CHEST

Original Research

TRANSPLANTATION

Impact of Lung Transplantation on Recipient Quality of Life

A Serial, Prospective, Multicenter Analysis Through the First Posttransplant Year

C. Ashley Finlen Copeland, MSW; David M. Vock, PhD; Karen Pieper, MS; Daniel B. Mark, MD, MPH; and Scott M. Palmer, MD, MHS, FCCP

Background: **Quality of life (QOL) is an important but understudied outcome after lung transplantation. Previous cross-sectional, single-center studies suggest improved QOL, but few prior longitudinal multicenter data exist regarding the effect of transplantation on the patient's QOL.**
Methods: **We hypothesized that lung transplantation confers a 1-year QOL benefit in both physical and psychologic well-being; we further hypothesized that the magnitude of benefit would vary by sex, native disease, age, or type of transplant operation. To test these hypotheses, we conducted a secondary analysis using QOL data prospectively and serially measured with the Medical Outcomes Study 36-Item Short-Form Health Survey, version 2 (SF-36) in a multicenter cytomegalovirus prevention clinical trial. Linear mixed-effects models were used to assess the impact of transplantation on the recipient's QOL.**
Results: **Over the first year after lung transplantation, the SF-36 Physical Component Score significantly increased an average of 10.9 points from baseline levels ($P < .0001$). A positive benefit was observed for all native diseases; however, the magnitude varied slightly by native disease ($P = .04$) but not by sex ($P = .35$), age ($P = .06$), or transplant type ($P = .30$). In contrast, the SF-36 Mental Component Score did not change from baseline ($P = .36$) and remained well below population norms.**
Conclusions: **Our results demonstrate that lung transplantation confers clinically important QOL benefits in physical domains but not in psychologic well-being. A better understanding of the barriers to psychologic well-being after transplant is critical to enhancing the benefits of lung transplantation.** ***CHEST 2013; 143(3):744–750***

Abbreviations: CF = cystic fibrosis; CMV = cytomegalovirus; IPF = idiopathic pulmonary fibrosis; MCS = Mental Component Summary; PCS = Physical Component Summary; QOL = quality of life; SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey, version 2

Advanced lung disease severely impairs the quality of life (QOL) and survival of millions of individuals and lacks highly effective medical therapies. Lung transplantation has emerged as a viable treatment option for select patients with end-stage lung disease, providing 1- and 3-year survival rates of 79% and 64%, respectively.[1] In fact, lung transplantation represents the only commonly transplanted solid organ with a steady rise in international volume in recent years, with 3,272 patients undergoing lung transplantation in 2009. Although lung transplant appears to provide a short-term survival benefit for most patients regardless

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Affiliations: From the Department of Medicine (Ms Finlen Copeland and Dr Palmer), Duke University Medical Center, Durham; the Duke Clinical Research Institute (Ms Pieper and Drs Mark and Palmer), Durham; and North Carolina State University (Dr Vock), Raleigh, NC.
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Correspondence to: C. Ashley Finlen Copeland, MSW, Duke University Medical Center, Box 103002, Durham, NC 27710; e-mail: Ashley.finlen.copeland@duke.edu

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of native disease,[2,3] its application remains controversial, in part, because of the intensive use of healthcare resources, high cost, poor long-term survival, and relative uncertainty regarding QOL benefits.

Measurement of QOL after lung transplantation has gained attention as a viable way to evaluate treatment effectiveness from a patient-centered perspective. Previous studies that have considered the impact of lung transplantation on QOL generally report enhanced QOL after transplant. However, many methodologic issues, including the use of small, single-center cohorts, analysis of patients transplanted in older eras, cross-sectional study designs, survivor bias, and lack of serial measurements,[4-16] limit the reliability and generalizability of these findings. Similar challenges confound the few studies that have examined QOL longitudinally after lung transplantation.[17-22] Therefore, despite the important observations made in previous studies, additional multicenter, prospective efforts are needed to assess the true impact of lung transplantation on an individual's physical, social, and emotional functioning.

In this study, we conducted a secondary analysis using QOL data prospectively and serially collected in a multicenter cytomegalovirus (CMV) prevention clinical trial.[23] We hypothesized that transplant confers 1-year physical and mental health QOL benefits and sought to determine whether these benefits vary by sex, native disease, age, or type of transplant operation.

Material and Methods

QOL Study Cohort

The study cohort consisted of 131 adult, first lung recipients who participated in a multicenter, prospective, randomized, placebo-controlled CMV prevention trial from July 2003 to January 2007. The clinical trial consisted of 136 patients who were randomized at the time of transplantation to either 12 or 3 months of valganciclovir prophylaxis (hereafter referred to as treatment group assignment) and followed for 1 year after lung transplant to monitor time to CMV disease or infection. Serial measurement of QOL was a prespecified secondary outcome. Trial design and enrollment criteria have been published elsewhere.[23]

Inclusion in the QOL analysis required patients to have completed one or more QOL measures post lung transplant. Five randomized patients did not complete any QOL measures after lung transplantation and, therefore, were excluded (Fig 1 depicts the study cohort). All sites obtained institutional review board approval (Duke Coordinating IRB Protocol number: Pro00016880), and patients provided written informed consent.

Measurement of Health-Related QOL

QOL was assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey, version 2[24] (SF-36) (e-Appendix 1), a generic measure of health-related QOL composed of eight subscales and two summary scores: physical functioning, role-physical, general health, bodily pain, role-emotional, social-functioning, vitality, mental health, Physical Component Summary (PCS), and Mental Component Summary (MCS). The summary scores aggregate the eight subscales, capturing approximately 80% of reliable variance measured by them,[25] and are calculated with norm-based scoring, which estimates scores in standard units relative to the US population mean of 50 and SD of 10.[26] A four-point change in PCS or MCS scores constitutes a minimal clinically important difference.[27]

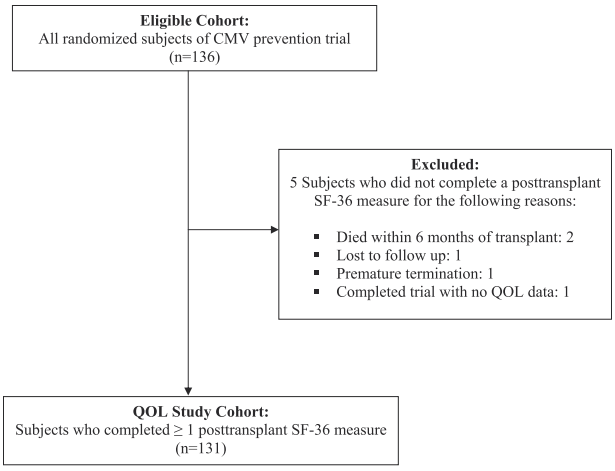

Figure 1. CMV prevention trial participants included in the QOL study cohort. CMV = cytomegalovirus; QOL = quality of life; SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey, version 2.

Randomized patients completed the SF-36 immediately prior to and at 3, 6, 9, and 12 months after lung transplantation. e-Table 1 outlines the patients remaining in the study and corresponding number of completed SF-36 measures at each time point. Because some patients were enrolled in the study after transplantation, missing QOL data are most common at baseline prior to transplantation. Reasons for premature termination, the most common being CMV infection or disease and physician discretion, are listed in e-Table 2.

Statistical Analysis

QOL was analyzed using the MCS and PCS scores measured at baseline and serially over the first posttransplant year. Because of the nature of the clinical trial, missing QOL data exist at various time points for individual patients. We, therefore, used a linear mixed model, a statistical approach appropriate for repeated measures and robust to handling missing data in longitudinal studies. Reliable estimates are produced because the model incorporates all QOL data available at any time point posttransplant, including QOL data obtained on patients who died or prematurely terminated the study.[28,29] This prevents having to limit the analysis to patients who completed a QOL measure at baseline and every subsequent time point. All models included terms for posttransplant indicator and linear time trend, to assess the impact of lung transplant on posttransplant MCS and PCS scores and determine if the trajectory changed over the course of posttransplant year one, and a random-subject effect, to account for within-subject correlation among all 131 study patients.

Separate models were used to assess the association of sex, indication for transplant, age, or transplant type on baseline and posttransplant QOL. In addition to the terms described previously, each included the covariate of interest and an interaction between the independent variable of interest and a posttransplant indicator term. We constructed a multivariable model to examine whether