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Quality of Life and Physical Activity in Liver Transplantation Patients: Results of a Case-Control Study in Italy

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ABSTRACT

The aim of the study was to assess the quality of life (QOL) and the physical activity of liver transplant recipients compared with the general population. The case-controlled pilot study was accomplished through the administration of 2 questionnaires: 36-item Medical Outcomes Study, Short-Form General Health Survey (SF-36) for quality of life (10 scores) and International Physical Activity Questionnaire (IPAQ) to estimate the physical activity (metabolic equivalent score). Fifty-four patients who underwent liver transplantation using the piggyback technique and 108 controls from the general population at the orthopedic ambulatories were enrolled between 2002 and 2009. Participants had a mean age of 55 years (range, 41–73). The multivariate analysis showed significant differences for some scales of the SF-36: liver transplant recipients displayed lower values for "Mental Composite Score" ($P = .043$), "physical activity" ($P = .001$), "role limitations due to physical health" ($P = .006$), "role limitations due to the emotional state" ($P = .006$), and "mental health" ($P = .010$). The metabolic equivalent positively associated with all examined SF-36 scales. The present study focused on the QOL and physical activity of liver transplant recipients, demonstrating that transplant recipients scored lower than the general population. Liver transplantation may allow full recovery of health status, but the physical and social problems persist in some patients. Interventions aimed at improving rehabilitation programs, regular psychosocial support, and follow-up in all phases of treatment may give patients a more satisfying lifestyle after transplantation.

LIVER transplantation has become a commonly used treatment for end-stage liver disease and acute liver failure because it represents the only chance of cure and long-term survival. In both cases survival and liver function are markedly improved after transplantation.[1–3] The rates of success and survival have increased from 30% in the 1970s to almost 80% today.[4,5]

This improvement in survival, which began in the early 1980s, is due to a number of factors. These include the refinement of harvesting techniques and organ preservation, the development of surgical techniques of transplantation, and new and more effective immunosuppressive drugs. However, at the same time, given the chronic shortage of donors compared with the number of patients on the waiting list, it was necessary to extend the eligibility criteria and increase the use of donor organs with suboptimal characteristics that may affect the immediate functional recovery of the body or the long-term survival.

A prospective study showed that limitations in activities due to patients' role and physical health problems improve significantly a year after liver transplantation.[6] It is well established that patients who have undergone liver transplantation regain their full capacity to lead a normal life within a few months after surgery, but these individuals must follow an immunosuppressive treatment for their entire life and undergo regular monitoring. A balanced diet

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and regular exercise are necessary to prevent, restrict, or delay any potential cardiovascular complications and bad prognosis.[7,8]

However, it was observed in several studies that, although the quality of life (QOL) and physical function improve after transplantation, a proportion of cases remain with limitations, such as fatigue, rheumatism,[1,9–12] difficulty in walking, and inability to work.[6] It was also reported that among transplant recipients those who had regular physical activity before the intervention had a much better QOL than those who did not practice any sport. These data have raised the question as to whether the inactivity of a transplant recipient is caused by concomitant health problems or vice versa, because it is indisputable that many chronic diseases (hypertension, diabetes, and heart failure) result in reduction of individual performance.[13] Certainly, the overall perception of QOL increases after surgical treatment but remains lower compared with the general population.[11] The aim of this study was to evaluate, for the first time in Italy, the QOL and physical activity of liver transplant recipients in comparison with the general population.

METHODS

Study Design

The epidemiological design chosen for the conduction of this study was case-control. The reporting of this study was carried out following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[14]

Sample Size

The present investigation is a pilot study; therefore, the sample is represented by an opportunistic sample. One-hundred seventy individuals were recruited.

Population and Setting

The questionnaire, explained in the following section, was administered to all transplant recipients (cases) with piggyback technique between 2002 and 2009 at the "San Camillo-Forlanini" General Hospital and the Transplant Center of the National Institute for Infectious Diseases "L. Spallanzani" in Rome. Patients were contacted during medical examinations at the clinic between May and June 2010. The period of follow-up between the surgical intervention and the interview for each patient was 1–8 years. Furthermore, the control group was enrolled in the waiting rooms of orthopaedic ambulatories at the University Hospital "Umberto I" in Rome. The sample was recruited from an orthopedic outpatient population because the probability to find patients with liver disease is comparable with the general population.

The exclusion criteria for the control subjects were as follows: liver transplantation and clinical manifestation of symptoms and signs of liver disease (jaundice, ascites, or edema). The information regarding liver disease was obtained from the questionnaire. The control group included subjects with minor routine, nonemergency orthopedic symptoms that did not affect their physical activity.

Participation in the study was voluntary.

Questionnaires

The QOL and physical activity in liver transplant recipients were evaluated with 2 instruments: 36-item Medical Outcomes Study, Short-Form General Health Survey (SF-36) and International Physical Activity Questionnaire (IPAQ).

The SF-36 is a 36-item, generic, and multi-dimensional questionnaire that includes 8 health components related to QOL:

physical activity (PF; 10 questions);
role limitations due to physical health (RP; 4 questions);
role limitations due to emotional problems (RE; 3 questions);
general health (GH; 5 questions);
body pain (BP; 2 questions);
social functioning (SF; 2 questions);
vitality (VT; 4 questions);
and mental health (MH; 5 questions).

Only one question was related to changes in health status.

The 8 scales are summarized in 2 scores: Physical Composite Score (PCS) for physical health and Mental Composite Score (MCS) for mental health. The PCS score includes PF, RP, BP, and GH scales. A low PCS value indicates severe physical dysfunction and severe pain, fatigue, and negative assessment of the general health status. The MCS score comprises RE, SF, and VT scales; a low MCS value indicates frequent psychological distress and serious social-emotional problems. These scales are scored from 0–100; higher scores are positively associated with good general health (ie, less pain, less limitations).

The standard questionnaire does not provide information on socio-demographic characteristics of the responders; for that reason it was integrated with questions regarding gender, age, marital status, residence, education, and present occupation.

In addition, the IPAQ questionnaire–short version was used[15]; it is an instrument for monitoring levels of physical activity of an adult population between 18 and 65 years and it is actually applied in 12 countries. The IPAQ includes 7 questions that compute the Metabolic Equivalent (MET). In particular, 6 items concerning the number of days and minutes in the last week spent in vigorous activity (VA; 2 questions) or moderate activity (MA; 2 questions) and walking (W; 2 questions) were used. The item about sedentary habits (1 question) was not considered.

The MET represents the time spent in physical activity, expressed in minutes per week, and is calculated from the following equation:

$$\mathrm{MET} = 4 * \mathrm{VA}\,(\mathrm{d} * \mathrm{min}) + 2 * \mathrm{MA}\,(\mathrm{d} * \mathrm{min}) + 1/3\mathrm{W}\,(\mathrm{min})$$

Statistical Analysis

Descriptive statistics (median, interquartile range, means, and standard deviation [SD]) were calculated for all quantitative variables; percentages and frequencies were generated for qualitative variables.

Univariate analysis was conducted to evaluate possible associations between cases and controls, with regard to socio-demographic variables, QOL, and physical activity. Chi-square and Mann-Whitney tests were used.

Linear multivariate analysis was conducted considering each scale of the SF-36 questionnaire as a dependent variable, and the following data as independent: educational level, living alone, gender, age, transplant status, and MET.

The regression models were constructed using the backward elimination procedure. The model's goodness of fit was evaluated using the R^2 index and the level of statistical significance was set at $P < .05$.

For data analysis we used the IBM software Statistical Package for Social Sciences (SPSS) version 19.0 for Windows (SPSS Inc. Chicago, Illinois, USA).

RESULTS

One-hundred seventy questionnaires were administered with a response rate of 95%. Table 1 shows the characteristics of the 162 participants in the study. There were 54 transplant recipients and 108 controls. The average age in both groups was 55 years (SD 6.38 and 6.50, respectively).

With regard to gender, 63% were male and 37% were females.

A significant difference regarding the level of education emerged. In fact, the control group had a higher education level compared with the cases ($P < .001$): 3% versus 22.2% for elementary school, 18% versus 41% for junior high school, 53% versus 35% for senior high school diploma, and 27% had an academic degree/postgraduate degree versus 2%, respectively (Table 1).

Another difference between the 2 examined groups regarded MET: transplant recipients had higher mean values compared with controls ($\bar{x}$ = 3719.01 min/wk and SD = 4980.22 vs $\bar{x}$ = 2880.05 min/wk and SD = 3863.32), but were not statistically significant ($P = .756$; Table 1).

Analysis of SF-36 scales (Table 2) indicated mean values significantly higher among controls than liver transplant recipients for the following data: MCS ($\bar{x}$ = 47.75 and SD = 9.20 vs $\bar{x}$ = 45.26 and SD = 10.06), PF ($\bar{x}$ = 82.63 and SD = 22.66 vs $\bar{x}$ = 71.48 and SD = 22.60), RP ($\bar{x}$ = 72.22 and SD = 35.57 vs $\bar{x}$ = 56.94 and SD = 41.61), RE ($\bar{x}$ = 74.07 and SD = 33.28 vs $\bar{x}$ = 59.87 and SD = 40.63) and MH ($\bar{x}$ = 71.77 and SD = 19.55 vs $\bar{x}$ = 65.11 and SD = 20.01).

The results of multiple linear regressions are shown in Table 3.

MET was associated positively and significantly with all examined scales, whereas the condition of transplants was negatively associated with MCS ($\beta = -3.087$; $P = .043$), PF ($\beta = -12.479$; $P = .001$), RP ($\beta = -17.181$; $P = .006$), RE ($\beta = -16.158$; $P = .006$), and MH ($\beta = -8.070$; $P = .010$). A higher level of education seems to be associated with better physical health ($\beta = 3.041$; $P = .040$).

Table 1. Socio-Demographic Characteristics of the Participants

Variables	Transplant Recipients N = 54 N (%)	Controls N = 108 N (%)	P*
Gender			
Male	33 (61.1)	67 (62.0)	.909
Female	21 (38.9)	41 (38.0)	
Mean age (SD)	55.15 (6.38)	55.26 (6.50)	.945†
Median age (IQR)	55.00 (9)	55.00 (9)	
Education level			<.001
Elementary school	12 (22.2)	3 (2.8)	
Junior high school	22 (40.7)	19 (17.6)	
Senior high school	19 (35.2)	57 (52.8)	
Academic degree	1 (1.9)	27 (25.0)	
Postgraduate degree	0	2 (1.9)	
Live alone			
No	44 (81.5)	84 (77.8)	.585
Yes	10 (18.5)	24 (22.2)	
Civil status			.239
Single	9 (16.7)	6 (5.6)	
Married	33 (61.1)	73 (67.6)	
Separated	3 (5.6)	10 (9.3)	
Divorced	3 (5.6)	10 (9.3)	
Widowed	2 (3.7)	4 (3.7)	
Cohabitant	4 (7.4)	5 (4.6)	
Mean MET (SD)‡	2880.05 (3863.32)	3719.01 (4980.22)	.756†
Median MET (IQR)	1413.00 (5827.50)	1448.50 (3674.25)	

Abbreviation: IQR, interquartile range.
*P-value; Chi-square test.
†P-value; Mann-Whitney test.
‡MET unit measure: min/wk.

Table 2. Univariate Analysis for 2 Groups, Transplant Recipients and Controls, Versus SF-36 Scales

SF-36 Scales	Transplant Recipients Mean (SD)	Controls Mean (SD)	P*
PCS	46.02 (8.79)	47.27 (9.54)	.178
MCS	45.26 (10.06)	47.75 (9.20)	.040
SF-36 PF	71.48 (22.60)	82.63 (22.66)	<.001
SF-36 RP	56.94 (41.61)	72.22 (35.57)	.029
SF-36 PI	73.79 (27.70)	70.91 (25.65)	.472
SF-36 GH	62.12 (20.76)	59.05 (22.29)	.815
SF-36 VT	58.14 (19.84)	59.49 (17.94)	.284
SF-36 SF	72.68 (23.55)	74.42 (23.33)	.624
SF-36 RE	59.87 (40.63)	74.07 (33.28)	.043
SF-36 MH	65.11 (20.01)	71.77 (19.55)	.030

Abbreviations: SF-36 PF, Physical Functioning; SF-36 RP, Role Physical; SF-36 PI, Pain Index; SF-36 GH, General Health; SF-36 VT, Vitality; SF-36 SF, Social Functioning; SF-36 RE, Role-Emotional; SF-36 MH, Mental Health.
*P-value test: Mann-Whitney.

DISCUSSION

QOL and physical activity evaluation in liver transplant recipients compared with the general population highlighted that patients are more subject to psychological/emotional distress and low physical function. Depressive symptoms, unfavorable medical conditions, and associated difficulties concerning work re-entry after transplantation can be considered as vulnerability factors responsible for the psycho-social difficulties.[16,17] The persistence of post-transplantation psychological impairment can be attributed to incomplete recovery from neurological damage caused by liver disease.[18–20]

Data analysis underlines that all scales of the SF-36 questionnaire are influenced by the total energy expenditure (MET). There were not significant differences between the transplant recipients and the controls regarding MET, however, the mean value is lower in liver transplant recipients (Table 1).

It is important to emphasize that MET was associated positively and significantly with all health-related QOL measures examined in the study. In addition, higher PCS mean ($\bar{x}$ = 47.9) was positively associated with higher educational level (academic degree/postgraduate degree); vice versa for lower PCS mean ($\bar{x}$ = 44.9), which was

Table 3. Models of Multiple Regressions Considering the Single SF-36 Scales as Dependent Variables and Transplant Recipients, High Educational Level, and MET Scores as Covariates

Linear Regression Models	Dependent Variables	Independent Variables			R^2
		Transplant Recipients β (P)	MET β (P)	High Education Level* β (P)	
1	MCS	−3.087 (.043)	0.001 (<.001)	−1.441 (.383)	0.116
2	PCS	−0.552 (.738)	0.001 (.001)	3.041 (.040)	0.095
3	SF-36 PF	−12.479 (.001)	0.002 (<.001)	0.250 (.149)	0.135
4	SF-36 RP	−17.181 (.006)	0.002 (.001)	0.156 (.430)	0.099
5	SF-36 PI	0.175 (.390)	0.001 (.010)	0.152 (.403)	0.041
6	SF-36 GH	0.074 (.660)	0.002 (<.001)	0.054 (.769)	0.138
7	SF-36 VT	−0.058 (.451)	0.001 (.001)	0.068 (.667)	0.063
8	SF-36 SF	−0.120 (.488)	0.001 (.011)	0.056 (.764)	0.040
9	SF-36 RE	−16.158 (.006)	0.002 (<.001)	−0.119 (.535)	0.109
10	SF-36 MH	−8.070 (.010)	0.002 (<.001)	−0.050 (.789)	0.153

*High school/academic degree/postgraduate.

associated with lower educational level (elementary, junior/senior high school diploma). It should be emphasized that in the 2 groups, transplant recipients and controls, there was a significant discrepancy in education levels; in the first group, 37% were graduates/postgraduates, whereas in the second group, there were 79.6%, and this may have affected the PCS values.

According to some studies, the liver transplant recipients with low MCS and PCS are more likely to suffer from cardiopulmonary complications and recurrent infections with hepatitis C virus (HCV). In addition, among them there are frequent cases of diabetes and smoking,[17,21] and years of survival after transplantation are reduced in patients with low PCS.[21] Other psycho-social aspects concerning liver transplant recipients include the effects of immunosuppressive therapy for their entire life, dependence on the health system for continuous monitoring, and potential discrimination at the workplace.[22–24]

There is a clear consensus in literature about patients who undergo major improvements, which are more likely to be used after the intervention, especially if they were professionally active even before the transplantation. The possibility to return to work after liver transplantation also depends on the type of work previously held.[25–27]

Interestingly, despite the socio-cultural differences that could affect the work patterns and perceptions of QOL, these results were found among transplant recipients in Japan,[28] Taiwan,[29] Sweden,[30] and the United States.[31,32]

The results of the present study show that liver transplant recipients have a significantly lower physical function than the general population ($P \leq .001$); according to the study carried out by Aadahl et al, patients with a low PF are often unemployed and more frequently experience fatigue than those engaged in any educational or working activity.[33] The association between external stimuli through work and sense of fatigue is also suggested in a Dutch study, which observed that an unemployed patient is less stimulated/motivated and being less active is more exposed to fatigue; thus, the patient has a reduced physical function.[34] Patients who return to work have a better QOL perception.[12,33,35]

This survey has limitations regarding the small sample size, and was conducted on an opportunistic sample. In particular, participation in the study was on a voluntary basis; therefore, it is not a perfect representation of the general population. In addition, there is heterogeneity in education levels; for that reason a multifactorial analysis was performed to control the distorting effect of this variable. The statistical significance was also adjusted for total energy expenditure. Other limitations of the study are the self-reported nature of the measures collected with the possible loss of information, although validated questionnaires were used. The validation studies demonstrated that the SF-36 questionnaire allows discrimination between groups of people with severe medical conditions from groups with mild conditions or healthy people. It also allows the evaluation of the benefits arising from the wide range of treatments available. The validation of IPAQ, as an instrument for monitoring physical activity levels, was realized in a pilot study conducted jointly by the "Sapienza" University in Rome, the University of Cassino, and the Catholic University of Sacred Heart in Rome.[15]

In this survey the previous employment status of respondents was not taken into account. To render the questionnaire complete other variables regarding comorbidity, smoking habits, consumption of alcohol/drugs, and previous employment status should be taken into consideration. Furthermore, the liver transplant recipients' heterogeneity in terms of follow-up time is not accounted for in the analysis. In fact, the average time posttransplantation of the liver recipients ranged from 1–8 years.

The strengths of this study are as follows: a high response rate (95.3%), strong levels of significance, and similarities between the 2 groups in gender, age, and marital status.

The aim of this survey was to highlight how physical activity and QOL are important parameters for the assessment of liver transplantation patient conditions. This is the first Italian study designed to investigate these aspects together in this category of patients.

Physical activity and work seem to be associated with the degree of functional recovery, whereas high PCS and MCS

scores have a protective effect relative to the QOL, and only in the case of PCS in terms of years of survival postintervention.

A more satisfying lifestyle after liver transplantation can be achieved through the improvement of rehabilitation programs, regular psychosocial support, and follow-up in all phases of therapy.

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