Review Article

The Effect of Pretransplant Depression and Anxiety on Survival Following Lung Transplant: A Meta-analysis

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Background: *Current lung transplant allocation guidelines recommend considering psychological function when assessing candidacy despite limited data on whether patients with conditions, such as anxiety and depression, have reduced benefit from transplant because of decreased survival after transplant.* **Objective:** *The aim of this article was to determine whether pretransplant depression and anxiety are associated with worse posttransplant survival.* **Methods:** *We searched Medline, Journal Storage, and Embase for original articles that assessed the effect of pretransplant depression and anxiety on survival following lung transplant published up to November 2015. We calculated a summary estimate of hazard ratios for death using a random effects model.* **Results:** *In total, 6 prospective longitudinal cohort studies were included in the meta-analysis, 4 of which used continuous scores on validated instruments to measure anxiety and depression. There were 711 patients of whom 345 (48.5%) died during the available follow-up time (mean = 7.8 years). Pretransplant anxiety and depression were not associated with posttransplant survival (hazard ratio = 1.009; 95% CI: 0.998–1.019). Heterogeneity was not detected ($I^2 = 0.00\%$, Q = 5.87, $p = 0.66$) and the results did not differ whether anxiety or depression was treated as the exposure of interest.* **Conclusions:** *There is sufficient evidence to conclude that scores on indices of depression and anxiety pretransplant are not associated with worse survival following lung transplant.*

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INTRODUCTION

Compared with other solid organ transplants, patients with lung transplant have higher rates of rejection and lower rates of survival at 1 and 5 years following transplant.[1] There have been ongoing efforts to identify pretransplant factors associated with decreased posttransplant survival, particularly those that may be amenable to clinical intervention. An area of focus has been pretransplant psychiatric disorders, particularly depression and anxiety.[2,3] Because patients with end-stage lung disease are more likely to have depression and anxiety, these disorders are more prevalent in the pretransplant population. In addition, several large cohort studies have suggested that comorbid psychiatric conditions are linked with decreased survival among patients with severe lung

disease, raising the possibility that this association may persist even after lung transplant.[4–6]

Drawing from this literature, some authors have considered whether pretransplant depression and anxiety may be associated with poor posttransplant outcomes.[7–9] Proposed mechanisms have included decreased rates of medication compliance or reduced motivation or engagement in essential posttransplant monitoring or clinic visits.[10,11] Studies from the heart transplant literature have suggested that pretransplant depression, in particular, may be associated with poor outcomes, including long-term mortality.[12,13]

Several single-center studies have examined the relationship among pretransplant anxiety and depression and survival following lung transplant.[14–17] Most have not identified either condition as associated with increased mortality, although a small study suggested that patients with depression or anxiety, when considered as a single group, may have increased survival at 1 year.[18] Overall, these studies have individually enrolled a relatively small number of patients raising the possibility that each is underpowered to detect differences in survival, especially given variability in time of follow-up. In this setting, a meta-analysis is indicated to identify true effect sizes through aggregation and comparison.

The objective of this meta-analysis is to review the current literature to assess the effect of pretransplant anxiety and depression on posttransplant survival.

METHODS

Information Sources

We searched Medical Literature Analysis and Retrieval System Online, Journal Storage, Social Sciences Citation Index, and Embase for English language studies between 1983 and 2015. We used the following key words in multiple combinations: lung transplant, lung transplantation, anxiety, depression, major depression, general anxiety, panic disorder, psychiatric disorders, diagnostic and statistics manual, Beck Depression Index (BDI), State Trait Anxiety Inventory (STAI), death, survival, and mortality. We reviewed the reference section of included articles to identify additional studies not found in our initial search. The last literature search was performed on November 1, 2015.

Selection of Publications

In total, 2 authors (AC and SS) performed the eligibility assessment in an unblinded manner and any disagreements were resolved by consensus among all authors. We initially screened studies using title and abstract and then reviewed full articles to assess for eligibility for inclusion. All studies that evaluated depression or anxiety and posttransplant survival were included in the qualitative synthesis. For the final meta-analysis, however, we selected only studies of patients with lung transplant that reported posttransplant mortality rates for patients with pretransplant depression and anxiety compared with patients without depression and anxiety.

Data Collection Process

We developed a data extraction sheet, which we further refined after the initial search. A total of 2 authors (AC and SS) independently entered the data that was included in the meta-analysis. All authors discussed any disagreements. We extracted the following data from each study: study type, method of diagnosing depression or anxiety, whether depression or anxiety was measured as a continuous or categorical variable, sample size, length of follow-up, and whether and which covariates were included in the survival analysis. We used the Newcastle-Ottawa Score to rank the study quality.[19] The Newcastle-Ottawa Score is a validated instrument for scoring the quality of nonrandomized studies, including case-control and cohort studies. Higher Newcastle-Ottawa Score scores (range: 0–9) indicate higher quality. Finally, we cross-referenced author names and institutions to ensure that each data set was used in only one of the included studies.

Statistical Analysis

The primary measure of effect was hazard ratios (HR) and 95% CI. We combined individual statistics using a random effects model, assessing for heterogeneity using a Q statistic and an I^2. Measures of HR were reported as point estimates with 95% CI. We anticipated heterogeneity in the study results and prespecified 2 hypotheses in this regard: that studies would differ by whether depression or anxiety was the exposure of interest and by whether depression and anxiety were treated as continuous or categorical variables. We assessed publication bias with a funnel