Quality of Well-being Predicts Survival in Lung Transplantation Candidates

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Predictors of survival were evaluated among 74 patients selected for a lung transplantation program. Each patient received the quality of well-being scale, a utility-based outcome measure that gives a score on a continuum ranging from 0 (for dead) to 1.0 (for optimum function), and a measure of depressive symptoms (Beck depression inventory). Over the course of follow-up, 24 patients died (ranging from listing date, 3 to 1,110 d). Of the 49 patients who received lung transplantation, 17 died. In a multivariate analysis, the most significant predictor of survival was quality of well-being (relative risk = 0.454, p < 0.05). Lung transplant status, when entered as a time-dependent covariate (a function of how long the patient waited for surgery) was not a significant predictor of survival (relative risk = 0.942, p > 0.05). Depression was not a significant predictor of survival (relative risk = 0.961, p > 0.05). We conclude that health-related quality of life is a significant predictor of survival for patients with serious lung diseases. Squier HC, Ries AL, Kaplan RM, Prewitt LM, Smith CM, Kriett JM, Jamieson SW. Quality of well-being predicts survival in lung transplantation candidates.


The quality of well-being scale (QWB) is a utility-weighted general health status index. The measure uses information on functioning and symptoms and attempts to estimate the construct of "health-related quality of life" (1). The measure can quantify health outcomes and is often used in cost-effectiveness evaluations (2). The QWB has been validated in diverse patient populations, such as those with chronic obstructive pulmonary disease (3), cancer (4-10), acquired immunodeficiency syndrome (11), cystic fibrosis (11-16), arthritis (11, 17), and coronary artery disease (18). Furthermore, quality of life may be an important outcome measure in future efficacy studies of pharmacotherapy and other treatments for a variety of diseases (19).

The recent focus on outcome assessment necessitates the evaluation of newer, high-technology, and more physically and emotionally complicated surgical therapies, such as organ transplantation. The validation of quality of life measurement in particular, as well as the assessment of its predictive ability for morbidity and mortality in patients with various end-stage diseases, has become an important focus of many investigations in medical outcome research.

The University of California, San Diego (UCSD) is one of many centers in the United States that performs lung transplantation. In the difficult process of selecting candidates for transplantation, the role and usefulness of non-physiologically based measures have not been clearly established. The purpose of this study is to examine the predictive value of baseline measures of health-related quality of life and depression on survival in candidates selected for the UCSD Lung Transplantation Program.

METHODS

Subjects
The subjects were selected from a cohort of 89 patients accepted as candidates for the Lung Transplantation Program at UCSD Medical Center from January 16, 1990 to October 30, 1993. Each patient had completed extensive physical and psychologic evaluation before being accepted for lung transplantation and placed on the waiting list (United Network for Organ Sharing, UNOS). Inclusion criteria for the present analysis required that patients were listed with UNOS and completed baseline evaluation before October 30, 1993. Inclusion criteria for UNOS listing included the following requirements: expected survival 12 to 18 mo; free of known systemic nonpulmonary or psychiatric disease; residence within 2 h of UCSD before transplant and in the San Diego area for 3 mo after surgery; demonstrated medical compliance, including no smoking and alcohol use; within 20% of ideal body weight; no corticosteroids for 2 mo; and adequate social support, including one person committed to the patient's care. Patients were encouraged to attend regular pretransplant pulmonary rehabilitation if they were able to exercise; patients with pulmonary vascular diseases were not exercised before transplant. After transplantation, all patients attended pulmonary rehabilitation for at least 3 mo during the recovery period. Baseline psychosocial measures were collected during the initial visit to the rehabilitation site at the time of UNOS listing. Data were updated before the final statistical analysis on June 1, 1994.

Of the 89 patients accepted for our lung transplantation program during the period of study, 15 were excluded from this analysis. The reasons for exclusion are summarized in Table 1.
TABLE 1

89 LUNG TRANSPLANTATION CANDIDATES ACCEPTED JANUARY 16, 1990 TO OCTOBER 1993

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Included in analysis</td>
<td>74</td>
<td>27</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Obstructive disease</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>Restrictive lung disease</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Pulmonary vascular disease</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Excluded from analysis</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Died before completing evaluation</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Transplanted at another center</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Transplanted before completing evaluation</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Of these 74 transplant candidates, 49 subsequently received lung transplantation at UCSD, 13 of the 49 died postoperatively during the period of follow-up (range from listing date = 3 to 1,110 d). Among the 25 patients who had not undergone transplantation at the time of analysis, 11 died while waiting.

Measurements

Quality of life. The quality of well-being scale (1), Version 7.0, was used for measurement of health-related quality of life at the baseline evaluation after UNOS listing. QWB interviewers were formally trained in the administration and scoring of the instrument. The QWB is administered in a structured interview and incorporates preference-weighted symptom-problem complexes and three similarly preference-weighted components of functioning: social activity, physical activity, and mobility. The result is a single score for each patient, ranging from 0.0 (dead) to 1.0 (optimum functioning), which is believed to provide a "numerical point-in-time expression of well-being" (11).

Depression. The Beck depression inventory (BDI) (20) was used for measurement of patient depressive symptoms at the baseline evaluation. The BDI is a cognitively based self-report assessment tool that has been widely used for the measurement of depression in many groups of medical and psychiatric patients.

Statistical Analysis

Kaplan-Meier product-limit: survival estimates for each disease category were computed using BMDP Function 1L (21). Previous preliminary analyses in this population (22) indicated that transplant candidates in these various disease categories differed significantly on several baseline variables. Therefore, survival curves were calculated separately for each of these disease categories. In addition, Kaplan-Meier survival curves and Mantel-Cox tests for group differences between transplant and non-transplant patients and for a median split of patient QWB scores were calculated using BMDP Function 1L (21).

The effect of covariates on survival for this cohort was evaluated using the Cox proportional hazards model, BMDP Function 2L (21). The proportional hazards model tests for relationships between prognostic variables at baseline and response time patterns and has been used in a number of survival analyses with various patient populations (23–25). General guidelines for survival analysis suggest limiting the analysis to one covariate for every 10 patients who respond (die). Because of the size of the sample and the number of overall deaths in the study population (23), the multivariate analyses were limited to two covariates. For these analyses, disease category was not entered as a covariate.

In the first analysis, baseline QWB score was entered as a fixed covariate, and transplantation status (whether the patient received a transplant) was entered as a time-dependent covariate by allowing the transplant status of the patient to vary, depending on the amount of time for which a patient waited for the surgery. The survival analysis was calculated using a multivariate model that included these two variables. Clinical meaningful intervals of change were 0.10 for the QWB and 1.0 for the BDI.

A second univariate analysis was conducted using a univariate model and entering baseline depression scores as a single, fixed covariate.

RESULTS

Kaplan-Meier Product-limit Proportional Estimates

Kaplan-Meier survival curves calculated for the obstructive, cystic fibrosis, and pulmonary vascular disease categories are shown in Figure 1. Because the restricted lung disease category contained only six subjects, this group was excluded from Figure 1. The other three groups appeared to follow similar survival curves through the period of follow-up until approximately 600 d survival, when the cystic fibrosis patients experienced a drop in survival probability. Likewise, at 1,000 d, the pulmonary vascular disease category dropped in probability of survival. The obstructive disease patients had the highest probability of survival at the 1,200 d end point. These differences between groups were not analyzed for statistical significance, however, because of the small numbers of patients for whom long-term follow-up data were available.

Kaplan-Meier survival curves calculated for patients who received a transplant versus those who did not are shown in Table 2. These results appear to show divergent curves between the two groups, indicating that a higher proportion of patients who underwent transplantation surgery survived during our period of follow-up. Mantel-Cox tests of group differences indicated a statistically significant difference between these two groups (statistic = 11.394, p < 0.01). There were 11 patients who died before being transplanted, all within the first year after UNOS listing.

Finally, Kaplan-Meier proportional estimates were calculated for survival functions of patients based upon a median split of QWB scores. The results of this analysis are shown in Figure 3. A higher proportion of patients whose QWB scores ranged in the upper median appeared to survive than those with lower scores. Again, Mantel-Cox tests of group differences indicated a statistically significant difference between groups (statistic = 5.320, p < 0.05).

Cox Proportional Hazards’ Model Survival Analysis

Two separate Cox proportional hazards model survival analyses
were conducted. A point estimate of relative risk was calculated for each covariate entered into the equation. In the first multivariate model, baseline measurement of patient quality of well-being was a significant prospective predictor of survival (relative risk = 0.454; 95% confidence interval, CI = 0.23, 0.91; p < 0.05). Furthermore, transplant status, allowed to vary depending upon wait time for surgery, was a weaker and nonsignificant predictor of survival (relative risk = 0.94; 95% CI = 0.84, 1.09; p > 0.05). Thus, being transplanted did not predict overall improved survival in this analysis. In the second univariate analysis, depression was not a significant predictor of survival (relative risk = 0.96; 95% CI = 0.28, 3.21; p > 0.05).

Because of the interesting results found in the Kaplan-Meier analysis of QWB median split, the survival, transplant status, and disease category of the QWB quartiles of our study cohort are shown in Table 2. Patients scoring in the lower three quartiles on the QWB had approximately the same survival rate. Patients in the highest quartile were more likely to survive to be transplanted, however, and more likely to survive after surgery. In addition, surgery was most protective for the lowest quartile group, because 6 of 8 patients not transplanted died but only 2 of the 10 patients transplanted died. For patients in the middle two QWB quartiles, the benefit of transplantation was less clear. That patients with COPD who were listed for transplant tended to have the lowest QWB scores and the cystic fibrosis group tended to have the highest is notable with regard to diagnostic differences in these quartile groups.

DISCUSSION

The results of these analyses suggest that health-related quality of well-being may be an important predictor of survival for patients with severe lung disease who have been accepted for lung transplantation (1). Although validated in other patient populations, the QWB has not been used previously as a predictor of survival in patients with chronic, end-stage pulmonary disease selected for lung transplantation. This result is consistent with other studies showing that measures of functional status can predict survival. For example, one study showed that a simple, five-point scale of functional status was the best predictor of survival for hypoxic patients with chronic obstructive pulmonary disease (COPD) receiving long-term oxygen therapy (26).

The results and interpretation of this study are complicated by several factors, including the relatively small number of patients and the heterogeneity of the study population. Further, there is an interesting anomaly. The findings suggested that there was better long-term survival for patients with COPD than with cystic fibrosis (CF); even though baseline QWB scores were higher for the patients with CF. This finding may confuse the assertion that QWB scores are the best predictor of survival across diagnostic groups. Within each subgroup, however, QWB scores do predict survival. Other studies have independently shown that the QWB or related measures predict survival in patients with COPD (27) and CF (15).
It appears that higher patient health-related functioning is associated with a better chance of survival, both before and after transplantation, regardless of what type of disease the patient has. It is important to differentiate between the constructs of study with a limited duration of follow-up might miss long-term benefits. Several researchers have also studied psychological variables in different populations of transplant patients. Cost effectiveness analysis of organ transplantation and the related question of optimal patient selection for the procedure have attracted considerable attention. Because of the scarce resource of donor organs and the great number of medically appropriate candidates, the psychosocial evaluation of these patients becomes an influential part of the team's decision process (31-33). Several groups have examined methods of assessment used in heart transplantation centers, as well as their psychologic contraindications to transplant. These studies suggest an overall lack of uniformity in the use of factors across centers (31, 34). Some researchers claim that psychologic factors may provide useful information for emotional outcomes but not for medical outcomes. One group followed 58 cardiac transplant patients for approximately 2 yr postoperatively and reported that self-reported psychologic distress did not significantly affect health-related morbidity or mortality (35). Similarly, another team conducted a review that found no evidence that preoperative psychopathology affects the overall heart transplantation outcome (36). Therefore, the predictive power of psychologic factors in transplantation medical outcomes appears limited.

This study examined baseline patient depression with the Beck depression inventory (20). A univariate survival analysis showed that baseline depression was not a significant predictor of survival. These results are consistent with other studies showing that psychologic variables are poor predictors of medical outcomes in transplantation patients (35, 36). Other psychologic variables, including anxiety, were not measured in these patients. It may be that there are many other psychosocial factors that are important to consider in future research endeavors.

It is important to recognize the limitations of this study. In particular, this study evaluated a modest number of patients with heterogeneous diseases and limited long-term follow-up. This creates considerable difficulties because of reduced statistical power and flexibility of approaches to regression modeling. Further, the experience is limited to a single medical center. Confirmation of these results by other investigators is necessary to affirm the findings.

In summary, the results of this study suggest that a simple measure of functional status may provide important predictive information in patients with severe lung disease who are candidates for lung transplantation. It is important to emphasize that QWB scores account for a small but significant portion of the variation in survival. At present, most of the variation in outcome remains unexplained. Thus, we strictly caution against using QWB scores for deciding which patients should undergo transplantation. Further studies are needed to identify the best predictors of survival before and after lung transplantation.

References


