



Utility of pretransplant psychological measures to predict posttransplant outcomes in liver transplant patients: a systematic review^{☆,☆☆}



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ABSTRACT

Objective: Evaluation of liver transplant (LT) candidacy involves psychosocial evaluation to ensure appropriate organ allocation. However, the utility of pre-LT psychiatric and neuropsychological factors in predicting posttransplant outcomes remains uncertain. We reviewed current evidence on the prognostic value of pre-LT psychological factors for outcomes after LT.

Method: We conducted a systematic review of studies with adult LT recipients that investigate the relationship between pre-LT psychiatric and neuropsychological variables and posttransplant outcomes. We searched Ovid, MEDLINE, PsycINFO, EMBASE/Scopus, Cochrane Controlled trials register and Web of Science (January 1975 to May 2015) for longitudinal, peer-reviewed studies of at least 20 subjects and written in English.

Results: The 19 studies included in this review are heterogeneous in population, prognosis and duration of follow-up (from 20 days to more than 3 years). Findings on the prognostic value of pre-LT depression or anxiety on post-LT outcomes are mixed, though depression appears to predict lower quality of life (QOL). Pre-LT suicidal thoughts in particular are associated with post-LT depression. High submissiveness may predict rejection within 20 days of LT, and low conscientiousness is associated with greater nonadherence. Whereas pre-LT cognitive performance has not been shown to predict survival, poorer performance may predict poorer QOL after LT.

Conclusion: Further studies are needed to examine this important element of LT candidacy evaluation. Studies should evaluate psychiatric factors in large samples, include systematic evaluations by mental health clinicians and explore broader neuropsychological domains in predicting posttransplant outcomes.

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1. Introduction

As liver transplantation (LT) has become the standard of care for patients with irreversible advanced liver disease and acute liver failure, nearly 16,000 adults and children are currently on LT waitlist in United States [1]. Currently, 10–20% of LT candidates die while on the waitlist [2,3] as the supply of donor livers has fallen and the waitlist has grown in size [4].

All potential LT candidates undergo psychosocial evaluation by a specialized transplant social worker and/or psychiatrist [5]. Substance

abuse before transplant has been implicated as a predictor of relapse to substance use after LT. Relapse has been associated with poorer long-term graft function, extrahepatic health and patient survival [6] [7–9]. Therefore, much of the psychosocial research related to LT candidacy has focused on substance use disorders, and they are considered a very strong relative contraindication for LT [10]. In fact, most centers' selection criteria require at least 6 months of documented abstinence before LT. Furthermore, relapse to alcohol use has been strongly associated with medication nonadherence after LT [9,11].

Nonsubstance-related psychiatric conditions are also common in people with advanced liver disease. The prevalence of significant depressive symptoms in cirrhosis has been reported to be as high as 63%. For instance, Guimaro et al. reported that among 73 patients with advanced liver disease, 17% were depressed, and 33% had symptoms of anxiety [12]. In addition, prevalence of subclinical cognitive deficits — for example, minimal hepatic encephalopathy — in patients with cirrhosis is estimated up to 60% [13,14]. Overt cognitive impairment occurs in 30–45% of cirrhotic patients [15,16]. Sorrel et al. recently reported that cognitive impairment defined as two standard deviations below the

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mean of age-matched standardized sample is highly prevalent and correlated with the model for end-stage liver disease score among 300 consecutive LT candidates [17].

There is growing interest in examining the impact of pretransplant psychological variables other than substance abuse on posttransplant clinical outcome [18]. Given the near-universal prevalence of psychosocial evaluation during LT patient selection, a better understanding of the predictive role of cognitive and psychological variables will be valuable. Therefore, we conducted a systematic literature review on the relationship between pretransplant nonsubstance related psychological variables and post-LT clinical outcomes for adult LT recipients. We included any nonsubstance use psychological factor that may predict outcome as measured by overall survival, graft rejection and hospital readmission, mental health, treatment adherence or cognitive status after LT.

2. Methods

We developed two sets of keywords: (a) those describing psychological domains and tests and (b) those describing LT. We included truncations and word spacing variation. Using Boolean logic in Ovid MEDLINE, we searched for articles including any keyword (using “or”) in both of the two keyword lists (using “and”) (Table 1). We adapted these terms to search PsycINFO, EMBASE/Scopus, Cochrane Controlled trials register and Web of Science, which do not index using keywords (Table 2).

The literature search was conducted in May 2015 (Fig. 1), and all citations were entered in an Endnote database where duplicates were removed using software deduplication followed by manual inspection. Three reviewers (SF, AW and PN) independently reviewed the title and abstract of each article applying the following inclusion criteria: (a) published in a peer-reviewed journal between 1975 and May 2015; (b) written in English; (c) describes adult LT recipients; (d) sample size at least 20; (e) pre-LT use of standardized scale or structured interview to assess for psychological symptoms; and (f) longitudinal study design with post-LT clinical outcomes. If the abstract of an article did not provide enough details to determine whether criteria were met, full text was obtained. Case reports and retrospective studies were excluded. Each result was reviewed by two independent personnel (including SF, AW, PN and HL). Inclusion decision for each article was compared between reviewers and consensus achieved. Information obtained from each study included pre-LT psychological factor including screening instrument, post-LT outcome measure, sample size, duration of follow-up and individual study results.

Table 1
Keywords for Ovid Medline

Keywords re: cognition/psychological function	Keywords re: LT
exp Hepatic encephalopathy/ Hepatic adj3 encephalopath*. mp. Liver adj3 encephalopath*. mp. exp Mental disorders/ exp Psychomotor Disorders/ exp Cognition disorders/ Delirium exp Neuropsychological Tests/ exp Psychometrics/ exp Psychiatry/ exp Psychological tests/ neuropsych*.mp. Cogniti*.mp. exp Personality Inventory/ exp Personality tests/ exp Language/ Adaptation, Psychological/	LT Liver adj3 transplan*.mp.

Table 2
Keyword correlates for non-Ovid databases

Ovid keyword	Keywords re: LT
exp Hepatic encephalopathy/ Hepatic adj3 encephalopath*. mp. Liver adj3 encephalopath*. mp.	hepatic encephalopath* liver encephalopath* (cut: very general keyword, no obvious text term)
exp Mental disorders/ exp Psychomotor Disorders/ exp Cognition disorders/ Delirium exp Neuropsychological Tests/ exp Psychometrics/ exp Psychiatry/ exp Psychological tests/ neuropsych*.mp. Cogniti*.mp. exp Personality Inventory/ exp Personality tests/ exp Language/ Adaptation, Psychological/ LT Liver adj3 transplan*.mp.	“psychomotor” “cogniti*” “delirium” “neuropsych*” “psychometrics” (cut – too broad without index terms) “psychological test*” “neuropsych*” “psychological test*” “personality” (cut – too broad without index terms) (cut: no good translation found) Liver transplant*

3. Results

In all, 5699 unique articles were identified. Based on title and abstract review, 118 full-text articles were retrieved. Ninety-eight of these were subsequently excluded upon review of full text: 14 included fewer than 20 subjects, 7 were not peer-reviewed manuscripts, 5 were duplicate entries, 7 included only subjects with alcoholic liver disease, 18 were not written in English, 10 did not include data describing psychiatric or neuropsychological variables before transplant, 33 did not include psychiatric or neuropsychological variables to predict posttransplant outcomes, 2 did not include LT and 2 were retrospective.

Nineteen articles met inclusion criteria. Their findings are organized below in four sections based on pre-LT predictor: (a) psychiatric variables; (b) personality traits; (c) cognitive performance; and (d) alexithymia.

3.1. Pre-LT psychiatric variables and post-LT clinical outcomes (Table 3)

The articles that examined pre-LT psychiatric variables as potential predictors of post-LT outcomes focused exclusively on depressive and anxiety symptoms. None of these studies examined the relationship between post-LT outcomes and pre-LT psychosis or mania.

3.1.1. Pre-LT mood and anxiety symptoms and post-LT survival

Four studies examined the association between pre-LT depression and post-LT mortality and reported conflicting results. Kober et al. found that depression scores based on the depression dimension of the European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire (EORTC QLQ C-30) were greater in a group of patients who died during the peritransplant period (2 weeks before or after transplantation) than in the patients who survived at least 6 months ($x = 1.82$, S.D. = 0.47 vs. $x = 1.2$, S.D. = 0.37) [19]. Similarly, Telles-Correia et al. found that pretransplant depression correlated with posttransplant mortality ($z = -2.00$, $P = .04$) in bivariate analysis, but in multivariate analysis that included pertinent sociodemographic and medical covariates, the association was no longer significant [20]. Similarly, a study by Goetzmann et al. based on 76 patients found that pretransplant depression was not correlated with posttransplant survival [21]. By contrast, Corruble et al. found that in their sample of 339 patients, those with pre-LT depression measured by short Beck Depression Inventory were more likely to survive at least 18 months (mortality: 4.6% vs. 11.6%, odds ratio [OR] = 0.37; 95% confidence interval [CI] = 0.16–0.88, $P = .02$) but that severity of depression was not predictive of survival [22]. Of note, the study sample of this fourth study was heterogeneous and included both kidney and

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