.O., and Sarabia, S. (2007). Factors influencing change in health-related quality of life after liver transplantation. *Clinical Transplantation*, 21, 481-490.
- Feurer, I.D., Wright, J.K., Payne, J.L., Kain, A.C., Wise, P.E., Hale, P., Chapman, W.C., Speroff, T., and Pinson, C.W. (2002). Effects of hepatitis C virus infection and its recurrence after liver transplantation on functional performance and health-related quality of life. *Journal of Gastrointestinal Surgery*, 6, 108-115.
- Forman, L.M., Lewis, J.D., Berlin, J.A., Feldman, H.I., and Lucey, M.R. (2002). The association between hepatitis C infection and survival after orthotopic liver transplantation. *Gastroenterology*, 122, 889-896.
- Goulding, C., O'Connell, P., and Murray, F.E. (2001). Prevalence of fibromyalgia, anxiety and depression in chronic hepatitis C virus infection: Relationship to RT-PCR status and mode of acquisition. *European Journal of Gastroenterology and Hepatology*, 13, 507-511.

- Herrero, M.J., Blanch, J., Peri, J.M., De Pablo, J., Pintor, L., and Bulbena, A. (2003). A validation study of the Hospital Anxiety and Depression Scale (HADS) in a Spanish population. *General Hospital Psychiatry*, *25*, 277-283.
- Jay, C.L., Butt, Z., Ladner, D.P., Skaro, A.I., and Abecassis, M.M. (2009). A review of quality of life instruments used in liver transplantation. *Journal of Hepatology*, *51*, 949-959.
- Jurado, R., Morales, I., Taboada, D., Denia, F., Mingote, J.C., Jiménez, M.A., Palomo, T., and Rubio, G. (2011). Coping strategies and quality of life among liver transplantation candidates. *Psicothema*, *23*, 74-79.
- Kallman, J., O'Neil, M.M., Larive, B., Boparai, N., Calabrese, L., and Younossi, Z.M. (2007). Fatigue and health-related quality of life (HRQL) in chronic hepatitis C virus infection. *Digestive Diseases and Sciences*, *52*, 2531-2539.
- Karam, V., Castaing, D., Danet, C., Delvart, V., Gasquet, I., Adam, R., Azoulay, D., Samuel, D., and Bismuth, H. (2003). Longitudinal prospective evaluation of quality of life in adult patients before and one year after liver transplantation. *Liver Transplantation*, *9*, 703-711.
- Marcellin, P., Chousterman, M., Fontanges, T., Ouzan, D., Rotily, M., Varastet, M., Lang, J.P., Melin, P., Cacoub, P., and for the CheObs Study Group (2011). Adherence to treatment and quality of life during hepatitis C therapy: A prospective, real-life, observational study. *Liver International*, *31*, 516-524.
- Martin, S.C., Stone, A.M., Scott, A.M., and Brashers, D.E. (2010). Medical, personal, and social forms of uncertainty across the transplantation trajectory. *Qualitative Health Research*, *20*, 182-196.
- Minazzato, L., Amodio, P., Cillo, U., Zanus, G., Schiff, S., Bombonato, G., Salari, A., and Bianco, T. (2009). Subjective satisfaction and quality of life in patients prior to listing for liver transplantation. *International Journal of Artificial Organs*, *32*, 39-42.
- Montero, I. and León, O.G. (2007). A guide for naming research studies in Psychology. *International Journal of Clinical and Health Psychology*, *7*, 847-862.
- O'Carroll, R.E., Turner, F., Flatley, K., McGregor, L.M., and Hayes, P.C. (2008). Functional outcome following liver transplantation - A pilot study. *Psychology, Health and Medicine*, *13*, 239-248.
- Pantiga, C., López, L., Pérez, M., Rodríguez, M., Linares, A., Dieguez, L.G., Alonso, P., Hernández, R., and Rodrigo, L. (2005). Quality of life in cirrhotic patients and liver transplant recipients. *Psicothema*, *17*, 143-147.
- Paterson, D.L., Gayowski, T., Wannstedt, C.F., Wagener, M.M., Marino, I.R., Vargas, H., Laskus, T., Rakela, J., and Singh, N. (2000). Quality of life in long-term survivors after liver transplantation: Impact of recurrent viral hepatitis C virus hepatitis. *Clinical Transplantation*, *14*, 48-54.
- Pérez-San-Gregorio, M.A., Martín-Rodríguez, A., Galán-Rodríguez, A., and Borda-Más, M. (2009). Living and deceased transplanted patients one year later: Psychosocial differences just after surgery. *International Journal of Clinical and Health Psychology*, *9*, 429-438.
- Santos, G.R., Boin, I.F., Pereira, M.I., Bonato, T.C., Silva, R.C., Stucchi, R.S., and da Silva, R.F. (2010). Anxiety levels observed in candidates for liver transplantation. *Transplantation Proceedings*, *42*, 513-516.
- Strauss, E. and Teixeira, M.C.D. (2006). Quality of life in hepatitis C. *Liver International*, *26*, 755-765.
- Sumskiene, J., Sumskas, L., Petrauskas, D., and Kupcinskas, L. (2006). Disease-specific health-related quality of life and its determinants in liver cirrhosis patients in Lithuania. *World Journal of Gastroenterology*, *12*, 7792-7797.

- Taylor, R.M., Franck, L.S., Gibson, F., and Dhawan, A. (2005). A critical review of the health-related quality of life of children and adolescents after liver transplantation. *Liver Transplantation, 11*, 51-60.
- Van Esch, L., Den Oudsten, B.L., and De Vries, J. (2011). The World Health Organization Quality of Life Instrument-Short Form (WHOQOL-BREF) in women with breast problems. *International Journal of Clinical and Health Psychology, 11*, 5-22.
- Verdugo, M.A., Arias, B., Gómez, L.E., and Schallock, R.L. (2010). Development of an objective instrument to assess quality of life in social services: Reliability and validity in Spain. *International Journal of Clinical and Health Psychology, 10*, 105-123.
- Watson, D., Clark, L.A., and Stasik, S.M. (2011). Emotions and the emotional disorders: A quantitative hierarchical perspective. *International Journal of Clinical and Health Psychology, 11*, 429-442.
- Zigmond, A.S. and Snaith, R.P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67*, 361-370.

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