

Quality of Life, Anxiety, Depression and Social Support in HCV Mono-Infected and HIV/HCV Co-Infected Patients Waiting for Liver Transplantation

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Abstract

Most studies focus on the outcomes of liver transplantation in HCV or HIV recipients but little is known about the psychosocial characteristics of HCV mono-infected or HIV/HCV co-infected patients waiting for a liver transplant. In order to study quality of life, anxiety, depression and social support, a cross-sectional study was conducted. Because only mono- or co-infected patients without a history of alcohol abuse listed at one regional center, only twenty-eight HCV patients registered on the national waiting list were enrolled. Two groups were constituted: 15 HCV mono-infected patients and 13 HIV/HCV co-infected patients. All participants completed three self-report scales. Quality of life was low and anxiety was high in both the study groups. HIV/HCV co-infected patients were younger ($p < 0.01$), reported a greater severity of physical ($p < 0.01$) and psychological symptoms ($p = 0.05$). The findings of this study highlight the importance of assessing psychosocial factors in HCV patients, and particularly in HIV/HCV patients, and indicate the need for specific interventions to improve their quality of life.

Keywords: Liver transplantation; Self-report; Psychological distress; Quality of life; Physical symptoms; Psychosocial factors; HCV; HIV/HCV; Co-infection

Introduction

Hepatitis C (HCV) is the most common, chronic, blood-borne infection in France. At present, nearly five million Europeans are infected, around 600,000 of them in France. HCV is the second most common indication for liver transplantation (LT) in France, and the leading indication in Europe [1]. Approximately 25% of people infected by the human immunodeficiency virus (HIV) are also infected by HCV. People who are co-infected have an increased risk of serious life-threatening complications [2]. Consequently, LT is a life-saving option for patients with end-stage chronic liver disease [3,4]. However, while end-stage liver disease due to HCV infection was sometimes considered a controversial indication for LT in HIV-infected patients, LT has now become common practice, especially with new treatment options [5,6]. According to Terrault et al. [7], the outcomes among HIV/HCV co-infected LT recipients are generally worse than those seen in recipients without HCV, and quality of life (QOL) may be poorer after LT for hepatitis C virus [8].

In fact, most studies focus on the outcomes of LT in HCV or HIV recipients, but little is known about the psychosocial characteristics of HCV mono-infected or HIV/HCV co-infected patients who are waiting for a liver transplant. Yet several studies have shown how psychosocial factors from the pre-transplant period can predict well-being and QOL after surgery [9,10]. More specifically, depression [11] and social support scores can predict life satisfaction with post-transplant outcomes [12]. Nevertheless, investigating pre-transplant psychosocial factors could be of value to the implementation of intervention programs when patients are on the waiting list. For these reasons, the aim of this study was to assess QOL, anxiety, depression and social support in patients waiting for LT, and to examine the relationships between these variables in HCV mono-

infected and HIV/HCV co-infected patients. More exactly, we tested the hypotheses that patients co-infected, in a cross sectional analysis, have significantly higher anxiety and depression scores and lower self-reported quality of life and social support than HCV patients.

Methods

Population and procedure

Adult patients were assessed while waiting for a liver transplant in the only LT center covering the southern Paris area (Centre Hepato-Biliaire at Paul-Brousse Hospital, Villejuif, France). Eligible participants were at least 18 years old and had been on the LT waiting list for less than one month, were co-infected by HCV ± HIV virus and had sufficient proficiency in French to complete the assessments. Patients unable to communicate or complete the questionnaires, waiting for a combined organ transplant (kidney and liver), who had been referred for an emergency transplant, or had an associated diagnosis of alcoholic cirrhosis, were excluded. Between January 2009 and June 2012, participation in this study was proposed to 37 patients, 28 (76%) of whom agreed to take part. Eight HCV mono-infected patients refused to participate, and one HCV mono-infected patient was excluded because he did not complete all the self-report scales.

Because of ethical considerations, and in order to avoid any bias arising from additional visits, the assessments were carried out when patients had an appointment at the transplantation center for their usual medical follow-up. Each patient was advised of his/her right to withdraw from the research, and was notified that the information would remain strictly confidential and only be used for scientific purposes. After giving their approval, each patient signed an informed consent form. Sociodemographic and medical data were then collected and several self-reported scales were completed.

The data were used according to the standard regulations determined by the French Network for Transplantation, and in compliance with the preservation of patient anonymity and privacy.

Measurements

The National Institute of Diabetes and Digestive and Kidney Diseases Pittsburgh, USA (NIDDK) instrument was used to assess QOL, as it had been proven to be reliable in assessing QOL among solid organ transplantation patients [13]. The French adaptation of the National Institute of Diabetes and Digestive and Kidney Disease Transplantation QOL (NIDDK-QOL) from Karam et al. [14] was used, and measured five QOL domains.

1. Measures of disease comprise 21 items describing physical symptoms; two subscores are generated: number of physical symptoms and severity of physical symptoms (a higher score indicating more symptoms or greater severity).
2. Psychological status consists of 14 items. Five items assess symptoms related to anxiety and depression and generate two subscores: number of psychological symptoms and severity of psychological symptoms (a higher score indicating more symptoms or greater severity). Nine items describe subjects' attitudes towards life and their personality (feelings of boredom, contentment, enjoyment, etc.) and generates an index of well-being (a higher score indicating greater well-being).
3. Personal function consists of nine items assessing ability to work and physical handicap (a higher score indicating better personal function).
4. Social and role function consists of eight items which measure the impact of a person's state of health on their social, emotional and professional life (a higher score indicating worse social and role function).
5. General health perception consists of five items that give an overall assessment of quality of life (a higher score indicating a better general health perception). In the present study, internal consistency was 0.87 for the number of physical symptoms, 0.85 for the severity of physical symptoms, 0.69 for the number of psychological symptoms, 0.76 for the severity of physical symptoms, 0.80 for the index of well-being, 0.90 for personal function, 0.71 for social and role function and 0.79 for general health perception.

The Hospital Anxiety and Depression Scale (HADS) were used to assess anxiety and depressive symptoms [15]. It consists of 14 items, seven which assess anxiety symptoms and seven for depressive symptoms (a higher score indicating greater anxiety or depressive symptoms). The cut-off score for an anxiety or depression disorder is 8. The HADS is a valid and reliable screening instrument to assess separate dimensions of anxiety and depression and to detect both disorders in patients in non-psychiatric hospitals. It provides clinically meaningful results for clinical group comparisons and correlational studies with various aspects of disease and QOL. The French adaptation displays good psychometric properties [16]. In our study, internal consistency was 0.74 for anxiety and 0.84 for depression.

The Social Support Questionnaire (SSQ) was used to assess social support [17]. The short form was selected, which consists of six items measuring two aspects of perceived social support: (1) *availability* which is an estimate of the number of people on whom a person can rely when assistance is needed, and (2) *satisfaction*, which is the perceived adequacy between the support received and expectations and needs. For each social support aspect, a higher score indicates a higher level of perceived social support. The French adaptation of this scale displays good psychometric properties [18]. In our sample, internal consistency was 0.88 for social support availability and 0.93 for social support satisfaction.

Statistical analysis

In order to compare HCV patients with HIV/HCV co-infected patients, the chi-squared test, analyses of variance and covariance were used. To investigate associations between QOL and anxiety, depression and social support, Pearson's parametric bivariate correlations were used. Parametric tests were used as all the scores, except the number of psychological symptoms from the NIDDK-QOL, were distributed normally according to Kolmorov-Smirnov's test. A *P* value of less than 0.05 was considered to be significant. Statistical analyses were performed using SPSS, version 18.

Results

Patient characteristics

Twenty-eight out of 37 patients agreed to contribute to the study, representing a compliance rate of 76%. Out of these 28 patients, 15 were infected with HCV and 13 with HIV/HCV. Their mean age was 50.7 years (SD=7.3). Most patients were men (85.7%), had attended college (66.7%), were married (70.4%), had at least one child (77.8%) and were disabled and not working (67.8%). HCV and HIV had mostly been transmitted through drug injection (60.7%); however, few patients were receiving drug replacement therapy (14.3%). In all patients, the primary liver disease was cirrhosis. At the time of their inclusion in the study, the Model for End-Stage Liver Disease (MELD) score was significantly lower for HCV patients (11.5 ± 4.6) than for HIV/HCV patients (16.1 ± 4.2; *p*<0.05). About one third of patients were receiving anti-HCV therapy (32.1%). They had received combined interferon-alfa and ribavirin therapy for more than 1 year. Treatment regimens were not standardized. All the HIV/HCV co-infected patients were being treated for their HIV. All had controlled HIV infection with a CD4 count > 100 cells/mm³, no previous AIDS events or opportunistic infections, and an undetectable HIV plasma viral load when they were placed on the waiting list.

All baseline characteristics were similar in the two groups with the exception of the age of patients; HIV/HCV co-infected patients were younger than HCV patients (*p*<0.01)

The results are presented in Table 1.

	Total N=28	HCV patients N=15	HIV/HCV patients N=13	χ ² /F	P-value
Sociodemographic data					
Mean age in years (SD)	50.7 (7.3)	54.6 (7.1)	46.2 (4.4)	13.30	<0.01
Male (%)	85.7	93.3	76.9	1.53	0.21
Education level					
Attended college (% vs. high school or lower)	66.7	60	75	0.68	0.41
Marital and living status					
Married (% vs. single)	70.4	66.7	75	0.22	0.64
At least one child (%)	77.8	86.7	66.7	1.54	0.24
Tenant or owner (% vs. guest)	82.1	86.7	76.9	0.45	0.50
Current occupational status					
Disabled (%)	67.8	60	76.9		
Employed (%)	17.8	20	15.3		
Retired (%)	10.7	20	0		
Other (%)	3.6	0	7.7		
Clinical information					
MELD score	13.6 (4.9)	11.5 (4.6)	16.1 (4.2)	7.29	<0.05
Virus transmission (%)					
Drug injection	60.7	40.0	84.6		
Sexuality	3.6	6.7	0		
Transfusion	10.7	13.3	7.7		
Unknown	25.0	40.0	7.7		
Treatment substitution (%)	14.3	6.7	23.1	1.53	0.22

Table 1: Baseline characteristics of participants

Comparison of quality of life (NIDDK-QOL), anxiety (HADS-A), depression (HADS-D) and social support (SSQ) between HCV and HIV/HCV patients by controlling MELD Score.

The results obtained for measures of disease, which is one domain of the QOL scale (NIDDK-QOL), were high in HCV and HIV/HCV groups (13.9 versus 17.2), but HIV/HCV patients reported a greater severity of physical and psychological symptoms ($p < 0.05$ and $p = 0.05$) than HCV patients, which means that they reported a worse QOL in these domains (Figure 1). The mean level of anxiety (HADS-A) was quite high, above the cut-off point in each group (> 8). In the sample of HCV mono-infected patients, 8/15 (53.3%) had a score > 8 , while in the sample of HIV/HCV co-infected patients, 7/13 (53.8%) had a score > 8 . The mean level of depression (HADS-D) was below the cut-off point, but 46.2% (6/13) of HIV/HCV co-infected patients obtained a score > 8 compared to 20% (3/13) among HCV mono-infected patients ($p = 0.63$). HCV mono-infected and HIV/HCV co-infected patients had similar levels of anxiety and depression. No significant differences were found between the groups with respect to social support availability and satisfaction (SSQ). These results are shown in Table 2 and Figure 2.

Relationships between the QOL (NIDDK-QOL), anxiety (HADS-A), depression (HADS-D) and social support (SSQ) scales.

In HCV mono-infected patients, depression was associated with the number and severity of physical symptoms ($r = .68$, $p < 0.05$ and $r = .75$, $p < 0.01$), with low well-being ($r = -.56$, $p < 0.05$), poor personal function ($r = .66$, $p < 0.05$) and a poor general health perception ($r = -.56$, $p < 0.05$). In HIV/HCV co-infected patients, anxiety was associated with a high severity of physical and psychological symptoms ($r = .61$; $p < 0.05$ and $r = .75$; $p < 0.01$), whereas depression was associated with poor social and role functions ($r = .76$; $p < 0.01$).

Social support satisfaction was only associated with a high index of well-being in HCV mono-infected patients ($r = .62$, $p < 0.05$).

These results are shown in Table 3.

Comparison of quality of life (NIDDK-QOL) between patients with and without anxiety (HADS-A), and with and without depression (HADS-D) by controlling MELD score.

Within the whole sample, the comparison between patients with and without anxiety showed that: patients with anxiety had more physical symptoms ($p < 0.05$), greater severity of physical and psychological symptoms ($p < 0.01$ and $p = 0.001$) and poorer social function ($p < 0.05$) than patients without anxiety. The comparison between patients with and without depression showed that: patients with depression had more physical symptoms ($p < 0.01$), greater severity of physical symptoms ($p < 0.01$), lower well-being ($p < 0.01$), poorer social function ($p < 0.01$) and lower general health perception ($p < 0.05$) than patients without depression. The results are shown in Table 4.

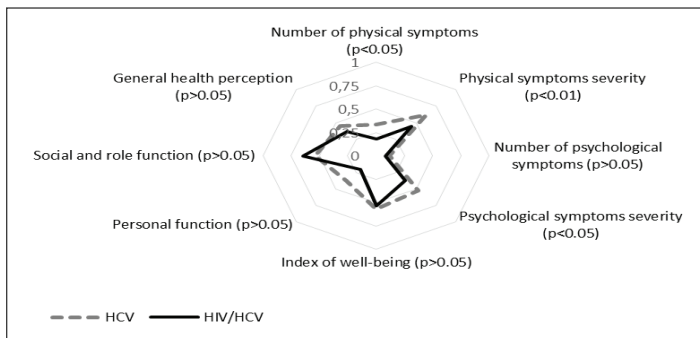


Figure 1: Quality of life of HCV and HIV/HCV patients
Note: Each quality of life score was transformed from 0 to 1, with 1 indicating a higher quality of life.

	Total N=28	HCV N=15	HIV/HCV N=13	F	P-value
NIDDK-QOL					
Measures of disease	15.4(4.2)	13.9(4.5)	17.2(3.2)	2.38	0.14
Number of physical symptoms					
Severity of physical symptoms	38.5(14.1)	31.6(11.9)	46.5(12.3)	5.35	<0.05
Psychological status					
Number of psychological symptoms	4.5(1.0)	4.4(1.1)	4.6(0.8)	0.71	0.41
Severity of psychological symptoms	11.0(4.1)	9.5(3.6)	12.6(4.3)	4.24	0.05
Index of well-being	9.1(2.2)	9.3(2.1)	8.8(2.4)	0.29	0.59
Personal function	1.2(1.3)	1.5(1.4)	0.8(1.2)	0.58	0.45
Social and role function	11.8(4.6)	10.8(4.4)	12.9(4.6)	0.07	0.79
General health perception	4.1(2.8)	4.5(3.1)	3.7(2.4)	0.00	0.95
HADS					
Anxiety (HADS-A)	8.6(4.1)	8.4(3.6)	8.8(4.7)	0.00	0.97
Depression (HADS-D)	6.6(4.7)	5.5(4.0)	7.8(5.4)	0.24	0.63
SSQ					
Social support availability	17.6(9.6)	21.4(10.4)	13.3(6.8)	2.60	0.12
Social support satisfaction	27.6(7.0)	29.3(4.9)	25.4(8.8)	2.22	0.15

Table 2: Comparison of quality of life (NIDDK-QOL), anxiety, depression (HADS) and social support (SSQ) between HCV and HIV/HCV patients by controlling MELD score

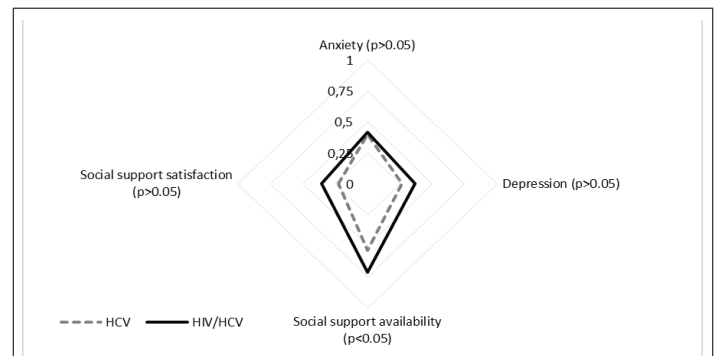


Figure 2: Anxiety, depression and social support of HCV and HIV/HCV patients
Note: Each score was transformed from 0 to 1, with 1 indicating high anxiety, depression, dissatisfaction with social support and weak social support availability.

Discussion

The aims of this study were to assess QOL, anxiety, depression and social support in HCV and HIV/HCV patients waiting for a liver transplant, and to examine the relationships between these variables. Only one significant difference in the sociodemographic data was found in our patients: HIV/HCV patients were younger than HCV patients ($p < 0.01$). Duclos-Vallée et al. [19] and Therrault et al. [7] also found that in a large sample of HIV/HCV co-infected and HCV mono-infected transplant recipients, HIV/HCV patients were younger. This might be attributed to the fact that HIV/HCV co-infected patients show faster rates of fibrosis progression when compared to mono-infected patients [20].

	HADS				SSQ			
	Anxiety		Depression		Social support availability		Social support satisfaction	
	HCV	HIV/HCV	HCV	HIV/HCV	HCV	HIV/HCV	HCV	HIV/HCV
NIDDK-QOL								
<i>Measures of disease</i>	.49	.51	.68**	.48	-0.12	.11	-.21	-.08
Number of physical symptoms								
Severity of physical symptoms	.50	.61*	.75**	.42	-0.16	.13	-.03	.12
<i>Psychological status</i>								
Number of psychological symptoms	.32	.30	.28	-.12	0.13	.06	-.30	.05
Severity of psychological symptoms	.50	.75**	.20	.36	0.17	-.20	.30	-.13
<i>Index of well-being</i>								
Personal function	-.14	-.15	-.66**	-.31	0.31	-.24	.09	.07
<i>Social and role function</i>								
Social and role function	.16	.24	.38	.76**	-0.19	-.19	-.34	-.45
<i>General health perception</i>								
General health perception	.10	-.16	-.56*	.50	0.46	-.44	.02	-.03

Table 3: Correlations between quality of life (NIDDK-QOL), anxiety (HAD-A), depression (HAD-S) and social support (SSQ)

Note: * $p < 0.05$ and ** $p < 0.01$; for the NIDDK-QOL: A higher score for the number and severity of physical and psychological symptoms indicates more symptoms or greater severity; a higher score of well-being, personal and social function and general health perception indicates higher quality of life.

	Anxiety				Depression			
	Low anxiety (N=13)	High anxiety (N=15)	F	P value	Low depression (N=19)	High depression (N=9)	F	P value
NIDDK-QOL								
<i>Measures of disease</i>	13.4(4.6)	17.2(3.0)	5.14	<0.05	13.9(4.3)	18.7(1.3)	8.67	<0.01
Number of physical symptoms								
Severity of physical symptoms	30.3(12.4)	45.6(11.6)	8.83	<0.01	33.7(13.9)	48.7(7.9)	7.15	<0.05
<i>Psychological status</i>								
Number of psychological symptoms	4.2(1.3)	4.8(0.4)	3.96	0.06	4.4(1.1)	4.7(0.7)	0.49	0.49
Severity of psychological symptoms	8.2(2.9)	13.3(3.6)	15.92	0.001	10.1(3.8)	12.8(4.4)	2.39	0.14
<i>Index of well-being</i>								
Personal function	1.6(1.6)	0.8(0.9)	1.62	0.21	1.5(1.4)	0.4(0.7)	3.28	0.08
<i>Social and role function</i>								
Social and role function	9.6(4.4)	13.7(3.9)	4.69	<0.05	10.1(4.3)	15.3(2.8)	9.07	<0.01
<i>General health perception</i>								
General health perception	4.9(2.8)	3.5(2.6)	1.06	0.31	4.9(2.9)	2.4(1.2)	4.51	<0.05

Table 4: Comparison of quality of life (NIDDK-QOL) between patients with and without anxiety, and with and without depression by controlling MELD score

Note: for the NIDDK-QOL: A higher score for the number and severity of physical and psychological symptoms indicates more symptoms or greater severity; a higher score of well-being, personal and social function and general health perception indicates higher quality of life.

The hypothesis that co-infected patients have significantly higher anxiety and depression scores was not supported. The scores obtained with HADS showed a high and similar level of anxiety in HCV and HIV/HCV patients waiting for an LT, as more than half of the sample had a score above the cut-off point. Anxiety is one of the most common symptoms recognized by clinicians who are caring for people with HIV and/or HCV disease [21,22]. However, several studies have found that not only anxiety but also depression is relatively higher among LT candidates than in healthy people [23,24]. According to Corruble et al. [11], among 339 patients, 51.6% on the waiting list reported depressive symptoms. In our study, the depressive symptom scores were not as high (around 32%) and no difference was found between the two groups. These findings differ from those published by Mrus et al. [25] in which HIV/HCV co-infected patients had significantly more depressive symptoms than HCV-infected subjects. However, they administered the CESD-10 depression scale rather than the HADS used in our work, which might explain the difference in results.

QOL is well-documented among LT recipients but very rarely in patients waiting for an LT. The hypothesis that co-infected patients have a significantly lower self-reported quality of life and social support than HCV patients was partly supported. The present study shows that HCV mono-infected and HIV/HCV co-infected patients reported a poor QOL. The scores obtained in the five domains of the QOL scale represented a lower QOL than that found by Karam et al. [14] in a sample of 67 French

patients with heterogeneous indications waiting for an LT. In our study, HCV mono- and HIV/HCV co-infected patients reported similar levels of well-being, personal function, social and role function and general health perception. Differences between the two groups were only observed with respect to measures of disease and psychological status: HIV/HCV co-infected patients had higher levels of physical and psychological symptoms compared to HCV mono-infected patients (severity of physical and psychological symptoms). Co-infection causes greater symptoms which can have a direct impact on the physical and psychological health of patients and thus influence their QOL, making it less satisfactory. Consequently, QOL needs to be included in clinical trials as a form of medical and psychological outcome assessment [26].

Regarding the associations between QOL, anxiety, depression and social support, it was very interesting to note that these differed in each group. Among HCV mono-infected patients, depression was associated with most dimensions of QOL, more severe depression being associated with a poorer QOL. In HIV/HCV co-infected patients, depression was only associated with social and role function, and anxiety was associated with the severity of physical and psychological symptoms. These results suggest that interventions during the waiting period to enhance QOL should differ depending on the patient's infection.

It was surprising to observe that social support was not associated with QOL, except among HCV mono-infected patients in whom a high degree of satisfaction with social support was associated with high well-being

scores. As early as 1990, a lack of social support was considered to be a possible risk factor for long-term survival in transplant recipients [27]. Since then, the positive contribution of post-transplant social support to the QOL of transplant recipients has been demonstrated [28]. It is possible that social support may evolve before and after transplantation, which could explain our finding. Further studies are necessary to explore this dimension and understand better how patients adapt to LT.

Another interesting result was that all patients, with depression and anxiety, had poorer social function. This finding leads us to question the assistance that teams might provide in order to encourage social support. For example, the setting up of support groups in care establishments, or online contact for those who cannot leave home [29]. A support group is defined as “a type of mutual helping group that comprises a group of people and a leader to share and deal with some common need” [30]. Support groups can provide patients with important resources, including information on their care and emotional and psychological support. The results of our study confirm the importance of adopting a comprehensive biopsychosocial approach towards clinical care in order to help HCV mono- and HIV/HCV co-infected patients to cope with physical and psychological diseases during the period before liver transplantation. Primary care clinicians could play a key role in identifying and responding to anxiety and depressive symptoms, which should be monitored and treated with medication, counseling and cognitive behavioral therapy focused on psychological distress. At the same time, particular attention needs to be paid to the number and severity of self-reported physical symptoms, so as to identify precisely those which cause patients the most problems by directly impacting their QOL.

Our study had some potential limitations. Firstly, the small sample size, the number of variables and the multiple comparisons limited the capacity and the power of statistical analysis. Caution needs to be exercised in the interpretation of the findings, as a lack of statistical significance may be due to the small number of patients rather than the absence of a true effect. Intensive recruitment efforts over a two-year period resulted in only 28 participants, because patients with HCV, and particularly those co-infected with HIV/HCV, who are waiting for an LT, are sparse in France. We are aware that a larger sample of participants might have produced more statistically significant results and enabled the effects of treatments, MELD score levels and gender to be controlled. Secondly, the study design was cross-sectional and compared two groups treated in just one University Hospital Center. As such, its findings might not be generalizable to a larger number of HCV and HIV/HCV patients waiting for an LT. It would also be preferable to examine the groups longitudinally before and after transplantation and to introduce a control group constituted by patients without viral infections.

Nonetheless, the originality of our study was its focus on psychosocial factors in HCV mono- and HIV/HCV co-infected patients waiting for an LT. The results obtained have contributed to well-known QOL, psychological distress and social support data, considering the impact of these variables on adherence to medical treatment and on post-transplant outcomes.

Conclusion

The findings of this study highlight the importance of assessing psychosocial factors and indicate a need for specific interventions to improve QOL. Early intervention and personalized medical care can increase patient well-being. These results might encourage the development of an interdisciplinary approach in order to help patients adjust to the pre-transplant process, to promote adherence and to maximize outcomes.

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