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LIVER TRANSPLANT RECIPIENTS: INDIVIDUAL, SOCIAL, AND ENVIRONMENTAL RESOURCES

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Abstract

CONTEXT—Patient characteristics are important in the liver transplant (LTX) population because of proven associations between individual and environmental factors, treatment adherence, and health outcomes in general medical and other transplant (txp) populations.

OBJECTIVE—The objective of this report is to determine generalizability of the sample to other LTX populations and to establish reliability of measures used to assess individual and environmental resources.

DESIGN—This is a cross sectional analysis of baseline data in a longitudinal study of adherence and health outcomes.

PARTICIPANTS, SETTING—Ninety first-time adult LTX recipients at the University of Pittsburgh Medical Center completed assessments of socio-demographic, health history, psychosocial and environmental factors shortly after surgery; adherence and health outcomes are tracked throughout the study.

RESULTS—The UPMC cohort is older, less racially diverse, and contains more living donors than the national sample. Our sample is generally comparable to the UPMC cohort on pre-txp socio-demographic and clinical characteristics.

Comparable reliability/internal consistency on psychological measures is demonstrated between our sample and most published norms. The mean scores on all coping scales in our sample are

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higher than normative. Our subjects indicated a more negative perception of family environment and perceived relationships with their primary caregiver more positively than the normative group.

CONCLUSION—The generalizability of our sample to the parent population and reliability of individual and environmental measures reported here will enable us to examine relationships and predictive capability of patient and contextual resources on treatment adherence and health outcomes among liver transplant recipients.

Keywords

liver; transplant; psycho-social; socio-demographic

INTRODUCTION

Transplantation (txp) is the only option for survival of end stage liver disease; demand for organs far exceeds supply. Advances in medical management and surgical technique account for the current success (72.5% 5 year survival rate in the US) (1) of liver transplantation (LTX); however, little is known about the personal characteristics of candidates associated with good prognosis. The LTX population varies widely on psychiatric history and etiology of end stage liver disease. Psychiatric disorders, including alcohol and/or drug abuse and cognitive dysfunction, are common in this population (2,3). Prevalence of personality disorders, primarily Anti-Social Disorder, approaching 30% in the LTX population has been reported (4). Similar levels of depression, anxiety and social support as well as similar mean scores of personality traits among candidates for lung, heart and liver transplantation have been reported (5). It would have been interesting to know range of scores on the personality measure as extreme values on some traits (e.g. high neuroticism, low openness) are consistently correlated with presence of personality disorders (6).

Patient characteristics are important in the LTX population because of proven associations between individual and environmental factors on treatment adherence and subsequent health outcomes in other populations. For instance, pre-transplant medication non-adherence, assessed with self-report, among candidates for cardiothoracic and liver transplantation was prevalent and similar in both cohorts (7) and was related to lower levels of trait conscientiousness and less social support among lung candidates (8). Previous studies of post-transplant adherence in this population have focused primarily on return to drinking among recipients transplanted for alcoholic cirrhosis (9). There are no consistent predictors of relapse, including a pre-transplant diagnosis of alcoholic liver disease (10,11); patients with a history of alcohol dependence rather than abuse are more likely to relapse (12). Neither is alcohol abuse or dependence a reliable predictor of pre-txp psychological morbidity (13). As with alcohol, pre-txp drug use is not related to post-txp mortality; while return to use does occur, history of use alone is not a reliable predictor of post-txp relapse (14,15).

There are clear links between adherence to treatment regimens and health outcomes both in general medicine and in transplantation (16-18) and between psychological and contextual factors, adherence, and health (19-21). Non-adherence is implicated in quality of life and morbidity in other transplant (txp) populations (22-25) and noncompliance is directly related (among other txp recipients) to the leading causes of late mortality (chronic rejection, de-novo malignancies) in the LTX population (26,27). No known studies have examined a broad range of patient and environmental factors that may be related to adherence with all aspects of the treatment regimen (appointment keeping, medication taking, life-style changes) and health outcomes in the general LTX population.

The LTX population may or may not be similar, with regard to adherence, to other whole organ txp groups. This study, based on Christensen's interactionist theory of adherence (28), is designed to examine the impact of individual and contextual factors on adherence and health outcomes among LTX recipients. Accordingly, one goal of this project is to prospectively assess potential correlates and predictors of adherence to the entire treatment regimen (appointment keeping, medication taking, abstinence from alcohol, tobacco, and non-prescription drugs) and health outcomes by LTX recipients. The first step in that process is to describe characteristics of the sample and internal reliability of the measures in this population. Given the wide range of pre-txp psychological characteristics (which underlie patterns of behavior) in this group, we focused on the patient as a unique individual in the context of highly stressful chronic illness and complex treatment regimens rather than on diagnosis of psychological or cognitive pathology. We chose to represent patient characteristics with patient and environmental factors that are relatively stable yet are amenable to change with appropriate interventions, could be assessed prior to transplantation, and have been identified as important predictors of adherence and outcome in medicine and transplantation.

This report focuses on background characteristics of the sample and on individual, social, and environmental resources of the initial cohort of LTX recipients. This information is critical to our long term objective of identifying LTX patients at risk of poor adherence and long-term prognoses early in the transplant process.

METHODS AND MATERIALS

Study Setting and Sample

All procedures are in accord with the Helsinki Declaration of 1975; approval from the University of Pittsburgh's Institutional Review Board and the Starzl Transplant Institute Data Safety and Monitoring Board were obtained prior to recruitment. Informed consent was obtained from all subjects at the time of enrollment, either in the hospital or at an outpatient clinic appointment within 1-2 months after discharge.

Subjects were recruited from the population of adult liver transplant recipients at the University of Pittsburgh Medical Center (UPMC), Starzl Transplant Institute. During the period from October 2006 to October 2007, 172 patients underwent a liver transplant. Of that group, 143 were eligible (first time liver transplant, English speaking, physically and cognitively able to participate in the study). One hundred twenty-two potential subjects (85% of those eligible) were told about the study by members of the clinical staff, 101 recipients (83%) agreed to be contacted by members of the research staff, 90 recipients (89% of those contacted) were enrolled (see Discussion for further explanation).

Procedure

Subjects, who were 2-4 months post-transplant at the time, completed a battery of self-report measures and participated in a baseline interview with a study team member. Adherence to the treatment regimen (appointment keeping, medication taking, life-style changes) and health outcomes (quality of life, morbidity and mortality) are being tracked with electronic monitoring and interviews for one year and with medical records for the duration of the study.

Measures

Sociodemographic Characteristics and Health History—Sociodemographic information was elicited during the baseline interview with a measure designed and used in the Center for Research in Chronic Disorders (CRCD) at the University of Pittsburgh.

Medical and mental health history were obtained at the baseline session with a comprehensive interview developed in research with chronic medical patients (CRCD) and cardiothoracic transplant (txp) recipients (22) and from medical records. The interview was modified to include additional information pertinent to LTX recipients (e.g., drug/alcohol use, addiction rehabilitation, and length of abstinence prior to transplant). When there was incongruity between self report and medical records, we relied on medical records data to determine history of substance abuse.

Transplant related information (e.g. documented history of substance abuse, pre-txp diagnosis, donor type), was obtained with medical records review.

Psychological, Social, and Environmental Factors—Coping style, as it pertains to LTX related health problems, was assessed with The Coping Responses Inventory this is a 48-item Likert scale instrument that assesses eight types of coping styles using the approach-avoidant framework (29). Each style of coping is represented by 4 scales, each comprised of 6 items scored 1-4. Higher scores reflect more frequent use of the coping response to problems.

Patterns of decision making, critical to sustaining adherence, were assessed with The Dysregulation Inventory a 92 item self-report developed by researchers at the University of Pittsburgh to determine risk of substance abuse. This is the first time the measure has been used in an organ transplant population and is particularly relevant given the life style changes required of many recipients. The Dysregulation Inventory assesses 3 types of dysregulation. Affective dysregulation represents degree of negative affectivity and irritability; behavioral dysregulation is impulsivity, sensation seeking and aggression; cognitive dysregulation is less strategic thinking, problem solving and self-monitoring. (30). Items are scored 0-3; the affective and cognitive scales are each represented by 28 items, the behavioral scale is comprised of 36 items. Higher score reflects more dysregulation.

Cynical hostility, an intrapersonal trait marked by mistrust, suspiciousness and easily aroused anger, has long been associated with high-risk behaviors and health outcomes and predicted medication non-compliance among patients in therapy for end stage kidney disease and hepatitis C (31). The Cook-Medley Hostility Scale assessed level of trait hostility. The scale is comprised of 50 true/false items; lower scores indicate higher levels of hostility (32).

Relationship with spouse/caregiver was assessed with the 32 item Dyadic Adjustment Scale which has been widely used in clinical and research work with couples. Items are scored 0-5, higher score represents a closer relationship. Norms are presented for married and divorced couples (33). We examine the total score to assess level of caregiver support.

Family support was assessed with the Family Relations Index from the Family Environment Scale (34); this index characterizes the recipient's perception of family cohesion, expressiveness, and conflict and yields a measure of positive vs negative perception of family support. Each scale is represented by 9 items answered true/false, lower score represents stronger perception of the construct. A total score is calculated by summing the cohesion and expressiveness scales and subtracting the conflict scale; a higher total Family Relations Index score represents a more positive perception of the family environment. This scale has been used with renal transplant patients (35).

Social network was evaluated with the Lubben Social Network Scale, an 8 item self-report instrument which describes family, friend and community networks and confidence in relationships (36,37). Each item is scored 0-5, higher score indicates more involvement with

others. A ninth item, scored 0-4 elicits information about composition of the household and reliance of others upon the subject for help with household chores (e.g. shopping, cleaning, child care), higher score indicates helping more often.

Access to health care facilities and personnel in the community is essential to post-transplant care. Proximity and accessibility (logistically and financially) to physicians, visiting nurses, social service professionals, hospital, laboratory, pharmacy, and transportation was assessed in interview with an investigator designed questionnaire.

Analytic Strategies

First, descriptive statistics were used to compare this sample on socio-demographic and transplant related characteristics with US liver transplant recipients based on data from United Network of Organ Sharing (UNOS) to assess generalizability of our parent population. Second, the sample was compared to data from the Starzl Transplant Intsitute registry to assess generalizability of our sample to other UPMC liver transplant recipients. And third, sample statistics (central tendency, range, and co-efficient alpha) on psychosocial measures were compared to published norms (when available) to assess for comparability of sample and normative data. Lastly, sample socio-demographic data were examined with t-tests and chi square analyses to explore differences between subjects with or without a history of substance abuse prior to transplantation.

RESULTS

Sociodemographic and transplant clinical characteristics of the national, UPMC populations, and our sample are illustrated in Table 1. The UPMC sample is less racially diverse and contains more older recipients than the national sample but is otherwise comparable. While there are some differences, our sample is generally comparable to the UPMC cohort on socio-demographic and clinical criteria. Our sample is older (7.9% fewer subjects in the under 50 age group) with a higher percentage of recipients transplanted for alcoholic cirrhosis or hepatitis C (55.5%) and more (5.2%) living donor transplants than the UPMC cohort. In addition to socio-demographic information in the table, most of our subjects were married and had completed some post-high school education. Twenty-five subjects (27.8%) reported annual household income of less than \$30,000, eleven subjects (12.2%) reported income of over \$100,000. Seventy-three subjects (81.1% of the sample) reported that their household income was adequate to meet basic needs. Recipients in every income bracket reported that revenue was inadequate to meet basic needs but the majority (47% of them) were in the lowest category.

As to general health history, twenty-two of our subjects reported more than one medical disorder; the most common diagnosis was diabetes (39 subjects, 43.3%); 33 subjects (36.7%) had a history of cardio-vascular disease; 3 subjects had a history of HIV disease. Twenty-five subjects (27.7%) reported more than one mood disorder; the most common psychiatric comorbidities were depression and anxiety, 3 subjects reported a history of bipolar disorder. Forty-two percent of the sample (38 subjects) had a documented history of substance abuse. Twenty-three LTX recipients had a history of alcohol abuse, 3 had a history of IV drug abuse and 12 had a history of both alcohol and IV drug abuse documented in medical records. Length of abstinence from alcohol prior to transplantation ranged from 3 months to 17 years with a median of 23 months; abstinence from drug use ranged from 1 month to over 30 years. Thirteen subjects went through alcohol rehabilitation treatment prior to transplant, 4 subjects participated in a drug rehabilitation program.

Normative data from publications and manuals and sample data on psychosocial measures are presented in Table 2. Coefficient alpha statistics demonstrate comparable reliability/

internal consistency on psychological measures between our sample and published norms. Reliability on measures of social support, except for the conflict scale on Family Relations Index, are acceptable but are slightly lower than the normative groups. The mean scores on all coping scales in our sample are higher than published norms. Our sample mean for total Family Relations Index score indicates a more negative perception of family environment than the normative group. At the same time, our subjects perceive relationships with their primary caregiver (usually the spouse) more positively than the normative group. Normative scores for the Cook Medley Hostility scale and the Lubben Social Networking Scale are unavailable. Forty-one subjects (45.5%) endorsed high (scores above the median) levels of hostility; 59 subjects (65.5%) reported very often or daily interaction with others. Distance to physician and pharmacy was a problem for 3 subjects, distance to hospital and laboratory was a problem for 2 subjects. All recipients would be able to get a nurse to come to the home, 18 subjects did not know if they would be able to arrange a home visit from a social worker but the rest of the sample reported that they could.

DISCUSSION

This report describes individual, social, and environmental resources, known to affect adherence and outcomes in other populations, among a sample of first time liver transplant recipients. This is the first known study to comprehensively assess these factors in the greater LTX population and significantly adds to the knowledge base about liver transplant patients. The long term goal of this research is to integrate findings about these resources with existing evidence about adherence in this population to improve outcomes and survival rates among LTX patients.

Our sample is generally comparable to the UPMC population of liver transplant recipients but generalizability to the national population may be somewhat limited. Recipients at UPMC and in our study are somewhat older, less racially diverse, and receive a larger percentage of living donor organs than the national population. It would have been informative to compare our sample to those who were eligible but either refused or were not contacted by clinical staff; HIPPA regulations prevent access to that data. It is noteworthy that all but one of the minority patients who were eligible for the study have been enrolled and that over 50% of our subjects were transplanted for disease generally precipitated by patterns of behavior.

Medical and psychiatric health history was obtained in interview and with medical records, data from both sources, including history of substance abuse, were generally congruent except for length of abstinence prior to transplantation. Policy at the Starzl Transplant Institute and other centers requires a 6 month period of abstinence prior to transplantation and all candidates in this sample met that requirement according to medical records. Two of our subjects stated (post-transplantation) they had abstained from alcohol less than 6 months, 2 others stated they had abstained from drug use less than 6 months. This inconsistency may be explained by the fact that pre-txp abstinence from both alcohol and drugs was documented with blood tests; since alcohol and most IV drugs are detectable in blood samples for a relatively short period of time, use may not have been detected by clinicians. Candidates are aware of the abstinence requirement and that detectable levels of alcohol and drugs are short lived; they are therefore less likely to disclose use to clinicians prior to transplant than they are to researchers post-transplant .

The stress of personal illness elicits more reliance on both approach and avoidant coping styles, particularly among problem drinkers (38). Mean scores for our sample were higher than the normative sample on all coping scales. While most coping studies report the predominant style, use of both styles of coping, particularly in stressful situations, is

considered adaptive (28). Fifteen (16%) of our subjects used what might be considered a “balanced” style of coping, relying on approach and avoidant strategies with approximately the same frequency when dealing with transplant related problems. This finding deserves more intensive exploration, particularly with regard to adherence and health outcomes in this population. Our sample mean on the perception of family environments, more negative than the normative group, is also somewhat consistent with prior studies of families under stress (34) although little is known about family environments among organ transplant recipients. This finding may seem incongruent with the higher than normative support of the primary caregiver but can be explained by some evidence that, while families often become more conflicted, couples sometimes become closer when dealing with serious illness (39).

While LTX recipients transplanted for alcoholic liver disease are more likely than others to resume drinking (9-12), few do and neither pre-transplant socio-demographic factors nor history of abuse is predictive of relapse (30). These results extend our earlier research on psychological characteristics among military veterans who were candidates for liver transplantation (40). In that study, candidates for LTX with a positive history of substance abuse used less adaptive coping styles and endorsed significantly higher levels of trait personality characteristics that underlie the behavioral and decisional patterns found in this study.

Limitations to this study include the possibility of sample bias, due in part to difficulty recruiting subjects. Some eligible subjects were too ill to approach during hospitalization and were discharged to skilled care facilities, then returned infrequently to the UPMC outpatient clinic. Recipients who refused at either the point of clinician or researcher contact were often overwhelmed with the complexity of the post-transplant regimen and reluctant to take on another responsibility. These constraints are likely to be found in many other sample of transplant recipients; they may be less pertinent to adherence research in that those potential subjects most often rely on others to manage the treatment regimen. We have modified our recruitment process to address these issues by extending the window of eligibility to include recipients who were transplanted longer than 3 months previously but have not been managing their treatment regimens. We also provide contact information to those who refuse initially so they may contact us later if they change their minds.

This longitudinal five year study will continue until December, 2010; recruitment began in October, 2006 and will continue until December, 2009. Adherence to the entire treatment regimen and health outcomes are being tracked with multiple methodologies during the first post-transplant year and with medical records review for the length of the study. The comprehensive data on individual and environmental resources reported here will allow us to create profiles of liver transplant recipients, examining main and interaction effects of patient and contextual factors, on trajectories of treatment adherence and health outcomes. While there are evidence based historical predictors (length of abstinence, amount consumed, psychiatric comorbidity, social stability) of relapse to alcohol among patients transplanted for alcoholic liver disease (ALD) (41,42), little is known about post-tpx behaviors and attitudes that may also contribute to recidivism in that cohort of recipients. By focusing on relatively stable characteristics that could be identified early in the transplant process, we hope to provide clinicians with guidelines to identify liver transplant candidates, regardless of pre-tpx diagnosis, at risk of non-adherence and poor outcomes. We hypothesize that, in addition to or in combination with known evidence based pre-tpx predictors of relapse of relapse to alcohol among ALD recipients, pre-tpx knowledge about behaviors and attitudes may also contribute to better health in that cohort of recipients. Some individual and environmental variables we have chosen to measure may be subject to modification with therapy (e.g. coping style, impulse control). Some factors may be fixed (e.g. age, access to medical care) but may be compensated for (e.g. with alternate

educational approaches, strengthening social and environmental supports). We report on correlates and predictors, described here, of adherence and health outcomes at six months in the another article (43); we are using that data to develop an assessment tool that will allow clinicians to target LTX candidates at risk of non-adherence and poor outcomes with interventions early in the transplant process. Intervention strategies that provide patients with insight into how their behaviors, attitudes, and environmental resources impact on their pre and post-tpx. health may stimulate change and improve health outcomes and survival rates in this population.

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Table 1

Background Characteristics of the 2007 National*,UPMC* Populations and the Sample of Liver Transplant Recipients

Socio-Demographic	National (6494)	UPMC (172)	Sample (90)
Age (N, %)			
<50	1703 (26.2%)	48 (27.9%)	18 (20%)
50-64	3539 (54.5%)	93 (54.1%)	54 (60%)
≥65	647 (10.6%)	31 (18%)	18 (20%)
Gender (% Male)	3993 (61.5%)	112 (65.6%)	57 (63.3%)
Race (% White)	4584 (70.6%)	160 (92.9%)	86 (95.6%)
Clinical			
Pre-txp Diagnosis (N, %)			
Alcoholic Cirrhosis	1018 (17.3%)	26 (15.3%)	22 (24.4%)
Hepatitis C	1373 (23.3%)	45 (26.2%)	28 (31.1%)
Non-Alcoholic Steatohepatitis	287 (4.9%)	18 (10.4%)	11 (12.2%)
Cryptogenic Cirrhosis	357 (6.1%)	12 (7.1%)	8 (8.9%)
Living Donor (N, %)	266 (4.1%)	17 (10.4%)	14 (15.6%)

* UNOS data (<http://www.optn.org>). Only 5,889 diagnoses were available for 2007.

Table 2

Means, Standard Deviations and Internal Consistencies for Normative Groups (ref) and the Sample of Liver Transplant Recipients on Measures of Psychosocial Function

Measure	Normative Group				Sample	
	Mean (sd)		Alpha		Mean (sd); range	Alpha
	M	F	M	F		
Coping Responses Inventory (20) Approach Responses						
	11 (4.0)	11.5 (3.9)	.67	.64	15.7 (3.9); 6-24	.67
Logical Analysis	10.3 (4.7)	10.7 (4.4)	.74	.71	18.1 (4.1); 6-24	.76
Positive Reappraisal	8.8 (4.0)	10.2 (4.0)	.61	.60	17 (4.0); 8-24	.69
Seeking Guidance & Support	10.8 (4.3)	11.2 (4.1)	.68	.63	18.2 (3.5); 5-24	.61
Problem Solving						
Avoidant Responses						
Cognitive Avoidance	6.7 (4.3)	6.8 (4.2)	.72	.70	13.6 (3.9); 6-23	.72
Acceptance/Resignation	7.2 (4.3)	7.6 (4.2)	.64	.60	13.9 (4.1); 6-23	.68
Seeking Alternative Rewards	5.2 (4.2)	6.6 (4.5)	.68	.71	12.4 (4.0); 6-22	.67
Emotional Discharge	3.4 (3.3)	4.1 (3.2)	.62	.58	10.6 (3.5); 6-20	.69
Dysregulation Inventory (21)						
Affective Dysregulation	NA (not available)		.89 ^I		17.7 (10); 3-50	.91
Behavioral Dysregulation	NA		.93 ^I		18.4 (10.1); 0-62	.88
Cognitive Dysregulation	NA		.86 ^I		28.4 (9.4); 4-53	.88
Cook Medley Hostility Scale (22)	NA		.86		82.9 (8.1); 62-98	.85
Family Relations Index (25)						
Cohesion	NA		.78		10.8 (1.3); 9-16	.67
Agreeableness	NA		.69		11.8 (2.0); 9-18	.60
Conflict	NA		.61		16.0 (2.1); 9-18	.70
Total FRI	9.91 (3.82) ²		NA		6.6 (4.0); 1-22	NA
Dyadic Adjustment Scale (24)	114.8 (17.8) ³		.96		126.8 (14.5); 91-154	.79
Lubben Social Network Scale (27)	NA		.78		34.3 (7.0); 13-49	.69

¹ data from parents of adolescents

- ² norm for kidney recipients of deceased donors
- ³ norm for married couples (most subjects who completed the DAS were married)