informa
healthcare

ORIGINAL ARTICLE

Profiles of health-related quality of life outcomes after liver transplantation: univariate effects and multivariate models

R. T. RUSSELL[1], I. D. FEURER[1,2], P. WISAWATAPNIMIT[3], E. S. LILLIE[1], E. T. CASTALDO[1] & C. WRIGHT PINSON[1]

[1]*Department of Surgery and Vanderbilt Transplant Center,* [2]*Department of Biostatistics and* [3]*School of Nursing, Vanderbilt University Medical Center, Nashville, Tennessee, USA*

Abstract

Aim. To test the effects of pre- and post-transplant clinical covariates on post-transplant health-related quality of life (HRQOL) score profiles in liver transplant recipients. *Material and methods.* HRQOL was measured before and after transplantation using the SF-36® Health Survey. Clinical data [diagnosis, model of end-stage liver disease (MELD) score, post-transplant rejection and infection episodes], pre-transplant functional performance (FP), and demographics were collected. Multivariate models for the eight SF-36 scales and two summary components were developed using multiple regression. Discriminant analysis was used to test whether the score profiles differentiated among recipients with and without hepatitis C virus (HCV) infection. *Results.* 104 adults reported pre- and post-transplant HRQOL. Time post-transplant averaged 9 ± 8 months (range 1–39). Scores on all SF-36 measures improved from pre- to post-transplant ($p < 0.001$), and 7 of 10 models were significant ($p < 0.05$). After controlling for pre-transplant HRQOL and time post-transplant, HCV infection had a negative effect on the role physical, bodily pain, and role emotional scales. History of a rejection episode had a negative effect on the bodily pain and vitality scales. MELD scores ≥ 18 had a positive effect on the role physical scale. Pre-transplant FP and post-transplant infection episodes did not affect post-transplant HRQOL. HCV infection had a significant effect on the SF-36 score profile (canonical correlation $= 0.50$; $p < 0.001$). *Conclusions.* Pre-transplant HCV infection, MELD score, and post-transplant rejection episodes have significant independent effects on HRQOL after liver transplantation. Their specific effects vary among the individual SF-36 scales, and HRQOL score profiles differ among HCV+ and HCV− recipients.

Key Words: *Graft rejection, HCV, liver transplantation, MELD, quality of life, score profile*

Introduction

Longitudinal assessments of health-related quality of life (HRQOL) after liver transplantation have increased over the past decade. Previous research demonstrated overall improvements in physical and mental HRQOL after liver transplantation [1–5]. One of the general conclusions gathered from these studies has been that the HRQOL of most liver transplant candidates starts below that of the general population. However, they experience a notable improvement in overall HRQOL during the first post-transplant year that is sustained over the next several years. In general, these improvements in global HRQOL are driven by improvements in physical HRQOL with smaller improvements in mental HRQOL. However,

there is a relationship between physical and mental HRQOL – those patients with better post-transplant physical HRQOL show greater improvements in mental HRQOL [6]. Although these findings characterize global improvements in HRQOL after liver transplant, the collective influence of pre-transplant factors and post-transplant clinical events on HRQOL outcomes has not been well described.

Score profiles reflect the pattern of scores for a collection of attributes, such as the eight individual SF-36 scales. Profiles can be reported for individuals or groups and are typically referenced to normative data [7]. The profile approach to reporting the SF-36 scales has been described by the instrument's developers [8], but this specific information is often not the focus of clinical reports. In this article, we refer to

"HRQOL profiles" as summaries reflecting how the eight HRQOL scales vary in relation to general population norms as a function of both liver transplantation (pre- and post-transplant profiles) and pre-transplant HCV infection (HVC+ and HCV– recipient profiles).

A specific understanding of HRQOL profiles will enable clinicians to recognize how clinical events affect the pattern of HRQOL scores, with some scales being within accepted limits of the general population and others being below that of the general population. For example, patients who were HCV+ before transplant have been reported to have deteriorating functional performance 3 years after liver transplant in comparison to HCV– recipients [9,10]. This effect may be reflected in HCV+ patients having a unique post-transplant HRQOL profile. Similarly, patients who experience an acute rejection episode may have a different HRQOL profile than those with an unremarkable clinical course. The aims of this study are: 1) to model the effects of pre- and post-transplant clinical covariates on individual post-transplant SF-36 scales and summary components; and 2) to evaluate whether HRQOL profiles differ as a function of liver transplantation and HCV.

Patients and methods

Patient and data acquisition

Beginning in January 2002, liver transplant candidates and recipients were asked to complete a battery of generic and specific HRQOL surveys at defined pre- and post-transplant time-points using a rolling enrolment system [11]. This IRB-approved protocol involved the administration of these surveys and integrating it with demographic and clinical data from Vanderbilt Transplant Center and Vanderbilt University Medical Center databases and records. Patients included in this study were liver transplant candidates listed after 1 January 2002 who received liver transplants through 1 May 2006. If pre-transplant HRQOL data were reported on more than one occasion, the observation closest to the date of transplant was selected as the baseline measure. In instances where patients had reported HRQOL on multiple occasions, post-transplant data from their last self-report were used.

Demographic and clinical measures

Pre-transplant demographic measures, which were collected for summary data reporting purposes, included age, sex, and race. Pre-transplant clinical measures included primary diagnosis and Model of End-Stage Liver Disease (MELD) score. Whether a candidate was infected with the hepatitis C virus (HCV) was diagnosed prior to transplantation with polymerase chain reaction amplification for detection of HCV RNA, and this diagnosis was confirmed with pathologic examination of the explanted liver after surgery. Post-transplant clinical outcomes that were hypothesized to have an effect on HRQOL were any infectious episode(s) and any rejection episode(s) that occurred prior to post-transplant HRQOL assessment. A rejection episode was defined by a liver biopsy confirming pathologic criteria for rejection; an infectious episode was defined as a positive blood or urine culture for bacterial, fungal, or viral pathogens that required treatment.

HRQOL and functional performance status

The Medical Outcomes Study Short Form 36® Health Survey (SF-36) was utilized for HRQOL assessment. Karnofsky functional performance (FP) status was also reported by transplant coordinators. Data collection occurred at specific time-points, as previously described: at initial evaluation, every 6 months while on the waiting list, and at 1 month, 3 months, six months, and annually post-transplant [11].

The SF-36 was used to assess generic physical and mental HRQOL. This 36-item questionnaire measures eight areas of functioning and well-being (role-physical, bodily pain, physical functioning, general health, vitality, social functioning, role-emotional, and mental health). Physical and mental component summary scales (PCS and MCS) are then computed as weighted composites of the 8 scales. Scale scores range from 0 to 100, with higher scores indicating a better health state. The PCS and MCS are standardized to the general population with a mean of 50 and standard deviation of 10. Thus, 68% of the general population are expected to score between 40 and 60 on the PCS and MCS scales [12].

Functional performance was evaluated by transplant coordinators at the same time-points at which patients completed the self-report surveys. Karnofsky FP scores can range from 10 to 100 and are stratified into 3 categories: 80 to 100 represents ability to carry out normal work and activity (able); 50 to 70 represents ability to care for most personal needs but with varying amounts of assistance and inability to work (unable); and scores from 10 to 40 represent patients who are unable to care for themselves and need chronic care (disabled) [11,13].

Statistical methods

The five pre- and post-transplant clinical covariates hypothesized to have potential effects on post-transplant HRQOL scores were identified prior to analysis. These included FP prior to transplant (encoded as 3 levels), HCV infection (positive or negative), and MELD score (≥ 18 or < 18). Occurrences of any episodes of rejection or infection after transplant (and prior to HRQOL) were encoded as dichotomous

Table I. Demographic and pre- and post-transplant clinical measures.

Age (years)	53.5±7.8
Gender (male)	73%
Race (Caucasian)	94%
Diagnosis – non-cholestatic	59% (51% HCV)
Metabolic/crypto/auto/NASH	26%
Cholestatic	13%
Other	2%
MELD	23±5
One or more rejection episodes	23%
One or more infectious episodes	21%

Values expressed as mean±standard deviation and percentages where appropriate. NASH =non-alcoholic steatohepatitis, MELD =model of end-stage liver disease.

covariates (yes/no). A statistical association between each subject's pre- and post-transplant HRQOL scores was expected, so the relevant pre-transplant HRQOL score was also included as a covariate in each model. Additionally, since patients were surveyed at varying times post-transplant, time post-transplant (months) was included in all models. Effect sizes for each covariate are reported as standardized regression coefficients, which allow the reader to infer the relative magnitude of individual effects. Standard collinearity statistics were examined for each model. The sample to covariate ratio (approximately 14:1) was adequate for each model and the power to detect a moderate ($R^2 \geq 0.15$) overall effect for each model was 86% at the 0.05 two-tailed alpha level.

Paired t-tests were used to determine the effect of liver transplantation (pre- vs post-transplant) on all SF-36 measures (the 8 scales and 2 summary components). Multiple regression was used to develop 10 multivariate models of the effects of each of the consistent sets of covariates on the individual HRQOL outcome measure. Models and effects with a p-value of ≤0.05 were considered statistically significant.

Score profiles for the 8 SF-36 scales were developed and summarized pre- and post-transplant. The effect of HCV infection on post-transplant score profiles was tested using discriminant analysis and the degree to which the discriminant function correctly classified cases was examined. Summary data are presented throughout as mean±standard deviation or percentages. All analyses were conducted using SPSS, version 15.0 (SPSS Inc, Chicago, IL, USA).

Results

One-hundred-and-four patients had pre- and post-transplant HRQOL data. This represented 66% of our non-veteran population over this time period. This population was predominantly male (73%) and an overwhelming majority were Caucasian (94%). The mean age at time of transplantation was 54±8 years, and the mean time post-transplant was 9±8 months (range 1 to 39 months). Indications for liver transplantation included: 59% for non-cholestatic cirrhosis (Hepatitis B, C, or Alcoholic Cirrhosis), 26% for metabolic liver disease, cryptogenic cirrhosis, non-alcoholic steatohepatitis, or autoimmune hepatitis, 13% for cholestatic cirrhosis (primary biliary cirrhosis and primary sclerosing cholangitis), and 2% for other indications (hepatocellular carcinoma and hepatic epithelioid hemangoendothelioma). The mean model of end-stage liver disease (MELD) score was 23±5, with a range from 12 to 40. Twenty-three percent of patients had one or more episode of rejection and 21% experienced one or more post-transplant infection (Table I).

In general, patients' HRQOL prior to liver transplantation was well below that of the general population (Table II). The greatest impairments were seen in the physical function and general health scales, which averaged >2 SD below the general population. This sample of liver transplant recipients was unable to function independently or work as classified by their pre-transplant FP scores. However, significant

Table II. Pre- and post-transplant HRQOL scores.

Instruments	General population	Pre-transplant score	Post-transplant score	n	p-value[a]
SF-36 scales					
1. Physical function	84±23	35±23	50±27	104	<0.001
2. Role physical	81±34	16±31	34±39	104	<0.001
3. Bodily pain	75±24	43±24	54±27	101	<0.001
4. General health	72±20	22±17	55±20	102	<0.001
5. Vitality	61±21	20±18	43±26	103	<0.001
6. Social functioning	83±23	43±25	63±30	107	<0.001
7. Role emotional	81±33	42±44	66±42	101	<0.001
8. Mental health	75±18	59±22	71±22	103	<0.001
SF-36 PCS	50±10	27±8	35±11	94	<0.001
SF-36 MCS	50±10	40±11	49±12	94	<0.001
Karnofsky functional performance status		59±23	84±12	104	<0.001

Values are expressed as means±SD.
[a]Pre-transplant vs post-transplant within-subject comparison.

improvement ($p < 0.001$) was observed on all 10 HRQOL measures and FP scores from pre- to post-transplant. Average post-transplant PCS and MCS scores (Table II), and scores on six of the eight individual SF-36 scales (Figure 1), approximated those of the general United States population. The pre-transplant profile demonstrates that patients were functioning at levels substantively below the general population on every scale except mental health. The post-transplant profile shows these same patients to be functioning within general population standards on all scales except physical functioning and role physical.

Seven out of 10 multivariate models of HRQOL were statistically significant ($p < 0.05$) (Table III). These included the SF-36 physical component summary, physical functioning, role-physical, bodily pain, social functioning, role emotional, and mental health scales. Collinearity statistics were acceptable for every covariate in all models (all tolerance values ≥ 0.83). Pre-transplant scores were positively associated with post-transplant HRQOL in every model (all $p \leq 0.10$). Time post-transplant had an inconsistent effect across the models and was positively associated with the PCS, role physical, and bodily pain scales (all $p \leq 0.10$). After controlling for pre-transplant HRQOL and time post-transplant, the collection of pre- and post-transplant clinical covariates that were statistically significant differed across the models. Pre-transplant HCV infection had a statistically significant negative effect on the post-transplant SF-36 role physical ($p = 0.018$), bodily pain ($p = 0.010$), and role emotional scales ($p = 0.003$), and a marginally significant effect on social functioning ($p = 0.099$). A history of one or more rejection episode had a negative effect on the bodily pain ($p = 0.007$) and vitality ($p = 0.029$) scales. Pre-transplant model of end-stage liver disease (MELD) scores ≥ 18 had a significant positive effect on the role physical scale ($p = 0.052$) and a marginal effect on bodily pain ($p = 0.072$). The history of one or more infectious episodes was not significantly associated with any post-transplant HRQOL measure and pre-transplant FP was not related to post-transplant HRQOL.

The data presented in Figure 2 and in Table IV summarize the effect of HCV infection on the SF-36 score profile. HCV-negative patients were within general population norms on six of eight SF-36 scales post-transplant. HCV positive patients were within general population norms on four of eight scales post-transplant; they differed from HCV-patients in this respect on the bodily pain and social functioning scales. Discriminant function analysis demonstrated that the score profiles for HCV+ and HCV− recipients differed significantly (canonical correlation = 0.50, $p < 0.001$). Table IV demonstrates that the discriminant function correctly classified 73% of cases (65% after cross-validation; kappa = 0.46, $p < 0.001$).

Discussion

Increasing emphasis has been placed on assessment of the impact of liver transplantation on recipients' HRQOL and functional status. Our analyses
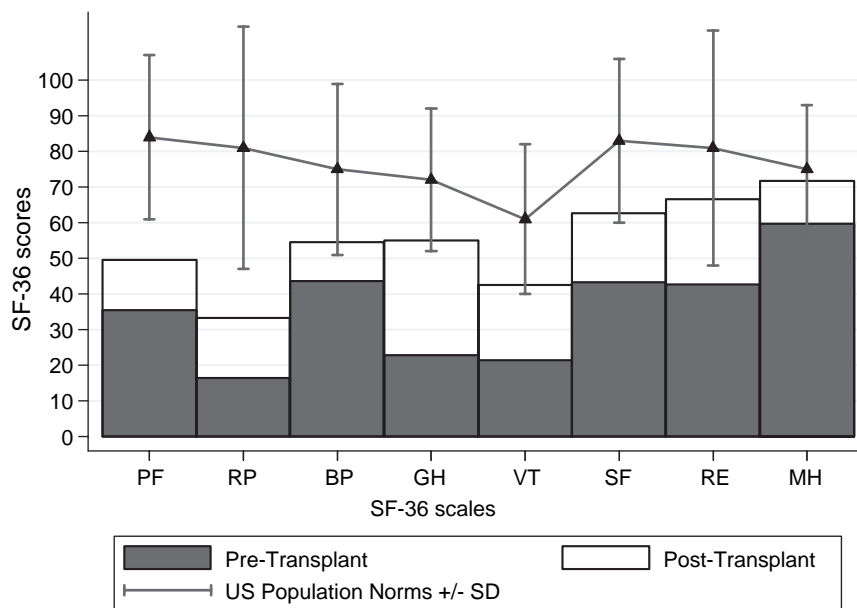

Figure 1. Pre- and post-transplant SF-36 score profiles. Shaded bar segments are average pre-transplant scores and unshaded segments the average post-transplant improvement in each scale. The full height of each bar represents the mean post-transplant score. Univariate tests of the effect of transplant on these scores demonstrated significant improvement ($p < 0.001$) on all scales after transplant. The line graph overlay represents the US population norms with error bars demonstrating ± 1 SD. The pre-transplant profile shows candidates to have substantively reduced HRQOL on 7 of 8 scales. The post-transplant profile shows recipients to have HRQOL that is within general population standards on 6 of 8 scales. Abbreviations for scales: PF = physical functioning, RP = role physical, BP = bodily pain, GH = general health, VT = vitality, SF = social functioning, RE = role emotional, MH = mental health.

Table III. Multivariate models of post-transplant SF-36 HRQOL.

Component/scale effect/parameter	PCS	MCS	PF	RP	BP	GH	VT	SF	RE	MH
Pre-transplant SF-36 score	0.394**	0.286*	0.195*	0.204*	0.319**	0.274*	0.199*	0.353**	0.172	0.306*
Time post-transplant	0.215*	−0.082	0.133	0.303*	0.146	−0.084	−0.035	−0.001	0.074	−0.084
FP at transplant	−0.022	−0.085	0.149	−0.050	−0.097	−00.47	0.012	−0.092	0.033	−0.041
Hepatitis C (Y/N)	−0.119	−0.169	−0.127	−0.232*	−0.252*	−00.47	−0.065	−0.162	−0.314*	−0.139
MELD ≥18	0.135	0.052	0.132	0.181*	0.155	0.032	0.099	0.129	0.101	0.103
Any rejection episode	−0.150	−0.073	−0.113	−0.077	−0.240*	−0.099	−0.227*	−0.143	−0.002	−0.060
Any infectious episode	0.162	−0.002	0.161	0.069	0.153	0.055	0.195	0.113	−0.107	0.076
Model p	<0.001	0.056	0.024	<0.001	<0.001	0.262	0.098	<0.001	0.020	0.018
Model R^2	0.298	0.147	0.151	0.244	0.391	0.091	0.120	0.236	0.164	0.163

Unless noted otherwise, table entries are standardized regression coefficients. **$p \leq 0.001$, *$p \leq 0.05$.
Model R^2 =squared multiple correlation coefficient.
FP =Karnofsky functional performance; MELD =model of end-stage liver disease.
Abbreviations for SF-36 components and scales: PCS =physical component summary, MCS =mental component summary, PF =physical functioning, RP =role physical, BP =bodily pain, GH =general health, VT =vitality, SF =social functioning, RE =role emotional, MH = mental health.

demonstrated significant improvement on all SF-36 measures and on FP. These findings confirm and also provide new information regarding factors that affect HRQOL after liver transplantation [1,2,14,15]. However, investigation into the effect of specific clinical covariates on a HRQOL profile after liver transplantation has not been reported.

HCV is the largest single cause of liver disease leading to cirrhosis and the need for organ transplantation. Half (51%) of our sample underwent liver transplantation secondary to HCV. For this reason, it is beneficial to characterize how this diagnosis may affect post-transplant HRQOL. Several studies have addressed the effect of HCV and recurrent post-transplant HCV on overall HRQOL, but no studies have described the effect of the diagnosis of HCV on individual post-transplant quality of life scales. Singh and co-authors compared HRQOL between liver transplant recipients with recurrent HCV to a group of recipients without recurrent HCV at different time-points. Six months after transplantation, both groups experienced significant improvement in Karnofsky functional performance scores, but improvement was less in patients with recurrent HCV. All other measures of HRQOL at 6 months, including depressive symptoms, mood disturbance, overall perceived
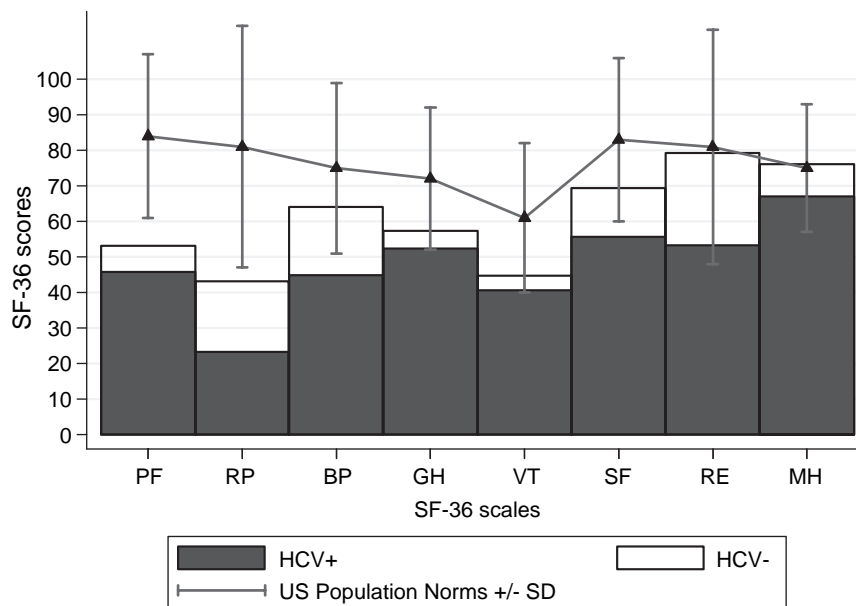

Figure 2. SF-36 post-transplant score profiles in patients with and without Hepatitis C (HCV+ and HCV −). Shaded bar segments are average post-transplant scores in HCV+ recipients, while unshaded segments are average post-transplant differences in HCV − recipients. The total heights of individual bars are mean post-transplant HRQOL scores in HCV − recipients. The line graph overlay represents the US population norms with error bars demonstrating ±SD. HCV+ recipients had post-transplant scores that were within general population standards on four of eight SF-36 scales. HCV − recipients were within general population standards on six of eight scales. Abbreviations for scales: PF =physical functioning, RP =role physical, BP =bodily pain, GH =general health, VT =vitality, SF =social functioning, RE =role emotional, MH =mental health.

Table IV. Discriminant analysis classification findings for the effect of SF-36 score profiles on HCV+ status.

			Predicted group membership		Total
	HCV (y/n)		No	Yes	No
Original	Count	no	36	13	49
		yes	13	34	47
	%	no	73.5	26.5	100.0
		yes	27.7	72.3	100.0
Cross-validated	Count	no	30	19	49
		yes	15	32	47
	%	no	61.2	38.8	100.0
		yes	31.9	68.1	100.0

In cross-validation, each case is classified by the functions derived from all cases other than that case.
73% of original grouped cases correctly classified.
65% of cross-validated grouped cases correctly classified.

QOL, and coping scores, improved significantly without differences between the two groups. At one year, patients with recurrent HCV hepatitis had significantly lower functional status, perceived QOL, and greater depressive symptoms compared to all other patients combined [16]. Likewise, Feurer and colleagues reported the negative effect of recurrent hepatitis C virus (HCV) infection on the trajectory of functional performance between post-transplant years two and three in liver transplant recipients. Using a multivariate model they demonstrated a negative effect of HCV on functional performance [9]. In our current report, we assessed whether the diagnosis of HCV, not post-transplant recurrence, had an effect on the HRQOL profile. The diagnosis of HCV had a significant negative effect on SF-36 role physical, bodily pain, and role emotional domains (Table III). Patients with HCV not only experience lower HRQOL in several physical domains, but also in one mental domain.

The model for end-stage liver disease (MELD) score is an objective liver disease scoring index that has replaced the Child Turcott Pugh (CTP) score for allocation of organs to patients with advanced, chronic liver disease awaiting orthotopic liver transplantation. The MELD score – calculated from total serum bilirubin, creatinine, and international normalized ratio (INR) – has been shown to be a reliable and valid predictor of short-term mortality in patients with end-stage liver disease [17,18]. Although the MELD score was originally proposed as a model to predict short-term mortality in patients with end-stage liver disease, in clinical practice it is often used as an overall indicator of the patient's functional health status. Several studies have reported associations between CTP, MELD scores, and HRQOL of patients with end-stage liver disease with conflicting results [19–23]. In patients awaiting liver transplantation, Saab and colleagues identified there to be no correlation between MELD score and HRQOL [21]. However, in the first report examining recipients, Kanwal and colleagues showed a small to moderate negative correlation between HRQOL and increasing MELD,

specifically in physical functioning [20]. In keeping with the previous findings, Rodrigue and colleagues showed that increasing MELD score was negatively associated with HRQOL after liver transplantation, especially as it relates to physical functioning [22]. Recently, Castaldo and colleagues, at our institution, have shown that recipients with higher pre-transplant MELD have better post-transplant physical HRQOL, but that MELD score is not correlated with post-operative mental HRQOL [23]. Despite the previous literature on MELD and HRQOL, there are no data evaluating the effect of MELD on individual HRQOL domains in a HRQOL profile. From our multivariate models, a MELD score ≥ 18 has a positive effect on SF-36 role physical and a marginal effect on bodily pain. This finding may be a function of self-perceived and self-reported improvement in HRQOL in comparison to their pre-operative status.

Twenty-three percent of our population experienced one or more rejection episodes confirmed by liver biopsy, consistent with rates reported at other centers with comparable immunosuppression regimens [24,25]. All patients experiencing rejection episodes required either an increase/change in their immunosuppression, pulse-dose steroids, or both. The additional procedures, inpatient admissions, more frequent outpatient visits secondary to these episodes had a negative effect on these patients' HRQOL. This group had significantly lower scores on SF-36 bodily pain and vitality scales. Knowledge of significant effects of rejection on certain HRQOL domains may enhance providers' abilities to care for these patients.

It is also important to recognize that pre-transplant functional performance measured by Karnofsky scores had no affect on post-transplant HRQOL. Pinson and co-authors described the trajectory of improvement of functional performance for patients after liver transplantation. Poorly functioning patients preoperatively reached equal functional performance plateaus as those patients with high preoperative functional status by 24 months [2]. Our findings support these previous findings that preoperative

functional performance was not predictive of post-operative status.

Strengths of this study include its prospective design, which allowed us to follow a specific population and characterize significant changes in QOL, affective status, and functional performance with a diverse battery of HRQOL measures. The broad assessment of HRQOL with well-validated instruments in a relatively large cohort makes it more likely that findings will generalize to other liver transplant populations. In addition, the multivariate modeling delineating positive and negative influences of certain pre-transplant and post-transplant covariates on a HRQOL profile helps clinicians recognize these effects in their liver transplant recipients. Due to our design requiring that both pre- and post-transplant data be available for several HRQOL measures, a limitation of this study is that the cohort that met our inclusion criteria represents only two-thirds of our total non-veteran population that was transplanted over this time period. Responder bias becomes a concern with any study relying on self-report of QOL depending on which population chooses to participate in the QOL evaluations. Despite the fact that our cohort had a broad range of scores on all HRQOL instruments prior to and after transplantation, consistent with previous literature [1,2,26,27], the possibility of this bias cannot be completely eliminated.

Overall improvement in mental and physical HRQOL of life after liver transplantation is well established. However, the effects of specific clinical covariates on a HRQOL profile have not been established and their effects are varied. HCV, MELD score, and biopsy-confirmed rejection episodes were influential on one or more HRQOL outcomes. Post-transplant scores on all SF-36 domains, except role emotional, were related to pre-transplant scores. Physical HRQOL and role physical improved with time post-transplant, while the remaining scales showed a sustained improvement that was not dependent on time post-transplant. Post-transplant infections and pre-transplant functional performance were not related to post-transplant HRQOL. These findings can aid clinicians in recognizing the varied effects of pre-transplant clinical conditions and post-transplant clinical events on a physical and mental HRQOL outcome profile.

Acknowledgements and disclosures

References

[1] Bravata DM, Olkin I, Barnato AE, et al. Health-related quality of life after liver transplantation: a meta-analysis. Liver Transpl Surg 1999;5:318–31.

[2] Pinson CW, Feurer ID, Payne JL, et al. Health-related quality of life after different types of solid organ transplantation. Ann Surg 2000;232:597–607.

[3] Whiting J, Nabel JPG, et al. Clinical determinants of health-related quality of life in recipients of solid organ transplants. J Surg Outcomes 1999;2:21–6.

[4] Bryan S, Ratcliffe J, Neuberger JM, et al. Health-related quality of life following liver transplantation. Qual Life Res 1998;7:115–20.

[5] Hellgren A, Berglund B, Gunnarsson U, et al. Health-related quality of life after liver transplantation. Liver Transpl Surg 1998;4:215–21.

[6] Russell RT, Feurer ID, Wisawatapnimit P, et al. The effects of physical quality of life, time, and gender on change in symptoms of anxiety and depression after liver transplantation. J Gastrointest Surg 2007.

[7] Anastasi A. Psychological testing. New York: Macmillan Publishing Company; 1988. p. 135–7; 492–6.

[8] Ware J, Kosinski M, Gandek B. SF-36 Health Survey: Manual and Interpretation Guide. Lincoln, RI: QualityMetric Incorporated; 2000. p. 3:10–11; 11:9–11.

[9] Feurer ID, Wright JK, Payne JL, et al. Effects of hepatitis C virus infection and its recurrence after liver transplantation on functional performance and health-related quality of life. J Gastrointest Surg 2002;6:108–15.

[10] Patterson D, Gayowski T, Wannstedt C, et al. Quality of life in long-term survivors after liver transplantation: impact of recurrent viral hepatitis C virus hepatitis. Clin Transplant 2000;14:48–54.

[11] Feurer ID, Moore DE, Speroff T, et al. Refining a health-related quality of life assessment strategy for solid organ transplant patients. Clin Transplant 2004;18(Suppl 12): 39–45.

[12] Ware J, Kosinski M, Keller S. SF-36 Physical and mental health summary scales: A users' manual. Boston: Health Institute, New England Medical Center; 1994.

[13] Grieco A, Long CJ. Investigation of the Karnofsky performance status as a measure of quality of life. Health Psychol 1984;3:129–42.

[14] Payne JL, McCarty KR, Drougas JG, et al. Outcomes analysis for 50 liver transplant recipients: the Vanderbilt experience. Am Surg 1996;62:320–5.

[15] Geevarghese SK, Bradley AE, Wright JK, et al. Outcomes analysis in 100 liver transplantation patients. Am J Surg 1998; 175:348–53.

[16] Singh N, Gayowski T, Wagener MM, Marino IR. Quality of life, functional status, and depression in male liver transplant recipients with recurrent viral hepatitis C. Transplantation 1999;67:69–72.

[17] Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001;33:464–70.

[18] Wiesner R, Edwards E, Freeman R, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology 2003;124:91–6.

[19] Marchesini G, Bianchi G, Amodio P, et al. Factors associated with poor health-related quality of life of patients with cirrhosis. Gastroenterology 2001;120:170–8.

[20] Kanwal F, Hays RD, Kilbourne AM, et al. Are physician-derived disease severity indices associated with health-related

quality of life in patients with end-stage liver disease?. Am J Gastroenterol 2004;99:1726–32.

[21] Saab S, Ibrahim AB, Shpaner A, et al. MELD fails to measure quality of life in liver transplant candidates. Liver Transpl 2005;11:218–23.

[22] Rodrigue J. Does MELD predict quality of life after liver transplantation? Transplantation 2006;82:1016.

[23] Castaldo ET, Feurer ID, Russell RT, Pinson CW. Does health related quality of life after liver transplantation correlate with the model for end stage liver disease score? Unpublished observation. 2007.

[24] Fisher RA, Ham JM, Marcos A, et al. A prospective randomized trial of mycophenolate mofetil with neoral or tacrolimus after orthotopic liver transplantation. Transplantation 1998;66:1616–21.

[25] Eckhoff DE, McGuire BM, Frenette LR, et al. Tacrolimus (FK506) and mycophenolate mofetil combination therapy versus tacrolimus in adult liver transplantation. Transplantation 1998;65:180–7.

[26] O'Carroll RE, Couston M, Cossar J, et al. Psychological outcome and quality of life following liver transplantation: a prospective, national, single-center study. Liver Transpl 2003; 9:712–20.

[27] Nickel R, Wunsch A, Egle UT, et al. The relevance of anxiety, depression, and coping in patients after liver transplantation. Liver Transpl 2002;8:63–71.