



## Psychiatric disorders and psychological distress in patients undergoing evaluation for lung transplantation: a national cohort study



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### ABSTRACT

**Objective:** We sought to investigate type and prevalence of psychiatric disorders and psychological distress in patients being evaluated for lung transplantation.

**Methods:** One hundred eighteen patients were assessed [74% with chronic obstructive pulmonary disease (COPD)] with the MINI Neuropsychiatric Interview, the General Health Questionnaire (GHQ), and Hospital Anxiety Depression Scale (HADS). Spirometry and the 6-min walk test (6MWT) assessed lung function with data subject to multivariate regression analyses.

**Results:** Current and lifetime prevalence for mental disorders were 41.5% and 61.0% respectively, with anxiety (39.8% of patients), mood disorders (11.8%), and subsyndromal disorders (8.7%) identified. 15% of patients reported feelings of panic during the last week, 9% reported hopelessness, and 3% felt that life was not worth living. Statistically significant correlates were derived for HADS-depression with lung function ( $P=.0012$ ) and 6MWT ( $P=.030$ ) for the entire group ( $P=.012$ ), and with lung function ( $P=.030$ ) for COPD patients ( $P=.045$ ), for whom higher chronic GHQ-scores correlated with poorer lung function ( $P=.009$ ). In multivariate regression analysis, history of mental disorder was strongest predictor of current distress.

**Conclusions:** Our findings underline the importance of assessing past, current, and sub-syndromal psychiatric disorders in addition to levels of distress in transplant candidates, with prospective studies needed to investigate impact on long-term outcome after transplantation.

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### 1. Introduction

Lung transplantation (LTX) is an established treatment, worldwide, for patients with end-stage lung disease with a life expectancy of <1–2 years [1]. Most LTX candidates suffer from chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF) and other parenchymal diseases, pulmonary hypertension or cystic fibrosis. These lung diseases differ in their pattern of development and course. For example, COPD patients slowly develop hyper-inflated lungs while patients with conditions such as IPF will develop fibrotic lung tissue within a few years. Patients suffering from other lung diseases (e.g., pulmonary

hypertension) may suffer dyspnea, which is relatively difficult to verify by routine investigation (e.g., spirometry/chest X-ray) and can therefore go undiagnosed, and untreated, for years. Smoking is the main cause of COPD, with genetic and environmental factors playing a more important role in the etiology of other lung diseases.

COPD patients suffer from increased levels of anxiety and depression [2–5], including suicidal tendencies [6,7]. Anxiety and depression are associated with inflammation [8,9], increased sympathetic tonus and dyspnea [10], and an increased frequency of aggravated disease [11]. In addition, anxiety and depression can increase the duration of hospital stays [12], and their associated costs [13]. Anxiety and depression can also increase the fear of exercise [14] which promotes functional impairment [15] and a deterioration in the quality of life [16,17], all of which increases the burden on the rest of the family [3,18]. Additionally, depression can reduce treatment compliance [19], with psychological

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distress known to be associated with increased long-term mortality in COPD patients [20,21].

Despite the severity of these associations, research on the topic of psychiatric disorders or distress in patients evaluated for LTX has been extremely limited. Thus far, only a few studies have been published, with these tending to focus on limited aspects of psychiatric morbidity [22], psychological distress [23], and quality of life [24]. There exists no single study that has addressed the full spectrum of mental health including an examination of diagnosable psychiatric disorders as well as psychological distress at a sub-syndromal level. From a clinical standpoint, both types of patients should be identified in order to provide appropriate intervention. Furthermore, some patients with chronic impaired lung function report feelings of panic, hopelessness, and suicidal ideation [7], suggesting that these should be included as assessable criteria for patients being evaluated for LTX.

### 1.1. Aims of the study

The primary aim of this study was to describe the prevalence of psychiatric disorders and levels of psychological distress in patients evaluated for LTX. Secondly, we wanted to study the prevalence of panic attacks, feelings of hopelessness, and suicidal ideation. Finally, we aimed to investigate the association between psychological distress, lung disease, and functional status.

## 2. Patients and methods

### 2.1. Subjects

Oslo University Hospital (OUH) is the only hospital in Norway (population about 5 million) currently performing organ transplantation. In Norway, taxation funds the costs related to the medical treatment of its citizens, including organ transplantation. I.e. economic status of the patient or having private insurance does not influence the possibility of receiving LTX if medically indicated. Specialists in lung medicine throughout the country refer possible candidates for LTX to OUH. Prior to referral, the referral physicians screen all patients for LTX eligibility as outlined in international guidelines [25]. Patients with substance abuse or dependence (e.g., alcohol, marijuana, or other illicit substances) or patients who have not quit smoking for at least 6 months are not referred to OUH. A history of mental disorders, including psychotic disorders, is not a contraindication for referral for possible LTX per se, but initiation of psychiatric treatment is required before referral. The number of patients evaluated by local specialists in pulmonary medicine with regard to possible LTX, but not referred to OUH, is unknown.

When admitted to the LTX unit at OUH, the patients underwent a comprehensive medical evaluation. We do not have information about the exact number of patients who were rejected for LTX based on the medical examination only. However, it is only a few patients. The local pulmonologists screen out almost all patients with medical contraindication for LTX prior to referral to OUH.

During the period 2006–2010, a complete psychiatric and psychometric assessment was routinely included as part of the assessment of adult patients with acquired lung disease ( $\geq 18$  years of age;  $n=121$ ) that passed the medical examination at the LTX unit. However, three patients were excluded from our study: Two failed to be interviewed due to logistic issues, while the psychiatric and psychometric records were lost for a third patient. The total cohort ( $N=118$ ) were categorized according to disease into three groups; COPD ( $n=87$ ), IPF ( $n=17$ ), and other lung diseases ( $n=14$ ), with the latter group including bronchiectasis ( $n=2$ ), lymphangioleiomyomatosis ( $n=2$ ), pulmonary hypertension ( $n=5$ ), sarcoidosis ( $n=3$ ), systemic sclerosis ( $n=1$ ), and obliterative bronchiolitis ( $n=1$ ). No patients were rejected based on the psychiatric evaluation only.

Of the 121 patients put on the waiting list after medical and psychiatric evaluation, 11 patients were not transplanted. Three patients died when on the waiting list and eight were removed from the waiting list due to severe worsening of their medical condition prohibiting LTX. None were removed from the waiting list for LTX for psychiatric reasons.

### 2.2. Psychiatric and psychometric assessments

The presence of any mental disorder was assessed using the *DSM-IV* version of the MINI neuropsychiatric interview (MINI), with additional modules from MINI-plus (melancholia, simple phobia, somatoform disorders [26]). Clinical psychologists and psychiatrists with at least 10 years' experience in consultation-liaison psychiatry, and who were trained in the use of MINI, conducted the interviews. The MINI is frequently used in psychiatric research and clinical psychiatry [26,27] including the study of psychopathology in patients with lung disease [28]. We measured psychological distress using the 30-item General Health Questionnaire (GHQ-30), and Hospital Anxiety and Depression Scale (HADS).

The 30-item General Health Questionnaire (GHQ-30) measures distress during the preceding two weeks [29]. Because the GHQ-30 does not include questions about somatic symptoms when addressing psychological distress, this measure is particularly useful for assessing psychological distress in patients with somatic disease. Each item is rated on a scale of 0–3, with 3 indicating the greatest distress. The sum of these scores (Likert score) is an overall measure of distress. Five subscores can also be calculated. In the present study, Cronbach's alpha, a measure of internal consistency, was found to be good for both the total GHQ Likert scores ( $\alpha=0.89$ ), and four of the GHQ-subcales; anxiety ( $\alpha=0.86$ ), depression ( $\alpha=0.77$ ), well-being ( $\alpha=0.69$ ), and social dysfunction ( $\alpha=0.71$ ). Cronbach's alpha  $\geq 0.60$  is commonly applied as cutoff for acceptable internal reliability [30]. Thus, the coping subscale ( $\alpha=0.53$ ) was excluded from this report.

We used two additional scoring methods for the GHQ-30 in the present study. First, a "case-score" can be generated to indicate whether a respondent has clinically significant distress (i.e., endorses 6 or more items at a level of 2 or higher). In the present study, if an individual had clinically significant distress (GHQ case score  $\geq 6$ ), but not fulfilling all criteria required for a mental disorder according to the *DSM-IV*, we considered them to have subsyndromal mental disorder.

Some authors advocate the use of a "chronic score (cGHQ)" to measure significant distress in patients with chronic disorders [31]. The cGHQ recognizes that a response of "not more than usual" to 15 negatively formulated questions (e.g., "felt that life is entirely hopeless") may in fact reflect chronic and significant clinical distress. In contrast, a response of "the same as usual" in the formulated questions (e.g., "been able to concentrate on whatever you're doing") does not signify significant distress. The cGHQ has, in some studies, been found to be superior to the conventional scoring method in yielding a wider range of scores and a more normal distribution, and may correlate more authentically with validated measures of non-psychotic psychiatric disorders [31].

The Hospital Anxiety Depression Scale (HADS) assesses symptoms of anxiety (e.g. internal psychological tension, restlessness, and concern) and depression (with an emphasis on anhedonia, such as the inability to experience pleasure from activities usually found enjoyable) during the past week [32]. The total score ranges from 0–21 for each subscale, with a higher score indicating greater distress. Cronbach's alpha for anxiety and depression subscales were 0.85 and 0.62 respectively. Scores  $\geq 8$  are most commonly used to indicate clinically significant distress, with a sensitivity and specificity of about 0.8 [5,33].

Patients may experience panic attacks without fulfilling the diagnostic criteria for panic disorder. Thus, we also counted affirmative statements to the HAD-A question "getting sudden feelings of panic", independently of positive answers to the MINI screen anxiety module. Prevalence for the following; "life is entirely hopeless", "isn't worth

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