

Quality of life in cirrhotic patients and liver transplant recipients

Carmen Pantiga, Laudino López*, Marino Pérez*, Manuel Rodríguez, Antonio Linares, Luisa G. Dieguez, Pilar Alonso, Radhamés Hernández-Mejía* and Luis Rodrigo
Central Hospital of Asturias and * University of Oviedo

This study analyses the health related quality of life in patients diagnosed with hepatic cirrhosis (HC) in the three Child-Pugh stages (A, B and C) and in liver transplant recipients (OLT). Health related quality of life was quantified by the multidimensional psychometric test PLC (Siegrits, Boer and Junge, 1996). In general, patients HC and OLT had a poorer scores than the control group in Physical Well-being, Physical Function, Positive Mood, Negative Mood and Psychological Wellbeing scales. Also, patients with OLT present a better quality of life than patients with advanced cirrhosis (Child B and C) in scales that evaluate Physical, Psychological and Social functions. The OLT group even obtained higher scores in the Positive Mood scale than Child-A cirrhotics. Our results suggest that although quality of life in OLT patients does not reach levels of healthy individuals, it is significantly better than in cirrhotic patients, especially than those in advanced stages.

Calidad de vida en pacientes cirróticos y trasplantados hepáticos. Este estudio analiza la calidad de vida relacionada con la salud en pacientes diagnosticados de cirrosis hepática (CH) en los tres estadios Child-Pugh (A, B y C) y en pacientes trasplantados (OLT). La calidad de vida ha sido cuantificada por la prueba psicométrica multidimensional PLC (Siegrits, Boer and Junge, 1996). En general, los pacientes CH y OLT presentaron peores puntuaciones que el grupo control en las dimensiones de Capacidad física, Función física, Ánimo positivo, Ánimo negativo y Bienestar psicológico. Aunque los pacientes OLT mostraron mejor calidad de vida que los pacientes con estados avanzados de cirrosis (Child B y C) en las escalas que evalúan las funciones física, psicológica y social. El grupo OLT presentan puntuaciones más altas en la dimensión Ánimo positivo respecto al grupo de pacientes cirróticos en estadio Child A. Nuestros resultados sugieren que la calidad de vida en pacientes OLT no alcanza los niveles de la población sana, pero es significativamente mejor que en pacientes CH especialmente en fases avanzadas.

For over 20 years, physicians specialising in a range of clinical areas, especially those working with chronic patients, have shown an increasing interest in health related quality of life evaluation (Testa and Simonson, 1996). The term quality of life can be interpreted as an attribute or a set of attributes inherent to a characteristic that permits this to be perceived as equal, better or worse than others of the same type (Definition of «Real Academia de la Lengua Española», 1984). In addition, the term of having diverse uses in the specialized scientific literature has, over the last decade, different meanings, such as relative conditions to the well-being, comfort, subjectivity, and multidimensionality (Padierna Sanchez, Fernández Rodríguez and González Menéndez, 2002). It has been observed in the last fifteen years an important increment of investigations in diverse fields like health, mental health, education, disability, labor world and services (Verdugo and Sabeh,

2002). Liver transplantation is currently considered to be the elective treatment for end-stage liver disease and approximately 80% of patients survive longer than one year post-transplantation and 61% have a survival of 8 years (Nickel, Wunsch, Egle, Lohse and Otto, 2002). Therefore, as well as knowing the survival of liver transplant recipients or patients diagnosed with chronic disease such as hepatic cirrhotics, it is also interesting to assess their health status in affective, psychological, emotional, social and work-related areas (Gill and Feinstein, 1994). Moreover, in clinical practise the physician is often ignorant of important changes taking place in their patients' all-round functioning (Deyo and Patrick, 1989).

A good evaluation of QOL is one that measures the health status on a wellbeing scale that covers aspects such as satisfaction, general perception of health, psychological wellbeing, physical wellbeing and disease and death. However, it should also include aspects that are not directly health-related such as: work, family, friends and other circumstances in the patients' lives (Gill and Feinstein, 1994; Patrick and Erickson, 1987). Moreover, QOL evaluation in transplanted patients is also interesting from the Health Service perspective because of the cost-benefit of surgical intervention as a treatment for these patients (Younossi and Guyatt, 1998).

The aim of this work is to assess quality of life in liver transplant recipients compared to that of cirrhotic patients and healthy individuals in its physical, social and psychological dimensions not directly related with liver function and clinical manifestations. For this purpose we chose a test, the PLC, that we consider to cover all the areas we wish to assess.

Material and methods

Subjects

A total of 150 patients were studied, 128 men and 22 women, with an average age of 56.2 ± 9.2 years. A total of 89 were diagnosed with hepatic cirrhosis and were classified into 30 patients in Child-Pugh A, 30 in Child-Pugh B and 29 in Child-Pugh C. Cirrhosis was diagnosed according to standard clinical and analytical criteria (Conn, 1981) and confirmed by liver biopsy when permitted by coagulation parameters (70% of cases).

Hepatic cirrhosis aetiology was excess alcohol consumption in 63%, a combination of alcohol intake and viral in 18%, only viral in 12% and 7% were due to other causes. The second group was comprised of 30 patients who had received a liver transplant because of a previous cirrhosis. Their pre-transplant aetiology was: 40% ethylic, 36% viral and 10% from other causes; 10% of patients had post-transplant liver disease. The control group (CG) was comprised of 31 health volunteer blood donors. The demographic, clinical and epidemiological characteristics of the study participants are given in Table 1. All participants gave their consent in writing for the study and were continually informed of the study objectives.

Methods

The Profile of Quality of Life in the Chronically Ill (PLC) (Siegrits, Boer and Junge, 1996) is a data collection instrument based on a well-known modular system. It consists of a central module with 40 items that measure 6 dimensions:

Physical capacity: 8 items, Psychological function: 8 items, Social function: 6 items, Positive mood status: 5 items, Negative mood status: 8 items, Social wellbeing: 5 items (see Table 2). It also has a variable module that covers aspects related to the chronic disease concerned, in this case liver disease. As well as the central module and the symptom list there is also a standardised record of the most important sociodemographic characteristics of the patients interviewed. The PLC have the following parts: central module (basic nucleus of the test), symptom list (specific to each disease) and sociodemographic appendix (including extra questions). In this study we used the PLC version validated for the Spanish population by Fernández-López and Hernández-Mejía (1997).

Process

Data for quality of life evaluation were collected from outpatients attending the Out Patients Clinic of the Digestive Medicine Service of the Central Hospital of Asturias, from September 1999 to December 2000. After the clinical check-up, patients were assessed for QOL and classified according to their Child-Pugh grade at that moment.

The group of liver transplant recipients (OLT) were chosen at random from all the patients in post-transplantation follow-up in

the Hospital. The average time elapsed from transplantation until QOL evaluation was 2.5 years (range 9-36 months). The control group (CG) was comprised of 31 healthy volunteer blood donors. This choice of control group ruled out the possibility of liver disease because of the periodic analytical tests these subjects had to undertake. Age, sex and cultural level of these individuals were similar to the cirrhotic and liver transplant groups (see Table 1).

Statistical Analysis

Differences between the sample groups in the dimensions that assess quality of life were studied by multivariate variance analysis followed by a Univariate Variance Analysis, with *a posteriori* between-group comparisons using the Sfeffe test, with a statistical significance of p<0.05. Statistical analyses were performed using the statistical package SPSS for Windows, version 8.5.0.

Results

The scores for the scales evaluated by the PLC test in the three study groups are recorded in Table 3. After transforming the *F*

Table 1
Characteristics of the sample

	A	B	C	OLT	CG
<i>n</i>	30	30	29	30	31
Sex, F/M	3/27	2/28	2/27	6/24	9/22
Education status					
Elementary school	27	23	24	18	24
High school	0	2	4	7	3
College / university	3	5	1	5	4
Age, years					
(mean ± SD)	57.26±9.05	58.06±9.03	55±9.21	54±9	54.70±6
Range (years)	39-73	34-69	35-73	34-69	46-67
Alcoholic	19	20	17	12*	-
Viral (B and /or C)	4	4	9	3*	-
Alcoholic + Viral	3	4	3	11*	-
Others	4	2	0	3*	-
HE / HE0	3/27	12/18	20/9	3/27*	-

A, B y C= Child-Pugh stage of cirrhosis; OLT= liver transplant recipients; CG= control group; n= number of subjects. HE / HE0= with / without clinical record of episodes of hepatic encephalopathy; *Before transplantation.

Table 2
Theoretical dimensions and factorial structure of the PLC

Dimension	Ability to function	Wellbeing
Physical	I. Physical function (8 items)	List of symptoms (10-15 items)
Psychological	II. Psychological function (8 items)	III. Positive mood status (5 items) IV. Negative mood status (8 items)
Social	V. Social function (6 items)	VI. Social wellbeing (5 items)

value a Wilk's Lambda of $F= 72.81$ ($P= 0.00$) was obtained and, consequently, ANOVA was applied individually to each dimension.

The Physical Well-being scale (PW) significant differences were found between the experimental groups and the control group (A,B,C and OLT vs CG, $p= 0.001$), and also between the subgroup of cirrhotic patients in Child-Pugh A and OLT compared to grade C cirrhotic patients (A and OLT vs C, $p= 0.001$). In the Physical Function scale (FF), significant differences were found between the patient groups and the control group (A, B, C and OLT vs CG, $p= 0.001$). In the dimension that measures Psychological Function (FP), there are significant differences between the control group and the three groups with hepatic cirrhosis (A,B,C vs CG, $p= 0.001$). There were also significant differences between the cirrhotic group with Child-C and OLT (OLT vs C, $p= 0.001$). Significant differences were also observed in the Positive Mood scale (PM) between the four experimental groups and the control (A, B, C and OLT vs CG, $p= 0.001$). Transplanted patients also presented significant differences in this dimension compared to the three groups of cirrhotic patients (OLT vs A,B,C, $p= 0.001$). There were significant differences in the Negative Mood dimension (NM) between the Child-C patient group and the control group (C vs CG, $p= 0.001$). The combination of the two scales NM and PM measure so-called Psychological Wellbeing.

The social function dimension (SF) there were significant differences between the four patient groups and the control group (A, B, C and OLT vs CG, $p= 0.001$), and also between the transplanted group and Child-C (OLT vs C, $p= 0.001$). The last scale, Social Wellbeing scale (SW), there were no significant differences between any of the groups ($p>0.05$).

Discussion

Our results suggest that cirrhotic patients and liver transplant recipients have a worse quality of life than healthy subjects. Also, liver transplant recipients appear to have a better quality of life than cirrhotic patients in most of the dimensions studied (Bravata, Olkin, Barnato, Keeffe and Owens, 1999). Cirrhotic patients with Child-A have similar scores to OLT patients in all the scales measured with the PLC, although these were not identical. In general, the OLT group had higher scores than the Child-A group

although these differences were not significant; differences may become significant if a larger sample were studied.

Most OLT patients showed an improvement in the Physical Wellbeing (PW) scale. However, these subjects are still on immunosuppressive maintenance therapy and this could, at least in part, explain their lower than normal values in the Physical Function (PF) scale. This scale evaluates the performance capacity and includes aspects related with corporal and intellectual functional capacity, the ability to perform intensive tasks, to concentrate and to cope with routine obligations in daily life and at work (Siegrits et al., 1996). In our work, cirrhotic patients presented a worsening of their physical health as the chronic liver disease progressed (Groeneweg, Quero, De Bruijn, Hartmann, Essink-Bot, Hop and Schalm, 1998; Wiesinger, Quittan, Zimmermann, Nuhr, Wichlas, Bodingbaver, Asari, Berlakovich, Crevenna, Fialka-Moser and Peck-Radosavljevic, 2001). However, immunosuppressive treatment with cyclosporin A caused nephrotoxicity and hypertension in 67% of transplant recipients and some OLT patients developed diabetes, although most patients achieved good liver function with liver function tests within normal limits (Eid, Steffen, Porayko, Beers, Kaese, Wiesner and Kiron, 1989; Tarter and Switala, 1991; Leyendecker, Bartholomew, Neuhaus, Hörhold, Blumhardt, Neuhaus and Klappo, 1993).

On the other hand, the Psychological Function dimension of tests measures the capacity for patients to enjoy themselves and to relax and the individual's ability for psychological recovery. Patients are asked about their ability to relax, the quality of their sleep, appetite and their ability to enjoy themselves. They are also asked about their ability to overcome day-to-day disappointments or setbacks and their ability to improve their own situation (Siegrits et al., 1996). The OLT patients also have the highest scores in this section and these differences are significantly better than those of Child-C patients. It is noteworthy that OLT patients receive treatment with steroids that can produce irritability, emotional lability, depression and impaired concentration and attention (De Bona, Ponton, Ermani, Iemmol, Feltrin, Boccagni, Gerunda, Naccarato Rupolo and Burra, 2000). However, as well as post-transplantation palliative treatments, psychological and social factors can also affect their QOL and are often somatised in these patients (Nickel et al., 2002). It is important to take into account the time elapsed since transplantation when evaluating QOL since these patients pass through a series of post-transplantation phases. Immediately after transplantation they tend to be euphoric and later gradually return to normal daily life (Leyendecker, Bartholomew, Neuhaus, Hörhold, Blumhardt, Neuhaus and Klappo, 1993; Commander, Neuberger and Dean, 1992). We must bear in mind that most of our patients have had a recent OLT. This is reflected in the dimensions that evaluate Positive Mood (PM) and Negative Mood (NM) that together measure Psychological wellbeing (PsyW). The OLT groups have significantly better PM scores than the three cirrhotic groups. The PM as a dimension of the PsyW contains essential aspects of positive mood such as good mood, emotional stability and optimism. In contrast, NM, measures essential aspects of negative mood such as melancholy, agitation, irritation, feelings of being under threat or despair (Siegrist et al., 1996). Only the Child-C group presented this type of behaviour with significantly different results to the control. However, it must be born in mind that these patients are in a terminal phase of the cirrhosis and fulfil several criteria to be candidates for OLT. They have similar scores in all

Table 3
Results of PLC quality of life test

Groups	Child-A	Child-B	Child-C	OLT	CG	p
Physical wellbeing	3.87±0.75 ^a	3.72±0.57 ^a	3.29±0.74 ^{a,b}	4.13±0.6 ^c	4.75±0.34	0.001
Physical function	2.42±0.89 ^a	2.24±0.98 ^a	2.07±0.94 ^a	2.56±0.98 ^a	3.61±0.33	0.001
Psychological function	2.67±0.79 ^a	2.82±0.78 ^a	2.34±0.86 ^{a,c}	3.02±0.84	3.59±0.35	0.001
Positive mood	2.37±0.82 ^a	2.31±0.86 ^a	1.19±0.91 ^{a,c}	2.74±0.88 ^a	3.52±0.48	0.001
Negative mood	3.21±0.72	3.15±0.57	2.78±0.85 ^a	3.28±0.58	3.56±0.4	0.001
Social function	2.86±0.94 ^a	2.86±0.97 ^a	2.27±1.2 ^{a,c}	3.09±1 ^a	3.92±0.18	0.001
Social wellbeing	3.58±0.7	3.78±0.4	3.57±0.56	3.8±0.4	3.96±0.21	0.001

Mean ± SE; ^a Significant differences with the CG; ^b Significant differences with Child-A and OLT; ^c Significant differences with OLT

the scales showing a correspondence between their physical condition and the other dimensions evaluated (Younossi, Guyatt, Kiwi, Boparai and King, 1999). Therefore, there are variability indicators in the QOL that depend on the subjects included in the study (Bravata et al., 1999; Younossi, Boparai, McCormick, Price and Guyatt, 2001). Other authors too found a poorer QOL in cirrhotic patients that worsened with hepatic disease course (Groeneweg et al., 1998).

Differences were also observed between patients and controls in the Social function scale (SF) that assesses the ability to start and to maintain communication with other people (Siegrist et al., 1996). Once again OLT patients presented better SF scores than the cirrhotic group, and this difference was significant between the OLT and the Child-C group. These results coincide with those obtained in the previous scales since, as other authors have shown, the QOL of cirrhotic patients considerably improves post-transplantation (Collis, Burroughs, Rolles and Lloyd, 1995; Bryan, Ratcliffe, Neuberger, Burroughs, Gunson and Buxton, 1998). However, in general, patients with a more severe pre-transplant Child-Pugh diagnosis tended to have better post-transplantation QOL levels (Bryan et al., 1998; Geervarghese, Bradley, Wright, Chapman, Feurer, Payne, Hunter and Pinson, 1998).

The Social Wellbeing scale (SW) measures aspects related with the social and emotional support the patient receives in the form of

proximity to other persons, their dedication and offers of help and no feelings of loneliness or exclusion. In this dimension no significant differences were found either among the patient groups or between these and the control group. These results emphasise the importance of health services specialised in caring for these patients. Hence, as well as the patient's family and social environment, close medical supervision by a specialised service plays an important role in maintaining and improving these patient's QOL (Hellgren, Berglund, Gunnarsson, Hansson, Norberg and Backman, 1998). There is also an OLT support group that gives information and help during the pre and post-transplantation phases.

On the whole, the QOL of these patients is no different from that of other types of transplant recipients (Lorenzon and Bäckman, 1999). Like other authors, we consider that pre and post-transplantation programmes offering both social and psychological support would improve QOL in OLT. Also, routine psychological and psychiatric tests before during and after transplantation to assess aspects such as the patient's personality would help in the face of a new crisis (Nickel et al., 2002).

In conclusion, we found quality of life in OLT to be significantly better than in cirrhotic patients although it will always remain below the levels experienced by the healthy population.

References

- Bravata, D.M., Olkin, I., Barnato, A.E., Keeffe, E.B. and Owens, D.K. (1999). Health-Related Quality of Life After Liver Transplantation: A Meta-Analysis. *Liver Transplantation Surgery*, 5(4), 318-331.
- Bryan, S., Ratcliffe, J., Neuberger, J.M., Burroughs, A.K., Gunson, B.K. and Buxton, M.J. (1998). Health-Related quality of life following liver transplantation. *Quality of Life Research*, 7, 115-120.
- Collis, I., Burroughs, A., Rolles, K. and Lloyd, G. (1995). Psychiatric and Social Outcome of Liver Transplantation. *British Journal Psychiatric*, 166, 521-524.
- Commander, M., Neuberger, J. and Dean, C. (1992). Psychiatric and social consequences of liver transplantation. *Transplantation*, 53, 1.038-1.040.
- Conn, H.O. (1981). Editorial. A peek at the Child-Turcotte classification. *Hepatology*, 1, 673-676.
- 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.
- Deyo, R.A. and Patrick, D.L. (1989). Barriers to the use of health status measures in clinical investigation, patient care, and policy research. *Medical Care*, 27(3 Suppl): S254-S268.
- Eid, A., Steffen, R., Michael, K., Porayko, M.K., Beers T.R., Kaese D.E., Wiesner, R.H. and Krom, R.A.F. (1989). Beyond 1 Year After Liver Transplantation. *Mayo Clinic Proceedings*, 64, 446-450.
- Fernández-López, J.A. and Hernández-Mejía, R. (1997). *Perfil de Calidad de Vida en Enfermos Crónicos (PECVEC)*. Versión española de la edición del Perfil der Lebensqualität Chronischkranken, by J. Siegrits, M. Broer and A. Junge. Oviedo: Servicio de Publicaciones de la Universidad de Oviedo.
- Geervarghese, S.K., Bradley, A.E., Wright, J.K., Chapman, W.C., Feurer, I., Payne, J.L. Hunter, E.B. and Pinson, C.W. (1998). Outcome analysis in 100 Liver Transplantation Patients. *American Journal Surgery*, 175(5), 348-353.
- Gill, T.M. and Feinstein, A.R. (1994). A Critical Appraisal of the Quality-of-Life Measurements. *Journal of The American Medical Association*, 272(8), 619-626.
- Groeneweg, M., Quero, J.C., De Bruijn, I., Hartmann, I.J.C., Essink-Bot, M.L., Hop, W.C.J. and Schalm, S.W. (1998). Subclinical Hepatic Encephalopathy Impairs Daily Functioning. *Hepatology*, 28(1), 45-49.
- Hellgren, A., Berglund, B., Gunnarsson, U., Hansson, K., Norberg, U. and Backman, L. (1998). Health-Related Quality of Life After Liver Transplantation. *Liver Transplantation Surgery*, 4(3), 215-221.
- Leyendecker, B., Bartholomew, U., Neuhaus, R., Hörhold, M., Blumhardt, G., Neuhaus P. and Klappo B.F. (1993). Quality of Life of Liver Transplant Recipients. *Transplantation*, 56(3), 561-567.
- Lorenzon, F.A. and Bäckman, F. (1999). Pain and health related quality of life after heart, Kidney, and liver transplantation. *Clinical Transplantation*, 13, 453-460.
- Nickel, R., Wunsch, A., Egle, U.T., Lohse, A.W. and Otto, G. (2002). The Relevance of Anxiety, Depression, and Coping in Patients After Liver Transplantation. *Liver Transplantation*, 8(1), 63-71.
- Padierna Sánchez, C., Fernández Rodríguez, C. and González Menéndez, A. (2002). Quality of life terminal oncological patientes, measured by the QL-CA-AFEX. *Psicothema*, 14, 1-8.
- Patrick, D.L. and Erickson, P. (1987). Assessing Health-Related Quality of Life for Clinical Decision Making. In S.R. Walker and R.M. Rosser (Eds.), *Quality of Life: Assessment and Application*. Lancaster: MTP Press Limited.
- Real Academia Española. Diccionario de la Lengua Española. Madrid: Espasa-Calpe, 1984.
- Siegrits, J., Boer, M. and Junge, A. (1996). Profil der Lebensqualität Chronischkranker (PLC). Göttingen: Hogrefe-Verlang GmbH and Co. K. G.
- Tarter, R.E., Switala, J., Arria, A., Plail, J. and Van Thiel, D. (1991). Quality of Life Before and After Orthotopic Hepatic Transplantation. *Archives International Medicine*, 151, 1.521-1.526.
- Testa, M.A. and Simonson, D.C. (1993). Assessment of Quality-of-Life Outcomes. *New England Journal Medicine*, 334(13), 835-840.
- Verdugo, M.A. and Sabej E.N. (2002). Perceived quality of life assessment in childhood. *Psicothema*, 14, 86-91.
- Wiesinger, G.F., Quittan, M., Zimmermann, K., Nuhr, M., Wichlas, M., Bodingbaver, M., Asari, R., Berlakovich, G., Crevenna, R., Fialka-Moser, V. and Peck-Radosevljevic, M. (2001). Physical Performance

- and Health-Related Quality of Life in Men on a Liver Transplantation Waiting list. *Journal Rehabilitation Medicine*, 33, 260-265.
- Younossi, M.Z., Boparai, N., McCormick, M., Price L.L. and Guyatt (2001). Assessment of Utilities and Health-Related Quality of Life in Patients With Chronic Liver Disease. *American Journal Gastroenterology*, 96(2), 579-583.
- Younossi, Z.M. and Guyatt, G. (1998). Quality-of-Life Assessment and Chronic Liver Disease. *American Journal Gastroenterology*, 93(7), 1.037-1.041.
- Younossi, Z.M., Guyatt, G., Kiwi, M., et al. (1999). Development of a disease specific questionnaire to measure health-related quality of life in patients with chronic liver disease. *Gut*, 45, 295-300.