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ORIGINAL ARTICLE

Liver versus cardiothoracic transplant candidates and their pretransplant psychosocial and behavioral risk profiles: good neighbors or complete strangers?

Fabienne Dobbels,[1,2*] Johan Vanhaecke,[2] Frederik Nevens,[3] Lieven Dupont,[4] Geert Verleden,[4] Dirk Van Hees[5] and Sabina De Geest[1,6]

1 Center for Health Services and Nursing Research, Katholieke Universiteit Leuven, Leuven, Belgium
2 Heart Transplantation Program, University Hospitals of Leuven, Leuven, Belgium
3 Liver Transplantation Program, University Hospitals of Leuven, Leuven, Belgium
4 Lung Transplantation Program, University Hospitals of Leuven, Leuven, Belgium
5 Abdominal Transplantation Surgery, Transplant Coordination, University Hospitals of Leuven, Leuven, Belgium
6 Institute of Nursing Science, University of Basel, Basel, Switzerland

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Correspondence
Fabienne Dobbels PhD, Center for Health Services and Nursing Research, Katholieke Universiteit Leuven, Kapucijnenvoer 35/4, B-3000 Leuven, Belgium. Tel.: +32 16 33 69 81; fax: +32 16 33 69 70; e-mail: fabienne.dobbels@med.kuleuven.be

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Summary

Research concerning pretransplant psychosocial and behavioral characteristics in different organ transplant groups is limited. The aim was to assess relevant psychosocial and behavioral pretransplant factors in heart, lung and liver transplant candidates, and their differences among groups. One hundred and eighty-six transplant candidates (i.e. 71 lung, 33 heart and 82 liver) were included (93% response rate). Demographics, clinical variables, co-morbidity, anxiety, depression, personality traits, received social support and adherence with the therapeutic regimen were assessed using validated self-report instruments and chart review. Because of significant differences in gender, age and co-morbidity among groups, analyses were controlled for these factors. Lung (8.2 ± 4.2) and heart (7.6 ± 3.5) transplant candidates tended to report more depressive symptoms than liver transplant candidates (6.5 ± 4.8) ($P = 0.05$). Groups were comparable for other factors, except for liver transplant candidates being more frequently active smokers (22%) compared with heart (3%) and lung candidates (0%), and more heart (36.4%) and lung candidates (33.3%) drinking alcohol than liver transplant candidates (6.3%). Psychosocial and behavioral characteristics are comparable among pretransplant candidates. Instead of performing the pretransplant psychosocial and behavioral screening in an organ-specific fashion, our data support the use of a more general screening protocol.

Introduction

Transplantation medicine is confronted with an increasing number of patients who could be helped by this treatment modality; yet, organ shortage remains a major limiting factor. Transplantation is also an expensive technology. Thus, an evidence-based decision process in the selection of organ transplant candidates is indicated.

There is growing awareness that pretransplant psychosocial and behavioral factors, besides medical criteria, are contributing to post-transplant outcome [1,2]. Consequently, most selection guidelines state that careful pretransplant screening should not only comprise a comprehensive medical evaluation, but should also involve a thorough psychosocial assessment [3–8]. Yet, these consensus guidelines do not systematically substan-

tiate what is meant by a 'thorough psychosocial assessment'.

The survey of Levenson and Olbrisch showed that different selection criteria were applied among transplant programs and organ transplant types [9]. More specifically, reasonable agreement is apparent on some criteria within, but not across heart, liver, kidney and lung transplantation. The origin of these inter-organ differences in the pretransplant evaluation process remains obscure. Current cigarette smoking, for instance, was an absolute contra-indication in 44% of the heart transplant programs participating at the survey of Levenson [9], while only 2.2% of liver transplant programs considered active smoking as an absolute contra-indication. Also, alcohol-related problems received much more attention in liver transplant candidates compared with heart or lung transplantation.

Just and fair access to transplantation is not served by widely differing psychosocial and behavioral criteria that are based on consensus within one center rather than on evidence. A patient being screened, for instance, at a center that is using a very liberal psychosocial screening protocol may have a higher chance of being placed on the waiting list than a patient being screened at a center using very stringent selection criteria. The results of the above-mentioned survey support the need for a systematic process to develop better and fairer psychosocial and behavioral criteria for the screening of transplant candidates. An important first step is exploring whether transplant candidates really differ on relevant characteristics to substantiate if and why different criteria should be applied among different organ transplant candidates groups.

Overall, studies comparing psychosocial and behavioral characteristics among organ transplant groups are scarce and mostly limited to the post-transplant period. To our knowledge, only three studies have performed a cross-organ comparison in the pretransplant period, with one small study looking at depressive symptoms in heart and liver transplant candidates [10], another study focusing on quality of life [11], and a recent study longitudinally investigating quality of life and psychosocial functioning [12]. The aim of this study was therefore to investigate similarities and differences in psychosocial and behavioral risk profiles among heart, lung and liver transplant candidates to understand better the overall, as well as organ-specific psychosocial and behavioral needs of these groups of transplant candidates.

Material and methods

Design, sample and setting

This cross-sectional study included all patients on the waiting list for a first heart, liver or lung transplantation at a single European TX center between May 2001 and May 2003. The setting is a compulsory health insurance system based on equity and solidarity for all citizens. Transplantation is therefore a therapeutic option, irrespective of the patient's economic means.

Eligible patients had to be Dutch speaking, ≥18 years, and being able to complete the self-report questionnaires independently. Patients on the waiting list for urgent, living donor or multiple-organ transplantation were excluded. We also decided not to include candidates for renal transplantation: patients with end-stage renal failure have access to renal replacement therapy, while alternative therapies for heart, liver and lung transplant candidates are still in their infancy. Secondly, most renal transplant candidates had been already included in another study on risk factors for nonadherence with the dialysis regimen. Asking them to complete additional questionnaires was judged inconvenient and burdensome for the patients.

Variables and measurement

Demographic characteristics

Age, gender and the presence of a stable partnership (i.e. being married or living together with a partner) were noted on a self-report questionnaire. The educational level of patients was ranked as 'low' (i.e. schooling <9 years), 'medium' (i.e. schooling 9–12 years) or 'high' (i.e. >12 years) [13].

Clinical characteristics

Medical characteristics related to severity of end-stage organ disease were retrieved from the medical files and are provided for each group (Table 1 for an overview).

The burden of co-morbidities was calculated using the Charlson Co-morbidity Index (CCI) [14]. The CCI consists of 19 categories of co-morbidity defined as ICD-9 diagnoses. Each category has an associated weight, based on the adjusted risk of one-year mortality [14]. The Index assigns a numerical value or 'weight' from 1 to 6 (e.g. peripheral vascular disease = score 1; diabetes with end-organ damage = score 2). Higher total scores represent a more severe burden of co-morbidity.

Pretransplant psychosocial and behavioral factors

Psychosocial factors assessed were anxiety, depression, personality traits and received social support. Behavioral factors assessed were adherence with therapeutic guidelines in view of medication taking, smoking cessation, diet, alcohol guidelines and overall adherence.

Anxiety and depression. The Hospital Anxiety and Depression Scale [15] is a valid 14-item self-report instrument assessing the prevalence and severity of anxiety (seven

Table 1. Medical characteristics of lung, heart and liver TX candidates.

Lung TX candidates (n = 71, %)	
Etiology of end-stage disease	
Chronic Obstructive Pulmonary Disease (COPD)/emphysema	35 (49.3)
Pulmonary fibrosis	13 (18.3)
Cystic fibrosis	7 (10.0)
α-1 Antitrypsin deficiency	5 (7.0)
Pulmonary hypertension	3 (4.2)
Bronchiectasis	3 (4.2)
Other	5 (7.0)
FEV1 (% predicted)	29.8 ± 16.1
FVC (% predicted)	55 ± 15.8
Patients with O_2 supplement (%)	45 (63.4)
6-min walking distance (m)	294 ± 101
Heart TX candidates (n = 33)	
Etiology of end-stage disease	
Ischemic cardiomyopathy	19 (57.6)
Dilated cardiomyopathy	11 (33.3)
Other	3 (9.1)
Left ventricular ejection fraction (%)	28.2 ± 13.3
VO_{2max} on cycle ergometer (ml/kg/min)	11.3 ± 2.9
Patients on ventricular assist device (%)	6 (18.2)
Liver TX candidates (n = 82)	
Etiology of end-stage disease	
Alcoholic liver cirrhosis	31 (37.8)
Hepatitis C virus	12 (14.6)
Cryptogenic cirrhosis	11 (13.5)
Primary sclerosing cholangitis	8 (9.6)
Hepatic carcinoma	7 (8.5)
Metabolic disease	4 (4.9)
Primary biliary cirrhosis	3 (3.7)
Hepatitis B virus	3 (3.7)
Other	3 (3.7)
Child–Turcotte–Pugh Score	10.7 ± 1.3
Albumin (g/dl)	32.6 ± 5.7
Total bilirubin (mg/dl)	3.1 ± 2.9
Alkaline phosphatase (U/l)	485.1 ± 472
Aspartate aminotransferase (U/l)	69.7 ± 59.7
Alanine aminotransferase (U/l)	57.6 ± 57.2
Gamma glutamyl transferase (U/l)	152.7 ± 204.8

Laboratory values of patients at time of admission to the waiting list are presented as mean ± SD; FEV1, forced expiratory volume within one second; FEVC, forced vital capacity; left ventricular ejection fraction was determined through echocardiography; VO_{2max}, maximal oxygen consumption during cycle ergometer testing; ventricular assist devices include incor, novacor, or implantable cardioverter defibrillator.

items) and depressive symptoms (seven items) in nonpsychiatric medical outpatients. Items are scored on a 4-point Likert-type scale increasing in degree of severity, resulting in a total score between 0 and 21 for each subscale. Established cut-off points were used to evaluate the severity of depressive, respectively anxiety symptoms: 0–7 no symptoms; 8–10 mild symptoms; 11–14 moderate symptoms; 15–21 severe symptoms.

Personality traits. The Neo Personality Inventory-Revised short form version [16] is a 60-item instrument that provides a general description of normal personality traits along five major domains of the five-factor model of personality of Costa and McRae, including neuroticism (=proneness to psychological distress), extraversion (=capacity for joy, need for stimulation), openness to experience (=toleration for and exploration of the unfamiliar), agreeableness (=one's orientation along a continuum for compassion to antagonism in thoughts, feelings and action) and conscientiousness (=degree of organization, persistence and motivation in goal-directed behavior) [17]. Item scores were summed and raw scores for each personality trait (12 items) were compared with norm data for gender and age. Raw scores were transformed in stanine (or 'standard-nine') scores following a normal distribution (mean = 5; SD = 2).

Received social support. Received social support were assessed by means of a self-report instrument adapted from previous research for the purpose of this study (Social Support Questionnaire or SSQ), as no reliable and valid instrument is available to assess specific social support in transplant populations for the Dutch speaking population. Factor 1 (based on Principal Component Analysis) was labeled as 'general received emotional, appraisal, instrumental and informational support', and consists of five items yielding a total score between 5 and 25. Factor 2 (six items, score 6–36) was labeled 'received specific support with medication taking'. Higher scores on each factor indicate more support.

Adherence with each aspect of the therapeutic regimen. We developed a self-report questionnaire to assess adherence with the various aspects of the therapeutic regimen.

Adherence with medication taking

Medication taking adherence was assessed by a single-item question: 'In the last 14 days, how often did you not take a dose of your medication'. Answering categories are: 'never', 'one', 'twice', 'three times' and 'four times or more'. Patients answering 'never' were considered to be adherent with medication taking. All other scores were considered as nonadherence. This stringent operationalization of nonadherence is based on the known underreporting of nonadherence by self-reporting techniques. Using this admittedly stringent cut-off, we were able to increase the sensitivity of self-report: convergent validity was tested in 78 HIV patients, indicating that the sensitivity of our question (i.e. ability to detect nonadherence)

was 64% compared with electronic monitoring, and 89% compared to pill count [18]. Moreover, a linear relationship between taking adherence, using the same cut-off, and optimal viral suppression in HIV patients has been demonstrated (i.e. nomological validity) [19]. Further work on validation in transplant patients is in progress.

Smoking status

Smoking status was assessed by self-report. Patients reporting to be an active smoker were considered to be nonadherent with smoking cessation guidelines. Smoking cessation is obligatory for heart and lung transplant patients from our center (i.e. stopped for at least 6 months before being placed on the waiting list) and is strongly recommended in liver transplant candidates (no specific criteria were used at our center).

Adherence with dietary guidelines

Nonadherence with dietary guidelines was assessed by two questions. Patients were asked if they currently followed a prescribed diet (yes/no answer). If yes, the frequency of noncompliance with dietary guidelines was assessed by asking: 'during the last 14 days, how often did you not follow your diet as prescribed'. Patients answering 'never' were considered to be adherent. Patients answering 'once', or more were considered to be nonadherent.

Adherence with alcohol guidelines

Amount of daily alcohol intake was explored by the following question: 'how many glasses of alcohol (beer, wine, and spirits) are you drinking per day? Based on the guidelines of the National Institute of Health, and the National Institute on Alcohol Abuse and Alcoholism [20], following cut-offs for nonadherence with alcohol guidelines were used: liver transplant candidates answering more than '0' were considered to be nonadherent, as strict abstinence is required in all liver transplant candidates with alcoholic cirrhosis and is strongly advised for the others (our center requires that liver patients are at least 6 months sober before being placed on the waiting list). For male heart and lung transplant candidates, all answers above '2' were considered as nonadherence. For female patients, all answers above '1' were considered as nonadherence [20]. These guidelines are also used in our center, although no formal assessment is taking place. The rationale for using different cut-offs in men and women is based on evidence that alcohol consumption above two drinks per drinking day in healthy men and 1 drink per drinking day in healthy women is associated with increased health risks, including increased risk of cancer, brain damage with functional and behavioral consequences, increased risk of liver disease, and mortality [21].

Patients were asked to complete the CAGE [an acronym formed from the first letter of the key words from each of the four questions (''cutting down drinking''; ''annoying people''; ''guilty about drinking''; and ''eye opener'')]. The CAGE is a brief, nonintimidating self-report instrument to screen for alcohol problems. The four questions have dichotomous answers (i.e. yes/no answer) [22]. Alcohol problems are suspected in patients reporting 'yes' at least once.

Overall adherence

A visual analogue scale of 10 centimeters ranging from '0' to '100' was used to assess global adherence with all prescribed therapeutic guidelines. The question was formulated in a supportive and nonjudgmental way: 'we know that it is difficult for many patients to follow all guidelines regarding medication taking, smoking, diet, and alcohol use. On a scale from '0' to '100', how well do you succeed in following all guidelines prescribed by the physician? Please draw a line indicating how well you succeed: '0' means 'I do not succeed at all' and '100' means 'I perfectly succeed'. Scores are expressed as percentages from 0% to 100%, with higher percentages indicating higher global adherence.

Data collection procedure

Patients were approached for participation 2–3 weeks after listing for transplantation between May 2001 and May 2003. The primary investigator (FD) contacted eligible patients by phone and explained the purpose of the study in a standardized way. Confidentiality of data was assured. After oral informed consent, the informed consent form and the questionnaires were sent to the patient's home address. The completed questionnaires and signed informed consent were returned to the research team in a prestamped, pre-addressed envelope. All questionnaires were coded, and stored in a locked closet in the office of the primary investigator. No reminders were sent.

The local ethics committee approved this study.

Data analysis

Data were checked for normality and descriptive statistics were calculated as appropriate (i.e. means, SD; medians, inter-quartile ranges; percentages). The demographic characteristics and severity of co-morbidity (CCI) were compared among the three groups, using ANOVA, Kruskal–Wallis or chi-square depending on the distribution and measurement level. We observed a significant difference in age, gender distribution and co-morbidity between heart, liver and lung transplant candidates. This

complicates the comparison of the psychosocial and behavioral factors among the three groups, as difference in these variables may be partly explained by differences in age, gender or co-morbidity, respectively. Therefore, we decided to use multinomial logistic regression analysis, controlling for age, gender and co-morbidity, to increase the likelihood of observing true differences in psychosocial and behavioral factors among the three groups. Multinomial logistic regression analysis is similar to logistic regression, but is more general because the dependent variable, i.e. organ transplant type, is not restricted to two categories.

Data were analyzed using the statistical package SPSS for Windows (version 14) (SPSS Inc., Chicago, IL, USA). We used the free statistical package (http://faculty.washington.edu/~jstorey/qvalue) to calculate the False Discovery Rate to correct for inflation of type I error caused by the multiple comparisons. This will be referred to as the *Q*-value. This technique was developed by Benjamini and Hochberg [23], and was adapted by Storey. Both the raw *P*-value and the *Q*-value will be presented.

Results

Sample

Between May 2001 and 2003, 282 patients were placed on the waiting list for heart ($n = 43$), liver ($n = 153$) and lung transplantation ($n = 86$), respectively. Eighty-two patients (29%) were excluded for the following reasons: not Dutch speaking ($n = 36$); re-transplantation ($n = 8$); multiple organ transplantation ($n = 18$); urgent transplantation or transplantation before inclusion was possible ($n = 15$); and patient death before inclusion ($n = 5$). Two hundred patients were eligible for participation in this study and were contacted by the primary investigator (FD) by phone. One patient did not give informed consent, three patients were transplanted before the questionnaires could be filled out and 10 patients dropped out because their questionnaires were not returned, although oral informed consent was provided (i.e. five lung, one heart and four liver transplant candidates). One hundred and eighty-six transplant candidates (i.e. 71 lung, 33 heart and 82 liver transplant candidates) were available for data analyses. Overall participation rate was 93%. Patients who did not give written informed consent ($n = 14$) were not significantly different from the patients included in this study ($n = 186$) with respect to age ($Z = -0.953$; $P = 0.340$) and gender (Fisher's exact = 1; $P = 0.549$). Etiology of end-stage organ disease and medical characteristics of the three groups are listed in Table 1.

Demographic characteristics and co-morbidity

There were differences between the organ groups in age ($P = 0.002$) and co-morbidity ($P = 0.003$), while the gender distribution also tended to be different ($P = 0.055$) (Table 2).

Post hoc tests revealed that lung transplant candidates tended to be younger than heart transplant candidates (*post hoc* Tukey's test: mean difference = −6.16 years; SE = 2.3; $P = 0.020$) and were significantly younger than liver transplant candidates (mean difference = −5.8; SE = 1.8; $P = 0.003$). There is also a tendency toward more female patients in the lung compared with the heart transplant candidate group ($\chi^2 = 4.9$; $P = 0.027$), but not compared with the liver transplant candidate group. Moreover, lung transplant recipients have a significantly lower co-morbidity score compared with liver transplant candidates (*post hoc* Tukey's test: mean difference = −1.03; SE = 0.30; $P = 0.002$). Because of the statistically and clinically meaningful differences in age, gender and co-morbidity, all further comparative analyses will be controlled for these variables.

Anxiety and depression

No significant difference in overall anxiety score could be observed among the three groups. Approximately half of

Table 2. Comparison of demographic characteristics and co-morbidity (Charlson Co-Morbidity Index) between lung, heart, and liver transplant candidates.

Variable	Total sample ($n = 186$)	Lung ($n = 71$)	Heart ($n = 33$)	Liver ($n = 82$)	*P*-value
Demographics					
Age (mean years ± SD)	52.2 ± 11.3	48.8 ± 12	54.8 ± 9.5	54.8 ± 10.4	$P = 0.002$*
Gender (% male)	66.3	56.3	78.8	69.5	$P = 0.055$†
Partnership (% stable)	70.4	73.2	72.9	67.5	$P = 0.73$†
Education (% Low)	48.1	47.9	53.1	48.1	$P = 0.97$‡
Co-morbidity					
Charlson index score (mean ± SD)	3.4 ± 1.9	2.9 ± 1.8	3.6 ± 2	3.9 ± 1.8	$P = 0.003$*

*ANOVA test; †chi squared test; ‡the Kruskal–Wallis test.

the pretransplant candidates showed mild to severe symptoms of anxiety. Yet, the three transplant candidate groups differed significantly with respect to depressive symptoms when controlling for age, gender and co-morbidity. *Post hoc* comparison, however, did not reveal significant differences between the highest score (i.e. lung transplant candidates) and the lowest score (i.e. liver transplant candidates) with respect to depression (Tukey's test: mean difference = 1.56; SE = 0.65; $P = 0.064$) (Table 3).

Received social support

No significant difference among the three patient groups could be observed for received general emotional, appraisal, instrumental and informational received specific support (factor 1), and received specific support with medication taking (factor 2) (Table 4).

Personality traits

No significant difference in personality traits could be observed between the transplant candidates. There was a tendency toward a difference for neuroticism (Table 4), with lung transplant candidates tending to show higher scores on neuroticism, explained in part by the higher scores on depression observed in lung transplant candidates (correlation between depression and neuroticism: $r = 0.507$; $P < 0.001$).

Adherence with the therapeutic regimen

There were more active smokers among the liver transplant candidates. One heart transplant candidate also admitted to continue smoking, despite the fact that active smoking is a contra-indication for listing on the heart transplant waiting list. Lung and heart transplant candi-

Table 3. Comparison of anxiety and depressive symptomatology among lung, heart, and liver transplant candidates.

Variable	Total sample (n = 186)	Lung (n = 71)	Heart (n = 33)	Liver (n = 82)	P-value	Q-value
Anxiety						
Total score (mean ± SD) severity (%)	7.4 ± 4.7	8.1 ± 4.5	7.9 ± 4.4	6.6 ± 4.9	$P = 0.057$	$Q = 0.13$
Not anxious	55.1	53.5	50	58.6		
Mild	17.8	14.1	18.7	20.7		
Moderate	19.5	23.9	25	13.4		
Severe	7.6	8.5	6.3	7.3		
Depression						
Total score (mean ± SD) severity (%)	7.5 ± 4.4	8.2 ± 4.2	7.6 ± 3.5	6.5 ± 4.8	$P = 0.013$	$Q = 0.05$
Not depressed	51.8	46.6	50	57.3		
Mild	22.2	23.9	21.9	20.7		
Moderate	21.1	23.9	28.1	15.9		
Severe	4.9	5.6	–	6.1		

Regression analysis with age, gender and co-morbidity controlled for in the analyses.

Table 4. Comparison of social support (SSQ) and personality traits (NEO-FFI) among lung, heart and liver transplant candidates.

Variable	Total sample (n = 186)	Lung (n = 71)	Heart (n = 33)	Liver (n = 82)	P-value	Q-value
*SSQ**						
Factor 1 (mean ± SD)	22.0 ± 3.9	22.4 ± 3.4	22.4 ± 3.8	21.6 ± 4.2	$P = 0.045$	$Q = 0.12$
Factor 2 (mean±SD)	14.5 ± 8.2	13.2 ± 7.9	14.3 ± 8	16 ± 8.4	$P = 0.32$	$Q = 0.57$
*NEO-FFI***						
Neuroticism (mean ± SD)	5.5 ± 2.0	6.1 ± 1.9	5.3 ± 2	5.1 ± 2.1	$P = 0.024$	$Q = 0.08$
Extraversion (mean ± SD)	4.9 ± 1.9	4.6 ± 2	5.4 ± 1.8	4.9 ± 1.9	$P = 0.64$	$Q = 0.84$
Openness (mean ± SD)	4.8 ± 1.9	4.9 ± 1.8	4.9 ± 2	4.7 ± 2	$P = 0.82$	$Q = 0.84$
Agreeableness (mean ± SD)	5.3 ± 2.1	5.2 ± 1.9	5.4 ± 1.9	5.3 ± 2.2	$P = 0.79$	$Q = 0.84$
Conscientiousness (mean ± SD)	5.1 ± 2.2	4.9 ± 2.3	5.3 ± 2	5.2 ± 2.2	$P = 0.84$	$Q = 0.84$

Regression analysis, corrected for age, gender and comorbidity.
Factor 1 = general received emotional and practical support; factor 2 = support with medication taking.
NEO-FFI: *Neuroticism* = proneness to psychological distress, excessive carvings or urges; *extraversion* = capacity for joy.
Need for stimulation; *openness to experience* = toleration for and exploration of the unfamiliar; *agreeableness* = one's orientation along a continuum from compassion to antagonism in thoughts, feelings and actions; *Conscientiousness* = degree of organization, persistence and motivation in goal-directed behavior.
*Social Support Questionnaire; **Neo Personality Inventory-Revised short form (NEO-FFI).

Table 5. Comparison of adherence (i.e. nonsmoking, diet, limited or no alcohol use, medication taking and general adherence) among lung, heart and liver transplant candidates.

Variable	Total sample (n = 186)	Lung (n = 71)	Heart (n = 33)	Liver (n = 82)	P-value	Q-value
Self-report						
% Current smoker	10.2	0	3	22	$P = 0.0001$	$Q = 0.0005$
% ≥1 on CAGE*	7.1	1.4	6.1	30.1	$P = 0.0001$	$Q = 0.0005$
% Using alcohol	22	33.3	36.4	6.3	$P = 0.0001$	$Q = 0.0005$
% NA with alcohol		8.7	9.1	5	$P = 0.609$	$Q = 0.84$
Patients following diet (n, %)	88 (47.3)	19 (26.8)	29 (87.9)	40 (48.8)	$P = 0.0001$	$Q = 0.0005$
% NA with diet	47.7	36.8	62.1	42.5	$P = 0.76$	$Q = 0.84$
% NA with medication taking	16.7	15.9	12.1	19.4	$P = 0.25$	$Q = 0.50$
General adherence (mean ± SD)	87.4 ± 13.9	87.3 ± 12.8	82.9 ± 17.6	89.5 ± 12.9	$P = 0.36$	$Q = 0.58$

NA, nonadherence.

Regression analysis corrected for age, gender and co-morbidity.

*Alcohol problems are suspected in patients reporting 'yes' at least once on the CAGE.

dates also used more alcohol compared with the liver transplant candidates (Table 5).

No significant difference in nonadherence with alcohol guidelines could be observed among the three groups, although approximately 10% of heart and lung transplant candidates were drinking above the safe limits. Also, a significant higher proportion of the liver transplant candidates had at least one positive answer on the CAGE. There was a contrast between CAGE scores and the proportion of liver transplant patients admitting alcohol use. Most likely, liver transplant candidates were referring to alcohol problems in the past. Patients with alcoholic cirrhosis significantly more answered yes to the first question of the CAGE (i.e. have you ever felt you should cut down on your drinking) (48.4% in patients with alcoholic cirrhosis versus only 9.3% in patients without alcoholic liver disease, $\chi^2 = 14.42$; $P < 0.001$).

No other differences in adherence behavior could be observed.

Discussion

This is the first study investigating psychosocial and behavioral factors concurrently in heart, liver, and lung transplant candidates. Demographics of the three cohorts were somewhat different. The younger age in lung transplant candidates can be explained by the presence of patients with cystic fibrosis (10%; patients in their 2nd and 3rd decade) and idiopathic pulmonary fibrosis (18%; patients in their 4th decade) in our sample [24]. Lung transplant candidates also have less co-morbidity, which may reflect the use of more stringent selection criteria. The male predominance in heart transplant candidates is well known and explained by the prevalence of ischemic cardiomyopathy as end-stage heart disease [25]. After controlling for these variations in demographic variables and co-morbidity, the three patient cohorts overall had a quite comparable psychosocial and behavioral profile.

Yet, there was a tendency toward more depressive symptoms in lung transplant candidates versus liver transplant candidates, while scores were similar to those observed in heart transplant candidates. Our findings are in contrast with the results of Riether *et al.* [10], who found no significant difference in the prevalence of depressive symptoms between liver and lung transplant candidates. However, these authors used the Beck Depression Inventory [26,27] assessing both the cognitive and somatic symptoms of depression. This makes it difficult to determine whether the somatic symptoms in chronically ill patients are part of the medical or psychiatric disease. The Hospital Anxiety and Depression Inventory, which we used was specifically developed for use in chronic patient populations [15].

It can be hypothesized that lung and heart transplant candidates experience their illness as more debilitating illness and experience more health-related problems compared with patients waiting for a liver transplantation. A life-threatening disease with severe somatic symptoms (e.g. breathing difficulties and limitations in exercise capacity) may challenge the patient's coping strategies, and may lead to depressive symptoms. Compared to the general population and patients with other chronic diseases, Stewart *et al.* [28] indeed showed that patients with heart failure and lung problems experienced the highest negative impact on physical functioning compared to the general populations and patients with other chronic diseases. On the other hand, several liver transplant candidates are suffering from subclinical or clinical chronic hepatic encephalopathy, which may intervene with their normal capacity to appreciate fully their critical situation as they may underestimate their disease condition. Half of the transplant candidates had some degree of depres-

sion, and one out of every four patients was moderately or severely depressed, a prevalence that is three to four times higher compared with that in the general population [29,30]. Yet, these numbers are highly comparable to prevalences found in other chronic disease populations including diabetes, cancer and cardiovascular disease [31].

Secondly, significantly more lung and heart transplant candidates admitted using alcohol than the liver transplant candidates. The fact that liver transplant candidates with alcoholic cirrhosis are explicitly advised to refrain from any alcohol can explain this. We found a prevalence of alcohol use (irrespective of severity) of 33.3% for lung and 36.4% for heart transplant candidates, which is considerably lower than the 82% prevalence of alcohol use reported for the general population [20]. To our knowledge, no data have been published on pretransplant prevalence of alcohol use in nonliver transplant groups. It can be hypothesized that transplant candidates who are experiencing a life threatening condition may be more aware of their fragile health and more motivated to change potentially dangerous health behavior [32].

In the absence of transplant-specific cut-off scores to define nonadherence with alcohol guidelines, we used the cut-off values developed by the World Health Organization to define health risk by alcohol intake [20]. Using these criteria, we observed that 5% of liver transplant candidates admitted nonadherence with complete sobriety. This number is slightly lower compared with the 12.5% relapse found by Isai *et al.* [33] in 66 liver transplant candidates with alcoholic liver disease. Moreover, 8.7% of the lung and 9.1% of the heart transplant candidates were drinking above the safe limits. Limited data exist on severe alcohol use as an etiological factor for cardiomyopathy [34]. To our knowledge, no data exist on severe alcohol use in other groups of nonliver transplant candidates. Regular screening for and quantification of alcohol use should be part of the pretransplant screening of all transplant candidates groups as evidence shows that heavy alcohol use may continue post-transplant and is related to a significant increase in all-cause mortality, organ damage, and psychosocial and social problems [35–38].

Thirdly, 22% of the liver transplant candidates were active smokers. This prevalence is significantly higher than in heart and lung transplant candidates, but comparable to the prevalence of active smokers in the Belgian population (i.e. 24%) [39]. Research on smoking behavior before and after surgery in liver transplant patients is limited, probably because tobacco use is not an etiological factor in the development of end-stage liver disease [40–43]. Yet, patients with an alcohol problem are at risk for poly-substance abuse, such as the use of tobacco and illicit drugs, both known risk factors for poor outcome after transplantation [37,43]. Our data are in line with the 27% active smokers in the study of Pungpapong *et al.* [40], but are higher than the 10% active smoking rate in the study of Ehlers *et al.* [41]. Despite the limited data in liver transplant patients, it is generally agreed that transplant candidates should refrain from smoking both before and after transplantation, because smoking after transplantation in combination with immunosuppressive medication is associated with poor graft function, mortality, cardiovascular disease and malignancy [44–47]. Explicit advice to quit smoking and referral to smoking cessation programs before placement on the waiting list are needed.

Although no difference in adherence with medication taking was observed among the three groups, its overall prevalence of 16.7% warrants further attention. The prevalence of pretransplant medication nonadherence is similar to prevalences found in other studies using self-report in heart failure and dialysis patients [48–50]. The meta-analysis of DiMatteo [51] reported a prevalence of 20.6% across chronic illness populations and measurement methods used. We expected a lower prevalence in our study, as the patients included in this study have end-stage organ disease and thus are severely ill: The World Health Organization report on nonadherence indeed indicated that having more severe symptoms, a higher level of physical disability, having a severe and rapidly progressing disease (such as end-stage organ failure) may be associated with better adherence [52]. It should be investigated further if nonadherent patients will also show higher nonadherence with the post-transplant immunosuppressive regimen and subsequent poor clinical outcome.

Limitations of the study

We did not use healthy subjects or renal transplant candidates as a comparison group. Neither did we include chronically ill subjects matched for disease severity but not included on the waiting list. Studying these populations could throw further light on the psychosocial and behavioral characteristics of transplant candidates.

All information regarding alcohol use and smoking behavior were obtained through self-report. This may have led to underestimation of the real prevalence of smoking and alcohol intake in our sample. One could try to validate these self-report measures against other methods, such as serum liver enzymes and red blood cell mean corpuscular volume. Yet, these methods should be interpreted with caution in patients with end-stage organ disease, as they are not always indicative of severe drinking [53,54]. Also, urine cotinine levels are only useful for detection of active smoking when determined by random checks. People may try to influence their results by smoking less the days before the scheduled appointment. Random checks are not feasible in transplant candidates,

because they only to the hospital come at scheduled appointments. Therefore, although further research on this topic could be useful, we decided not to use more objective measures of medication use, alcohol use or smoking.

However, to increase the likelihood of truthful answers on the self-report questions, we adopted the following strategies. The questions were formulated in a neutral, nonthreatening way. Further, the primary investigator was not a member of the transplant teams. Disclosure to an independent researcher seems to be more accurate than disclosure to clinical staff [55]. Also, it was assured in the informed consent that no individual data would be disclosed to the treatment team and that information conveyed remains confidential with no impact on patient's pretransplant status (i.e. receiving higher priority on the waiting list or removal from the waiting list). Finally, all questionnaires were coded to increase anonymity.

Clinical implications

Our results underscore the importance of including assessments for smoking and drinking patterns in the pretransplant psychosocial and behavioral screening protocol for all transplant candidates. Further, pretransplant candidates should be regularly screened for presence of depression. Adequate psychopharmacological and/or psychotherapeutic treatment should be provided, as evidence from other chronic disease populations shows that even minor symptoms of depression are associated with mortality and morbidity [56,57]. Post-transplant recurrence of untreated depression is also possible [58,59]. For most centers, this means that their screening protocol and content of pretransplant care need a thorough revision.

In addition, this study provides the basis for prospectively investigating the relationship between these pretransplant factors and post-transplant outcome, which is an important step toward the development of a standardized pretransplant evaluation protocol for the psychosocial and behavioral screening process of transplant candidates.

Authorship

FD designed the study, performed the study, analyzed the data, and wrote the paper. JV provided medical data for heart transplant patients, assisted in interpreting the medical data, and participated in study design and revised the manuscript critically. FN provided medical data for liver transplant patients, assisted in interpreting the medical data, and contributed to writing of the manuscript by critically revising its content. LD provided medical data for lung transplant patients, assisted in interpreting the medical data, and contributed to writing of the manuscript by critically revising its content. GV provided medical data for lung transplant patients, assisted in interpreting the medical data, and contributed to writing of the manuscript by critically revising its content. DVH substantial contribution to data collection and interpretation of medical data. Sabina De Geest assisted in designing the study, supervised the statistical analyses, and contributed to writing of the manuscript by critically revising its content.

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