

Psychiatric disorder and quality of life in patients awaiting lung transplantation

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Abstract:

Study objective: To examine the relationship between psychiatric comorbidity and quality of life in patients awaiting lung transplantation. **Setting:** Duke University Medical Center/Lung Transplantation Program. **Participants:** One hundred patients with end-stage pulmonary disease listed for lung transplantation. **Measurements and results:** Twenty-five percent ($n = 25$) of the sample met diagnostic criteria for at least one current mood of anxiety disorder. Controlling for age, gender, ethnicity, percentage of predicted FEV₁, and lung disease diagnosis, patients with a current psychiatric diagnosis reported poorer general quality of life ($p < 0.0001$), poorer disease-specific quality of life ($p < 0.0001$), greater shortness of breath ($p = 0.01$), more symptoms of psychological distress ($p < 0.0001$), lower levels of social support ($p < 0.0001$), and fewer positive health habits ($p < 0.04$) than their counterparts without a psychiatric diagnosis. **Conclusions:** Psychiatric comorbidity affects a significant portion of patients awaiting lung transplantation and is associated with decreased health-related quality of life.

Keywords: anxiety | depression | lung transplantation | psychiatric disorder | quality of life

Article:

Since the first successful human lung transplant operations were performed in the mid 1980s, cadaveric lung allotransplantation has grown into an acceptable therapy for many end-stage pulmonary diseases. Unfortunately, there are many more patients awaiting lung transplantation than there are organs available.¹ Furthermore, short- and long-term outcomes for lung

Abbreviations: DSM IV = Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition; FEV₁% = percentage of predicted FEV₁; GHQ = General Health Questionnaire; INSPIRE = Investigational Study of Psychological Intervention in Recipients of Lung Transplant; MANCOVA = multivariate analysis of covariance; PQLS = Pulmonary-Specific Quality of Life Scale; SF-36 = Short Form-36; SOBQ = UCSD Shortness of Breath Questionnaire

transplantation lag behind those of other solid-organ transplants, with 1-year and 5-year survival rates of 76% and 43%, respectively, for lung transplant recipients.² Given the scarcity of donor lungs and the risk associated with the transplant surgery, careful screening of potential lung transplant candidates is essential to ensure optimal outcomes. This screening process not only involves a comprehensive medical evaluation, but also includes a thorough psychological assessment.

End-stage pulmonary disease is associated with significant psychological distress,³⁻⁵ with up to 47% of lung transplant candidates meeting criteria for at least one psychiatric disorder.⁵ Previous studies have found that psychiatric illness and other psychosocial problems are related to poor posttransplant outcomes, such as more rejection episodes,⁶ increased length of hospitalization,⁷ and higher levels of emotional distress.^{8,9} Although quality of life is considered an important measure of outcome following lung transplantation, little attention has been devoted to the relation between psychiatric illness and quality of life in candidates for this surgery. Because many patients awaiting lung transplantation will not survive long enough to receive a transplant, it is important to examine factors influencing quality of life before as well as after transplant. Therefore, the purpose of the present study was to examine the relationship of psychiatric comorbidity and various measures of quality of life in a relatively large series of patients awaiting lung transplantation.

MATERIALS AND METHODS

Patient Population

Patients who were candidates for lung transplantation at Duke University Medical Center between November 2000 and January 2002 were recruited for this study. Inclusion criteria were as follows: age ≥ 18 years, current placement on the waiting list for an initial single or bilateral lung transplant, and the ability to complete written and telephone assessments (ie, basic English proficiency; lack of significant hearing, speaking, or visual difficulties; and a working telephone number). Participants agreed to enroll in a clinical trial of a telephone-based stress management intervention being conducted at Duke University and Washington University Medical Centers in which they would be randomly assigned to either stress management or usual care. This report presents baseline data from 100 patients who enrolled in this clinical trial at Duke University.

A total of 236 patients were approached to participate in this study. Of these, 98 patients (42%) were ineligible for the following reasons: not listed for lung transplantation ($n = 54$), listed for lung retransplantation ($n = 1$), required multiple-organ transplants ($n = 12$), underwent transplantation before enrolling in the study ($n = 17$), died before enrolling in the study ($n = 8$), difficulty speaking due to damaged vocal cords or shortness of breath ($n = 2$), could not be reached by telephone ($n = 3$), and already participating in a competing protocol ($n = 1$). Of the remaining eligible patients, 38 patients (28%) refused to participate in the study. There were no significant differences with respect to age, gender, time waiting on the transplant list, or disease severity (measured by percentage of predicted FE₁ [FE₁%]) between those who declined to participate and those who participated.

Procedure

Patients were initially contacted either by mail or in person during their pulmonary clinic appointment. After patients provided written informed consent to participate, they were given a battery of psychosocial measures, which they were asked to complete and return by mail. Participants were then administered a psychiatric diagnostic interview over the telephone by a trained clinical psychologist (K.M.). Pulmonary function data were obtained from medical records. The consent form and all study procedures were approved by the institutional review board at Duke University Medical Center.

Psychosocial Measures

Medical Outcomes Survey, Short Form-36: The Medical Outcomes Survey, Short Form-36 (SF-36) is a questionnaire that measures quality of life by assessing eight life domains: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, pain, mental health, vitality, and general health perception.¹⁰ The SF-36 has been used with patients with chronic lung disease.^{11,12} Higher scores indicate better health-related quality of life.

Pulmonary-Specific Quality of Life Scale: The Pulmonary-Specific Quality of Life Scale (PQLS) was developed for use with persons with chronic lung disease.^{13,14} The PQLS has seven subscales: physical functioning, psychological/emotional status, functional status/activities of daily living, social activities, intimacy/relationships/sexuality, occupational functioning, and view of self. Lower scores indicate better functioning.

Beck Depression Inventory II: The Beck Depression Inventory II is a 21-item self-report scale measuring cognitive, affective, and somatic symptoms of depression.¹⁵ A higher score indicates more severe depressive symptoms.

Spielberger State Anxiety Inventory: The Spielberger State Anxiety Inventory consists of 20 items assessing current anxiety level.¹⁶ This scale was originally developed to investigate anxiety in normal populations and has also been used in medical and surgical patients. A higher score indicates greater anxiety.

General Health Questionnaire: The General Health Questionnaire (GHQ) is a 60-item scale developed to screen for nonpsychotic psychiatric disorders by assessing somatic symptoms, symptoms of anxiety, social dysfunction, and depressive symptoms.¹⁷ A higher score indicates greater psychological distress.

Perceived Stress Scale: The Perceived Stress Scale is a 14-item scale that measures perceived stress, which is the extent to which life events are viewed as unpredictable and uncontrollable.¹⁸ A higher score indicates greater stress.

Life Orientation Test-Revised: The Life Orientation Test-Revised is a 10-item scale assessing generalized optimism, broadly defined as the expectation that positive events will occur.¹⁹ A higher score indicates greater optimism.

Perceived Social Support Scale: The Perceived Social Support Scale consists of 12 items assessing perceived social support from family, friends, and significant other.^{20,21} A higher score indicates greater overall perceived support.

UCSD Shortness of Breath Questionnaire: The UCSD Shortness of Breath Questionnaire (SOBQ) is a 24-item scale assessing the degree of shortness of breath experienced while performing various daily activities.²² A higher score indicates greater overall shortness of breath.

Health Practices Index: The Health Practices Index is a 15-item survey assessing a variety of health indicators, including body mass index, cigarette smoking, alcohol use, sleep habits, and physical activity level.²³ A higher score indicates a greater number of positive health habits.

Psychiatric Diagnosis

A modified version of the Structured Clinical Interview for *Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition* (DSM-IV), Axis I Disorders Nonpatient Edition²⁴ was administered to participants by telephone in order to determine the presence of current and past psychiatric diagnoses. Modules A (mood episodes), B/C (psychotic symptom screen), and I (adjustment disorder) were included in their entirety. Also included were the portions of module F (anxiety disorders) assessing panic disorder, social phobia, generalized anxiety disorder, anxiety disorder due to a general medical condition, substance-induced anxiety disorder, and anxiety disorder not otherwise specified. Finally, the section of module J (optional disorders) assessing minor depression also was included. It should be noted that minor depression is not a DSM-IV diagnosis, but is instead considered a research diagnosis for further study. However, patients with minor depression do meet criteria for the DSM-IV diagnosis of depression not otherwise specified. The Axis I Disorders Nonpatient Edition was administered and scored by a clinical psychologist unaware of responses to the quality-of-life test battery and medical measures.

Pulmonary Function

FE₁% was obtained for all but one of the participants. Because patients usually underwent spirometry testing as a routine part of their pulmonary clinic visits, medical charts were reviewed to obtain FE₁% values closest to the date of the psychosocial assessments. The average interval between FE₁% testing and the quality-of-life measures was 56 days (SD, 98 days; range, 0 to 724 days).

Statistical Analysis

To determine whether patients with a current psychiatric diagnosis differed from patients without a current diagnosis with respect to demographic variables, χ^2 tests and independent two-tailed t tests were conducted. To determine whether patients with a current psychiatric diagnosis differed from patients without a current diagnosis with respect to psychosocial measures, multivariate analysis of covariance (MANCOVA) and analysis of covariance models were used. Two MANCOVA models were performed with the subscales of the SF-36 and the subscales of the PQLS as the dependent variables, respectively. Analysis of covariance models were performed

for all other psychosocial measures and for each of the individual subscales of the SF-36 and PQLS. All models included absence/presence of a current psychiatric diagnosis as a between-subjects factor and age, gender, ethnicity, FE₁%, and lung disease diagnosis as covariates. FE₁% was unavailable for one patient, so we imputed this value by substituting the median FE₁% of the other nine patients in our sample with the same lung disease diagnosis, primary pulmonary hypertension. All statistical analyses were performed using SAS 8.2 software (SAS Institute; Cary, NC).

RESULTS

Sample Demographic Characteristics

The sample consisted of 57 women (57%) and 43 men (43%) with a mean age of 48.6 years (SD, 11.7 years). The most common lung diseases were COPD (42%) and fibrotic lung disease (31%). The majority of participants were white (82%), married (67%), and had at least a high school education (87%). Only 12% of the sample were employed full-time. There were no significant differences between patients with at least one current psychiatric diagnosis and those with no current psychiatric diagnosis on any demographic variables (Table 1).

Table 1. Demographic Characteristics of Patients Awaiting Lung Transplantation*

Characteristics	No Current Psychiatric Diagnosis (n = 75)	At Least One Current Psychiatric Diagnosis (n = 25)	Entire Sample (n=100)
Age, yr†	48.4 (12.5)	49.2 (9.1)	48.6 (11.7)
Male gender	32 (42.7)	11 (44)	43 (43)
White race	61 (81.3)	21 (84)	82 (82)
≥ High school education	65 (86.7)	22 (88)	87 (87)
Married	49 (65.3)	18 (72)	67 (67)
Employed full-time	10 (13.3)	2 (8)	12 (12)
6-minute walk in feet†	1,139 (418.3) [n = 71]	1,097 (370.8) [n = 24]	1,129 (405.4) [n = 95]
FEV ₁ %†	32.7 (19.6)	34.5 (18.7)	32.9 (19.6)
Oxygen dependent	64 (85.3)	22 (88)	86 (86)
Lung disease diagnosis			
COPD	33 (44)	9 (36)	42 (42)
Cystic fibrosis	11 (14.7)	5 (20)	16 (16)
Fibrotic disease	21 (28)	10 (40)	31 (31)
Other	10 (13.3)	1 (4)	11 (11)

*Data are presented as No. (%) unless otherwise indicated.

†Mean (SD).

Prevalence of Psychiatric Disorders

Among our sample of patients awaiting lung transplantation, 25% (n = 25) had a diagnosis of at least one current mood or anxiety disorder. Of these, 28% (7 of 25 patients) had two current psychiatric disorders. Panic disorder and anxiety disorder not otherwise specified were the most common current diagnoses, identified in 7% and 6% of the sample, respectively. The prevalence of a past psychiatric disorder was 18%, with a history of major depression being the most common, identified in 15% of the patients. Among patients with a current psychiatric diagnosis, 24% reported treatment with antidepressant medication, 8% reported treatment with anxiolytic medication, 32% reported treatment with both antidepressant and anxiolytic medications, 8%

reported combination treatment consisting of psychotropic medication plus counseling, and 36% reported no current mental health treatment. Table 2 presents the prevalence of all psychiatric disorders identified in our sample.

Table 2. Prevalence of Mood and Anxiety Disorders in Patients Awaiting Lung Transplantation*

Disorders	Current	Past
Mood		
Major depression, single episode	1	11
Major depression, recurrent	4	4
Dysthymic disorder	1	0
Mood disorder due to general medical condition	1	0
Depression NOS (minor depression)	5	0
Anxiety		
Panic disorder	7	1
Generalized anxiety disorder	3	0
Social phobia	3	1
Adjustment disorder with anxiety	1	0
Anxiety disorder NOS	6	1

*Data are presented as %. NOS = not otherwise specified.

Table 3. Health-Related Quality of Life in Patients Awaiting Lung Transplantation*

Quality-of-Life Measure	No Current Psychiatric	At Least One Current	Entire Sample (n = 100)
	Diagnosis (n = 75)	Psychiatric Diagnosis (n = 25)	
SF-36 scales			
Physical functioning	31.8 (23.7)	23.9 (22.2)	29.8 (23.5)
Physical role limitations	36.3 (40.7)	9.0 (22.7)‡	29.5 (38.8)
Pain	70.2 (23.2)	56.8 (26.6)†	66.9 (24.6)
General health	27.7 (19.7)	27.3 (15.9)	27.6 (18.7)
Vitality	42.3 (22.3)	31.2 (19.0)†	39.5 (22.0)
Social functioning	50.0 (18.7)	49.0 (23.9)	49.8 (20.0)
Emotional role limitations	87.1 (26.2)	44.0 (35.6)‡	76.3 (34.3)
Mental health	81.8 (12.2)	61.9 (14.0)‡	76.8 (15.3)
PQLS scales			
Physical functioning	4.1 (1.0)	4.5 (0.7)†	4.2 (0.9)
Psychological status	2.0 (0.7)	3.1 (0.7)‡	2.3 (0.9)
Activities of daily living	2.3 (0.9)	2.9 (1.2)†	2.4 (1.0)
Social activities	3.5 (0.9)	3.8 (0.9)	3.6 (0.9)
Relationships	3.0 (0.7)	2.9 (0.8)	3.0 (0.7)
Occupational functioning	4.1 (1.2)	4.5 (0.9)	4.2 (1.2)
View of self	2.7 (1.1)	3.4 (1.0)‡	2.9 (1.1)
Total	21.7 (4.3)	25.1 (3.5)‡	22.6 (4.3)
SOBQ	61.2 (22.5)	72.0 (23.3)†	63.9 (23.1)

*Data are presented as group mean (SD). On the SF-36 higher numbers indicate better functioning, whereas on the PQLS and SOBQ lower numbers indicate better functioning.

†p < 0.05, patients with vs patients without current psychiatric diagnosis.

‡p < 0.01, patients with vs patients without current psychiatric diagnosis.

Health-Related Quality of Life

SF-36: A MANCOVA performed on the set of SF-36 subscales revealed a significant group effect ($p < 0.0001$), indicating that, controlling for age, gender, ethnicity, FEV₁%, and lung disease diagnosis, there were differences in quality of life between patients with at least one current psychiatric diagnosis and those without a diagnosis. Examination of univariate analyses

indicated that compared to patients without a comorbid psychiatric diagnosis, patients with a psychiatric diagnosis had greater physical role limitations ($p = 0.002$), physical pain ($p = 0.01$), and emotional role limitations ($p < 0.0001$), along with less vitality ($p = 0.02$), poorer mental health ($p < 0.0001$) and a tendency toward poorer physical functioning ($p = 0.09$) [Table 3].

PQLS: There was a significant multivariate group effect for the set of PQLS subscales ($p < 0.0001$). Results of univariate analyses revealed that as compared to patients who did not have a current psychiatric diagnoses, patients with a psychiatric diagnosis reported poorer physical functioning ($p = 0.04$) and psychological status ($p < 0.0001$), decreased ability to perform activities of daily living ($p = 0.01$), a more negative view of the self ($p = 0.007$), and a tendency toward poorer occupational functioning ($p = 0.08$) [Table 3].

Shortness of Breath: Patients with a current psychiatric diagnosis reported greater shortness of breath ($p = 0.01$) than patients without a psychiatric diagnosis.

Psychosocial Measures

After controlling for age, gender, ethnicity, FEV₁%, and lung disease, patients with at least one current psychiatric diagnosis were found to report greater depressive symptoms ($p < 0.0001$), greater anxiety symptoms ($p < 0.0001$), more psychological distress as assessed by the GHQ ($p < 0.0001$), and higher levels of stress ($p < 0.0001$) than patients without a current psychiatric diagnosis. Patients with a psychiatric diagnosis also reported lower levels of optimism ($p = 0.004$), fewer positive health habits ($p = 0.04$), and less perceived social support ($p < 0.0001$) than their counterparts without a current psychiatric diagnosis (Table 4).

Table 4. Psychosocial Measures in Patients Awaiting Lung Transplantation*

Psychosocial Measures	At Least One Current		
	No Current Psychiatric Diagnosis (n = 75)	Psychiatric Diagnosis (n = 25)	Entire Sample (n = 100)
Beck Depression Inventory II	8.5 (6.0)	15.6 (5.5)‡	10.3 (6.6)
Anxiety (Spielberger State Anxiety Inventory)	33.4 (9.9)	42.8 (8.7)‡	35.8 (10.4)
Psychological distress (GHQ)	41.9 (18.0)	63.3 (20.3)‡	47.3 (20.7)
Perceived stress	17.2 (7.2)	26.7 (5.9)‡	19.6 (8.0)
Optimism (Life Orientation Test-Revised)	16.9 (3.9)	14.4 (4.1)‡	16.2 (4.1)
Social support	77.0 (7.3)	67.7 (11.0)‡	74.7 (9.2)
Health Practices Index	3.2 (0.9)	2.9 (1.1)†	3.1 (1.0)

*Data are presented as group mean (SD).

† $p < 0.05$, patients with vs patients without current psychiatric diagnosis.

‡ $p < 0.01$, patients with vs patients without current psychiatric diagnosis.

DISCUSSION

In the present study, one fourth of patients with end-stage pulmonary disease awaiting lung transplantation met diagnostic criteria for a current mood or anxiety disorder. Psychiatric comorbidity in these patients was associated with significantly decreased quality of life across a number of domains. Specifically, lung transplant candidates with a psychiatric diagnosis reported poorer physical functioning, more shortness of breath, fewer positive health habits, less social support, more stress, and more symptoms of depression and anxiety than their counterparts with no current psychiatric disorder. Because persons with chronic lung disease exhibit decreased

quality of life in comparison to healthy persons,²⁵ our results indicate an additional burden of impaired quality of life associated with comorbid psychiatric disorder. This effect on quality of life occurred independent of age, gender, ethnicity, and even severity and type of lung disease. One implication of these findings is that identifying and treating psychiatric disorder in patients awaiting lung transplantation may improve their overall quality of life. In our study, 36% of the patients with a current psychiatric diagnosis were receiving no treatment, suggesting that mental disorders are generally underidentified and undertreated in this population. Indeed, inadequate mental health treatment may partially explain our finding of poorer quality of life in patients with current psychiatric disorders. Unfortunately, we were unable to compare quality of life between patients with treated psychiatric disorder and patients with untreated psychiatric disorder because of limited statistical power due to small sample size. Additional studies are needed to determine the optimal treatment of psychiatric disorders in these medically ill patients and to determine the degree of impact mental health treatment might have on quality of life.

Our finding that mood and anxiety disorder, particularly panic disorder, is common among patients with end-stage lung disease is consistent with previous studies.³⁻⁵ Because patients with major nonpulmonary medical conditions and severe psychosocial dysfunction are excluded from listing for lung transplantation, our rate of 25% psychiatric comorbidity is likely to underestimate the true rate of psychiatric disturbance in a broader sample of end-stage pulmonary patients. Our results suggest that even when patients undergo extensive screening and self-selection for lung transplantation, psychiatric comorbidity is significant. The occurrence of frequent episodes of dyspnea and hyperventilation, symptoms of lung disease as well as triggers of anxiety, may explain why individuals with pulmonary disease are particularly susceptible to panic and anxiety.²⁶ However, another possible explanation for findings of a high rate of anxiety disorders in patients with pulmonary diseases is an increased false-positive rate for the diagnosis of panic and anxiety disorders due to symptom overlap with lung disease.

Patients with end-stage pulmonary disease who also are awaiting lung transplantation experience unique stressors, including separation from their support system due to relocation, a progressing course of illness, and fear of not receiving donor lungs in time,²⁷ that make the waiting period a time of especially high risk for psychological distress. For example, Craven³ found that 21% of patients acquired psychiatric symptoms while on the waiting list for lung transplant, highlighting the importance of continuing mental health follow-up of these patients after the initial evaluation. Similarly, in our previous work, we have shown that patients awaiting lung transplant tend to show declines in social support and other indexes of quality of life with increasing time on the waiting list.¹⁴ However, in the same study, improvement in quality of life, including better physical functioning, was reported in patients who received a psychosocial intervention, despite the fact that these patients did not necessarily have any psychiatric diagnosis. Therefore, we might expect even greater improvement in quality of life upon treatment of psychiatric disorder in lung transplant candidates. However, it should be noted that even in the current sample, greater psychological distress (as measured by the GHQ) was associated with decreased pulmonary-specific quality of life and greater shortness of breath independent of the presence of a current psychiatric diagnosis (data not shown). This suggests that psychosocial interventions should be considered even for those pulmonary patients who do not meet criteria for a psychiatric diagnosis.

Psychiatric disorder in patients awaiting transplant may be linked to adverse health outcomes as well as reduced quality of life. For example, one study²⁸ identified quality of well-being, a measure of physical and social functioning, as the strongest predictor of survival in lung transplant candidates. Notably, we found that patients with a comorbid psychiatric condition reported more dyspnea, which has been shown to be a better predictor of survival than FEV₁ in patients with chronic lung disease.²⁹ Our study also demonstrated that patients with a current mood or anxiety disorder practiced fewer health-promoting habits, suggesting that psychological disturbance could lead to poorer health outcomes by influencing compliance, especially in light of other studies^{6,30} demonstrating that psychosocial issues are related to poor medical compliance.

There are several methodologic issues that deserve comment. First, because we only studied patients on the waiting list for lung transplantation, our sample may not be representative of all patients with end-stage lung disease, as pulmonary patients with especially severe and intractable psychiatric or social problems would not have been listed for transplant. Also, it should be noted that the association of psychiatric disorder with poor quality of life does not imply a causal relationship. Although it is possible that a psychiatric disorder may result in decreased quality of life, indexes of poor quality of life (such as marked functional impairment and high levels of pain) could increase the risk of psychiatric illness. It is unclear whether the patients in our study who met criteria for a current psychiatric disorder were more physically ill than their counterparts without psychiatric disturbance. The patients with psychiatric disorders did report greater shortness of breath and reduced physical functioning; however, their mean FEV₁% was not statistically different from that of patients without current psychiatric disorder. A prospective study design would be needed to determine if more severe physical illness plays a causal role in poorer psychiatric and quality-of-life outcomes in patients awaiting lung transplant. Finally, although we suggest that the presence of psychiatric disorder may be associated with adverse medical outcomes and effective treatment of psychiatric disorder may be associated with improvements of physical health, long-term follow-up data are needed. The INSPIRE (Investigational Study of Psychological Intervention in Recipients of Lung Transplant) trial hopes to provide these data in the future.

In summary, we found that the presence of current mood or anxiety disorder was related to significantly decreased quality of life in patients with end stage pulmonary disease awaiting lung transplantation. Our results suggest that identifying and treating psychiatric disorder in this population could result in improved psychosocial and medical outcomes for these patients.

APPENDIX

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