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Illness apprehension, depression, anxiety and quality of life in liver transplant candidates: Implications for psychosocial interventions

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Abstract

Objective—End stage liver disease is associated with diminished quality of life. Numerous physical and psychosocial problems that impact quality of life are common in those undergoing evaluation for liver transplantation. Identifying which of these challenges are most closely associated with quality of life would be helpful in developing priority targets for evidence-based interventions specific to those undergoing transplant evaluation.

Method—108 adults undergoing psychological assessment for liver transplant completed clinical interview, neuropsychological testing, and self-report inventories of depression, anxiety, cognitive appraisal characteristics, support resources, and quality of life.

Results—Multiple regression analyses revealed that while emotional symptoms (anxiety and depression) were primarily associated with mental quality of life, illness apprehension was the only variable uniquely associated with physical quality of life after accounting for severity of liver disease, cognitive status, emotional symptoms, and support resources.

Conclusion—Findings suggest that psychosocial interventions prioritizing reduction of illness related fear and symptoms of anxiety/depression will likely have the greatest impact on quality of life in persons with end stage liver disease awaiting transplantation.

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Introduction

Living with end stage liver disease (ESLD) presents various physical, cognitive, emotional, and social challenges. For those in need of liver transplantation, the evaluation and waiting process is wrought with uncertainty. Quality of life (QOL) generally improves following transplant (1–5), even when some physical symptoms remain (6), which highlights the inherently stressful nature of the process of evaluation and waiting for a life-saving transplant. Some investigators emphasize that the psychosocial and physical demands on patients and families shift throughout the different stages of transplantation and call for the development and implementation of stage-specific evidence-based treatment strategies in order to optimize outcomes (7). Identifying the most critical factors in determining QOL during this stage may help to focus interventions to maximize QOL for patients undergoing transplant evaluation.

Multiple life domains impacted by ESLD/chronic liver disease are linked to poor QOL. Individuals with ESLD have elevated rates of depression and anxiety, and associated decreases in QOL (8, 9). Restricted social functioning and low religious faith have been linked to poor QOL in persons with hepatitis C virus (10). Spiritual well-being has been demonstrated to be associated with lower death distress in persons living with other life-threatening medical conditions (11), and post liver transplant patients have described spirituality as an important determinant of their QOL (12). In regards to styles of cognitive appraisal, patients with hepatitis C virus who have negative reactions to diagnosis or who have pessimistic explanatory styles report poorer QOL (10, 13). In one longitudinal study, pessimism prior to heart transplant remained predictive of depressive symptoms up to five years after transplant while optimistic individuals maintained greater QOL over the same period (14). Taken together, these findings suggest that affective symptoms, cognitive appraisal (e.g. pessimism vs. optimism and reactions to illness), and psychosocial resources (e.g. social support and spirituality) are likely important mediators of QOL in persons with ESLD.

Physical and neurocognitive symptoms which negatively impact QOL are also common in patients undergoing liver transplant evaluation (15). While overall illness severity, indicated by Model End-Stage for Liver Disease (MELD) score, has been linked to QOL in persons with ESLD (16), the presence of specific symptoms such as ascites and overt hepatic encephalopathy have been better predictors of QOL in some samples (17, 18). Hepatic encephalopathy (HE) negatively impacts mental QOL (18), and successful management of encephalopathy with rifaximin improves QOL in persons who have experienced this complication (19).

In summary, studies to date indicate that greater illness severity, cognitive impairment, dysphoric mood (e.g. depression, anxiety), negative appraisal style (e.g. pessimism, fearful reactions to illness), and lack of psychosocial resources (e.g. social isolation and spirituality) may adversely impact QOL while living with a life-threatening illness such as ESLD. In a limited-resource environment, identifying which of these domains are most strongly related to QOL for individuals undergoing evaluation for liver transplantation would help prioritize aspects of care and specific interventions during this phase of illness.

Guided by the domains identified in prior research, we selected measures of illness severity, cognitive function, affect, styles of appraisal, and psychosocial resources to relate to QOL during our assessments of candidates for liver transplant. We predicted that this broad range of factors would be associated with QOL. An exploratory analysis was planned to assess the relative contributions of the leading factors from each of these domains in order to help providers prioritize resources when caring for patients during the pre-transplant stage of illness.

Method

Participants

The participants were 108 adult candidates for orthotopic liver transplantation at a large, urban medical center in central Virginia who had completed a multidisciplinary assessment for liver transplantation. Individuals suffering neurocognitive impairment due to other medical conditions, acute illness, or poorly controlled psychiatric disorder were excluded from this study. Individuals for whom English was not their first language were also excluded. The mean age of the sample was 53.3 ($SD = 7.5$) and mean education level was 12.8 years ($SD = 2.4$). Demographic and illness data are summarized in Table 1 and complete details have been published at (20). This archival study was approved by the Virginia Commonwealth University Institutional Review Board.

Measures and Procedures

All participants completed a clinical interview, self-report inventories, and neuropsychological testing as part of their standard psychological evaluation for liver transplantation. Model for End-Stage Liver Disease (MELD) score was obtained by medical record review and was used to assess liver disease severity. All testing and interviews were completed by a doctoral level psychologist or a doctoral level trainee being supervised by the psychologist. See (20) for a full description of the measures from which predictor variables were derived. Self-reported depression, anxiety, illness apprehension, future pessimism, social isolation, and spiritual absence were selected as the variables of interest from the Millon Behavioral Medicine Diagnostic, and recommended cutoff of 75 or greater was used to detect clinically significant concerns in each domain (21). Mental and physical component scores (MCS and PCS) for QOL were obtained from the SF-36 (22).

Age-adjusted scores were used for all neuropsychological variables. Neuropsychological assessment included estimated Full scale IQ from the Weschler Abbreviated Scale of Intelligence (23); total score and index scores for immediate memory, delayed memory, visuospatial-construction, attention, and language from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (24); and a measure of visuomotor speed and attention (Trail Making Test) (25).

Statistical Analyses

Five hierarchical multiple regression analyses were completed for each of the QOL component scores (MCS, PCS) as dependent variables. All analyses controlled for education and MELD score. Independent variables in the first four regressions for MCS and PCS were:

1) global cognition: WASI FSIQ, Trails B time, and RBANS total score, 2) specific RBANS cognitive domains: immediate memory, delayed memory, visuospatial-construction, attention, and language, 3) affective symptoms: anxiety and depression scores, and 4) cognitive appraisal style and psychosocial resources: illness apprehension, social isolation, and spiritual absence. We originally planned to include future pessimism as a cognitive appraisal measure, however, pessimism was highly correlated with illness apprehension ($r=0.76$, $p<.001$), so we elected to exclude this variable to avoid problems with multicollinearity. Following review of the results of these planned regressions, independent variables were selected for a final regression model which included measures that were closely associated with quality of life in the previous models. SPSS v. 20.0 (IBM) was utilized for all analyses.

Results

Table 1 presents demographic, health, and psychosocial characteristics of the sample. Surprisingly, mental QOL score was in the average range compared to normative population data, however physical QOL was more than a standard deviation lower than seen in the general population. While mean levels of depression symptoms were in the average range, rates of clinically elevated symptom levels were highly prevalent (23.1% of the sample). Only mean levels of illness apprehension and future pessimism scores were noted to be significantly above levels seen in the general population, and unfortunately, approximately 50% of individuals reported clinically significant illness apprehension.

Correlations among all major study variables are presented in Table 2. Results of the first four planned regression analyses for MCS (see Table 3) indicate that anxiety, depression, illness apprehension, and social isolation were associated with mental QOL after controlling for education and severity of liver disease. These four were subsequently entered as independent variables in the fifth regression analysis. In this final model, depression ($\beta=-.43$, $p<.001$) and anxiety ($\beta=-.22$, $p<.05$) were inversely associated with mental QOL after controlling for education and disease severity, and social isolation approached significance ($\beta=-.17$, $p=.06$).

Results of the first four planned regressions for PCS (see Table 4) indicate that depression and illness apprehension were associated with physical QOL after controlling for education and severity of liver disease. These two variables were then entered into the final regression analysis for PCS and only illness apprehension remained significantly inversely associated with physical QOL ($\beta=-.46$ $p<.001$). MELD score was not significantly associated with PCS score.

Discussion

Undergoing liver transplant evaluation and waiting for transplant may be one of the most stressful phases of the transplantation process and warrants the development of evidence-based interventions that target the specific challenges of this period (7). Many physical, cognitive, emotional, and social challenges occur during this time. The current study was designed help identify which of these multiple life domains are most closely related to QOL

in order to guide the development of interventions specific to the needs of individuals in this challenging situation. Somewhat surprisingly, our participants reported mental QOL that was in the average range, however, it is noteworthy that these data were collected as part of their psychological evaluation for transplant candidacy, thus there likely was a degree of positive impression management to this finding. Nonetheless, a subset of individuals (13%) did report poor mental QOL and not surprisingly, depression, anxiety, and to a certain extent social isolation emerged as the most important concomitants of this variable. Intriguingly, illness apprehension and not severity of liver disease emerged as the main factor associated with physical QOL.

Depression correlated with anxiety, illness apprehension, pessimism, and social isolation in our sample. While a broader construct such as trait neuroticism might subsume susceptibility to each of these symptoms/characteristics, the cognitive-affective aspects of depression and anxiety each uniquely contributed to mental QOL in this patient population. Because pre-transplant depression is also an important predictor of QOL six months after transplant (26), targeting these symptoms early is important. Furthermore, addressing negative appraisals and expectations is a well-established cognitive behavioral treatment of depression and anxiety (27). Additionally, interventions for depression and anxiety commonly target reduction of emotional avoidance, the restructuring of maladaptive behavior patterns, and use of medications (27). Based on our findings, interventions for pre-transplant individuals with poor mental QOL could focus on a) teaching skills for monitoring and tolerating the emotional distress associated with uncertainty of waiting for life-saving treatment, b) modeling strategies for restructuring of unrealistically negative or fearful thoughts (27), and c) implementing behavioral strategies to increase daily reinforcement opportunities that are consistent with the individual's physical functioning (28).

Poor physical QOL was rather common in our sample, and illness apprehension was predictive of poor physical QOL over and above the impact of severity of liver disease. Apprehension is to be expected during a time of uncertainty about one's health, and a degree of fearfulness may be necessary to mobilize appropriate coping resources and maintain vigilance over illness-related threats. High levels of apprehension, however, impairs QOL and potentially interferes with effective self-care behaviors during surgical recovery (29). We did not find an association between illness apprehension and disease severity in our sample, indicating that degree of apprehension was largely psychologically determined. A phenomenological study has shown that patients describe difficulty dealing with uncertainty and lack of control during the transplant process (30), which would seem likely to be associated with high fearfulness. Providing education about the transplant process, and directly addressing fearfulness about one's illness then, may be critical in optimizing physical QOL. Our transplant program (and many others) offer patient support groups that are open to both pre- and post-transplant recipients. Anecdotally, patients who are in the waiting phase have reported that it is comforting to meet and interact with short- and long-term survivors who are part of this group. Hearing from survivors that they were once equally sick and scared before their own transplants provides some hopeful illumination of the path ahead. This particular type of social support may be distinct from that provided by friends, family, and neighbors, who lack personal experience with transplant. Knowing that one is not alone and that others have survived this frightening path may be uniquely suited

to reducing illness apprehension. Future studies might assess the relative impact of such disease-specific social support in contrast to that provided by friends and family.

There are some limitations to this study. The cross-sectional nature of the design allows only for a snapshot of what happens in the lives of persons with ESLD at the time of their psychological evaluation for transplant. Future studies might prospectively assess the impact of QOL pre-transplant on post-transplant adjustment and adherence to medical regimen. Because this study focused on the pre-transplant psychological evaluation, our sample likely includes individuals who were ultimately not listed for transplant for any number of medical or psychosocial reasons. Being deemed an unsuitable candidate for transplant would undoubtedly impact QOL, and may necessitate different intervention approaches. Finally, there is some conceptual and content overlap between predictor variables and the outcome measure of mental QOL (MCS). Specifically, MCS includes some items pertaining to depressive symptoms (SF-36 item “have you felt downhearted and blue”), social isolation (SF-36 item “to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, and groups?”), and anxiety (SF-36 item “have you been a very nervous person”). However, this overlap is minimal in that of a total of 14 items, three represent possible symptoms of depression, one represents anxiety symptoms, and two represent social functioning, and the latter is somewhat conceptually distinct from social isolation. Mental QOL represents a broader construct that includes the perceived impact of such symptoms on daily functioning and ability to enjoy life. Our use of multiple regression analysis allowed for an assessment of the degree to which these specific symptoms and characteristics relate to this broader construct while simultaneously accounting for the relation between QOL and other potential physical concerns.

In summary, although multiple factors contribute to QOL in individuals undergoing psychological evaluation for liver transplant, depression, anxiety, and illness apprehension emerged as the primary domains most closely linked to QOL. In particular, poor physical QOL was quite common, and was associated with illness apprehension, highlighting the importance of addressing fearfulness about illness at this stage of ESLD. Psychosocial interventions should also target symptoms of depression and anxiety and adaptive styles of cognitive appraisal to improve QOL during this challenging phase of life with ESLD. Liver patient support groups that include individuals who are post-transplant may provide one of the best opportunities to reduce fear about illness, depression, and anxiety in those who are undergoing the evaluation and waiting process. Skills commonly addressed in treatment of depression and anxiety (e.g. tolerating emotional distress, restructuring unrealistic thinking, and increasing participation in reinforcing behaviors) should be incorporated into such groups for individuals during this difficult phase of illness.

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Abbreviations

ESLD	End Stage Liver Disease
MELD	Model End-Stage for Liver Disease
QOL	Quality of Life
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status

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Table 1

Sample demographics, health, cognitive, and psychosocial status

Demographics	
Age M(SD)	53.3(7.5)
Gender (% male)	70.4
Ethnicity	
Caucasian	82.4
African American	13.7
Hispanic	3.7
Years of Education M(Range)	12.8 (5– 18)
Health Status	
MELD score M(Range)	14.6 (6–27)
Cause of ESLD (% of sample)	
Hepatitis C Virus	40.7
Alcoholic Cirrhosis	25.0
Other	34.3
(e.g. non-alcoholic steatohepatitis, cryptogenic, biliary cirrhosis, etc.)	
Cognition	
WASI Full Scale IQ M(SD)	95.4 (16.3)
Trails B (z-score)	2.0 (3.5)
RBANS total	83.4(14.0)
Immediate Memory	87.0 (16.5)
Visuo-Construction	85.1 (17.6)
Language	90.8 (11.1)
Delayed Memory	88.4 (15.2)
Affective symptoms, cognitive appraisal styles, psychosocial resources	
(MBMD prevalence scores; scores 75 indicate clinically significant problem area)	
Depression M(SD, % above 75)	48.2 (27.9, 23.1)
Anxiety	43.4 (26.7, 13.9)
Illness Apprehension	68.1 (22.2, 50.9)
Social Isolation	40.4 (24.1, 7.4)
Future Pessimism	64.5 (18.3, 34.3)
Spiritual Absence	41.1 (31.0, 19.4)
Quality of Life	
(Normative data M= 50 SD =10)	
Mental Component Score M(SD, % below 40)	50.2 (9.4, 13.0)
Physical Component Score	37.3 (10.7, 51.9)

MELD: Model for End Stage Liver Disease; ESLD: End Stage Liver Disease; MBMD: Millon Behavioral Medicine Diagnostic; RBANS=Repeatable Battery for the Assessment of Neuropsychological Status; WASI FSIQ = Weschler Abbreviated Scales of Intelligence Full Scale IQ

Table 2

Correlations among study variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. Education																
2. MELD score	.24*															
3. FSIQ	.54**	.05														
4. Trails B time	-.33**	.16	-.48**													
5. RBANS total	.44**	.06	.62**	-.58**												
6. Immediate memory	.47**	.04	.43**	-.46**	.81**											
7. Visual Construction	.29**	.18	.50**	-.35**	.70**	.36**										
8. Language	.29**	.01	.50**	-.43**	.69**	.44**	.41**									
9. Attention	.25**	-.05	.52**	-.49**	.74**	.51**	.34**	.45**								
10. Delayed Memory	.30**	.00	.40**	-.50**	.80**	.66**	.43**	.44**	.50**							
11. Anxiety	-.12	.02	-.18	.19	-.25*	-.24*	-.14	-.19*	-.08	-.27**						
12. Depression	-.20*	.10	-.22*	.21*	-.22*	-.19*	-.13	-.21*	-.16	-.16	.47**					
13. Illness App.	-.15	.05	-.23*	.11	-.20*	-.19*	-.12	-.13	-.17	-.10	.47**	.52**				
14. Future Pessimism	-.17	.03	-.22*	.13	-.17	-.09	-.13	-.16	-.19	-.05	.34**	.57**	.76**			
15. Social Isolation	-.05	-.05	-.03	.18	-.06	-.11	.12	-.06	-.09	-.11	.24*	.33**	.06	.01		
16. Spiritual Absence	-.17	.01	.09	.02	-.06	-.17	.11	-.07	-.05	-.02	-.04	.14	-.11	-.08	.08	
17. Mental QOL	.20*	-.05	.19	-.25*	.32**	.31**	.13	.29**	.16	.31**	-.56**	-.63**	-.48**	-.31**	-.01	
18. Physical QOL	.21	-.09	.18	-.03	.14	.13	.18	.11	.05	.02	-.14	-.35**	-.53**	-.55**	-.05	-.12

Note: MELD=Model for End-stage Liver Disease, RBANS=Repeatable Battery for Assessment of Neuropsychological Status, QOL=Quality of Life

Table 3
Hierarchical Multiple Regression analyses using mental component QOL score as the dependent variable.

	<i>B</i>	<i>SE B</i>	β	<i>t</i>	<i>Sig. (p)</i>
Model 1: Global Cognition					
Step 1:					
Education	.919	.395	.264	2.330	.022
MELD	-.225	.209	-.122	-1.076	.285
Step 2:					
Education	.542	.474	.155	1.142	.257
MELD	-.188	.214	-.102	-.879	.382
WASI FSIQ	-.025	.082	-.046	-.300	.765
Trails B	-.261	.343	-.108	-.761	.449
RBANS total	.124	.097	.195	1.270	.208
Model 2: Specific cognitive (RBANS) domains					
Step 1:					
Education	.919	.395	.264	2.330	.022
MELD	-.225	.209	-.122	-1.076	.285
Step 2:					
Education	.443	.446	.127	.992	.324
MELD	-.174	.209	-.094	-.829	.410
Attention	-.022	.078	-.038	-.285	.776
Visuo-construction	-.051	.065	-.100	-.784	.436
Immediate memory	.078	.089	.142	.877	.383
Language	.082	.111	.098	.737	.464
Delayed memory	.127	.087	.220	1.458	.149
Model 3: Affective Symptoms					
Step 1:					
Education	.919	.395	.264	2.330	.022
MELD	-.225	.209	-.122	-1.076	.285
Step 2:					
Education	.302	.301	.087	1.003	.319

	<i>B</i>	<i>SE B</i>	<i>β</i>	<i>t</i>	<i>Sig. (p)</i>
MELD	-.092	.155	-.050	-.593	.555
Anxiety	-.092	.032	-.271	-2.923	.005
Depression	-.167	.031	-.509	-5.401	.000
Model 4: Cognitive appraisal style and psychosocial resources					
Step 1:					
Education	.919	.395	.264	2.330	.022
MELD	-.225	.209	-.122	-1.076	.285
Step 2:					
Education	.569	.344	.163	1.655	.102
MELD	-.207	.178	-.112	-1.161	.249
Illness Apprehension	-.143	.036	-.380	-3.961	.000
Social Isolation	-.133	.036	-.345	-3.674	.000
Spiritual Absence	-.010	.028	-.033	-.354	.724
Model 5: Multi-dimensional					
Step 1:					
Education	.919	.395	.264	2.330	.022
MELD	-.225	.209	-.122	-1.076	.285
Step 2:					
Education	.316	.298	.091	1.059	.293
MELD	-.122	.154	-.066	-.788	.433
Illness Apprehension	-.025	.038	-.067	-.660	.511
Depression	-.142	.035	-.434	-4.096	.000
Anxiety	-.076	.033	-.223	-2.272	.026
Social Isolation	-.064	.034	-.166	-1.880	.064

Note: ESLE=End Stage Liver Disease; MELD= Model End-Stage for Liver Disease; QOL=Quality of Life; RBANS=Repeatable Battery for the Assessment of Neuropsychological Status; WASI FSIQ = Weschler Abbreviated Scales of Intelligence Full Scale IQ

Table 4
Hierarchical Multiple Regression analyses using physical component QOL score as the dependent variable.

	<i>B</i>	<i>SE B</i>	β	<i>t</i>	<i>Sig. (p)</i>
Model 1: Global Cognition					
Step 1:					
Education	1.231	.449	.306	2.742	.008
MELD	-.351	.237	-.165	-1.480	.143
Step 2:					
Education	1.247	.547	.310	2.279	.026
MELD	-.415	.247	-.195	-1.680	.097
WASI FSIQ	.062	.095	.100	.656	.514
Trails B	.514	.396	.184	1.299	.198
RBANS total	.020	.112	.028	.182	.856
Model 2: Specific cognitive (RBANS) domains					
Step 1:					
Education	1.231	.449	.306	2.742	.008
MELD	-.351	.237	-.165	-1.480	.143
Step 2:					
Education	1.293	.526	.321	2.457	.016
MELD	-.417	.247	-.196	-1.687	.096
Attention	.006	.092	.009	.067	.947
Visuo-construction	.085	.077	.146	1.112	.270
Immediate memory	.023	.106	.037	.222	.825
Language	-.073	.131	-.076	-.562	.576
Delayed memory	-.102	.103	-.152	-.987	.327
Model 3: Affective Symptoms					
Step 1:					
Education	1.231	.449	.306	2.742	.008
MELD	-.351	.237	-.165	-1.480	.143
Step 2:					
Education	.952	.449	.237	2.118	.037

	<i>B</i>	<i>SE B</i>	β	<i>t</i>	<i>Sig. (p)</i>
MELD	-.282	.232	-.132	-1.218	.227
Anxiety	.021	.047	.053	.441	.660
Depression	-.116	.046	-.308	-2.527	.014
Model 4: Cognitive appraisal style and psychosocial resources					
Step 1:					
Education	1.231	.449	.306	2.742	.008
MELD	-.351	.237	-.165	-1.480	.143
Step 2:					
Education	.878	.404	.218	2.175	.033
MELD	-.243	.209	-.114	-1.165	.248
Illness Apprehension	-.216	.042	-.497	-5.089	.000
Social Isolation	.058	.043	.130	1.358	.179
Spiritual Absence	.006	.033	.016	.169	.867
Model 5: Multi-dimensional					
Step 1:					
Education	1.231	.449	.306	2.742	.008
MELD	-.351	.237	-.165	-1.480	.143
Step 2:					
Education	.827	.408	.205	2.026	.046
MELD	-.259	.210	-.121	-1.231	.222
Illness Apprehension	-.200	.049	-.461	-4.070	.000
Depression	-.014	.043	-.038	-.330	.742

Note: ESLE=End Stage Liver Disease; MELD= Model End-Stage for Liver Disease; QOL=Quality of Life; RBANS=Repeatable Battery for the Assessment of Neuropsychological Status; WASI FSIQ = Weschler Abbreviated Scales of Intelligence Full Scale IQ