Weighing Projections of Physical Decline in Lung Cancer Surgery Decisions

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Abstract: *Background:* Patients with early-stage lung cancer often have comorbid illnesses and fear debility and death when contemplating surgery. However, data that compare physical function of patients who receive surgery with similar patients who do not are sparse. The authors report 1-year outcome results for surgical and nonsurgical patients in a prospective lung cancer cohort to address this gap. *Methods:* The authors enrolled 386 patients with early-stage lung cancer. A 106-item survey was completed at the time of enrollment including the Short-Form 12 (SF-12) Health Survey to assess functional status. Patients were followed for a year. Chart abstractions were obtained to determine comorbid illnesses and surgical status. Death was ascertained through vital records. The SF-12 was repeated 1 year after the enrollment. Regression models were constructed to identify predictors of 1-year mortality and decline in physical function. *Results:* Fifty-nine patients (15.3%) died before 1-year follow-up. Mortality in the surgical group was 10.8% compared with 22.8% in the nonsurgical group ($P < 0.001$). In regression analysis controlling for age and comorbidities, surgical treatment was associated with a reduction in 1-year mortality (odds ratio: 0.5 and 95% confidence interval: 0.3–1.0) but did not worsen physical function relative to the untreated group (average decrease in physical component score of SF-12 = 1.9 for surgery group and 2.5 for no surgery group, $P = 0.66$). *Conclusions:* Functional decline between surgically treated and untreated patients did not differ. This result casts doubt on its value as a treatment determinant. Cancer mortality seems to be a more essential issue in treatment decisions.

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Patients diagnosed with early-stage non–small cell lung cancer fear debility and death when facing the specter of surgery. These patients assign extremely low value to states of severe postoperative debility such as limitations in activities of daily living or a bed to chair existence while perceptions of states of less debility, such as cutting current walking ability in half, are more acceptable as a treatment result.[1] Because lung cancer patients have impaired physical functioning compared with healthy individuals of similar age[2,3] and often have comorbid illnesses, surgical decisions can be equivocal and vary not by strict medical contraindication but by nonmedical factors, such as race or geography, despite the dire consequences of untreated cancer.[4,5] Further complicating difficult decisions for complex patients and their doctors is that the interplay of patients' race, and personal perceptions result in lower surgical rates especially for African Americans particularly when comorbidities are considered.[6] Given these circumstances, the use of postoperative physical functioning could emerge as an objective criterion in the calculus of lung cancer surgery decisions. Past reports have compared postoperative with preoperative functional status in lung resection patients and show some decrement,[2,3,7] but these decrements are usually small and 1 report describes the return to baseline function within 3 months.[7] In addition, a patient with non–small cell lung cancer who does not undergo an operation with curative intent will either face the consequences of progressive disease and/or alternative therapies. Although functional status has been amply described for lung cancer surgery patients relative to populations without cancer or relative to the preoperative state, significant gaps in this literature exist regarding functional status comparisons to similar patients who do not receive surgical care. We, therefore, pose the question, if patients with early-stage non–small cell lung cancer who undergo lung resection surgery are compared with patients with similar disease who do not undergo surgery, will physical functioning significantly differ a year after diagnosis? By comparing functional status to a nonsurgical group with lung cancer, a true decrement in physical functioning would argue that postoperative functional status should be a significant determinant of surgical decisions, whereas similar decrements in functioning between the groups would lead to the opposite conclusion. We recently performed a prospective cohort study examining decisions in lung cancer surgery[6]; we now report 1-year outcome results to address the described gap regarding functional status change in a nonsurgical lung cancer group compared with a group treated with lung resection for cure.

METHODS

This study was approved by the Institutional Review Boards of all participating institutions. Full details of recruitment and study protocols are published elsewhere.[6] In brief, patients with early-stage non–small cell lung cancer were identified in pulmonary, oncology, thoracic surgery and generalist practices in 5 communities. Patients were included if they were at least 21 years of age, had either biopsy-proven disease or a lung lesion demonstrating a high probability of lung cancer using a Bayesian algorithm and had stage 1 or 2 disease as defined by clinical, radiological and/or mediastinoscopic criteria. Informed consent was obtained. Patients were either referred by the clinical practices or found through a chest computerized tomography review protocol. Patients who were identified using the computerized tomography protocol were

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contacted through the ordering practice unless the ordering physician of the scan was based on the emergency department and no documented follow-up occurred. In these cases, the research associate was allowed to contact the patient directly and arrange further care. Pneumonectomies were infrequently performed at the participating study sites (N = 9). Given our inability to perform meaningful statistical comparisons for pneumonectomy patients, they were excluded from analysis.

All participants were administered a 106-item survey at the time of enrollment. Demographic data were obtained while other survey items explored perceptions of patient-physician communication, attitudes about lung cancer and surgery, religiosity, past health care experiences and access to a regular source of care. Race and ethnicity were self-reported. Physical function was ascertained using the Short-Form 12 (SF-12) Health Survey.[8]

Chart reviews were performed starting 4 months after enrollment. The chart abstraction included lung surgery status, date of surgery if it occurred, preoperative stage, medical comorbidities and preoperative pulmonary function tests. Physical function was reassessed using the SF-12 by telephone 1 year after enrollment. For patients who had died, death and date of death were verified by searching state vital records.

The primary outcomes for this analysis are mortality and physical function as assessed by the SF-12 physical component score (PCS) 1 year after lung cancer diagnosis. Significant physical deterioration was defined as a drop of 5 or greater in the PCS 12 months after diagnosis given that a 4.5-point gain in SF-36 PCS was linked to improved (66 m) 6-minute walk distance in pulmonary rehabilitation research[9] and the SF-12 PCS is highly correlated with the SF-36.[8,10,11] The physical function outcome is reported for the group of 1-year survivors who completed both the initial and 12-month phone assessment. To account for death as a condition of physical deterioration, we also examined a combined outcome of 5-point decrement in PCS and death reflecting a state of global worsening 1 year after diagnosis inclusive of all enrolled patients.

Descriptive statistics including selected bivariate associations were computed for demographic variables, surgical rate, religiosity, a sum of comorbid conditions relevant to lung resection surgery (chronic obstructive lung disease, congestive heart failure, renal insufficiency, poor mobility, cerebrovascular disease, obstructive sleep apnea, oxygen dependence), a history of coronary artery disease, known diabetes, the mental component score (MCS) of the SF-12 and the 3 outcomes noted above. All outcome variables were dichotomous, so a generalized linear model for clustered data with multiple predictors was used to assess the simultaneous effect of predictors on outcome.[12] Given that the major goal of this analysis was to gauge the effect of surgery on 1-year mortality and physical functioning, receipt of surgery was a variable in all models. Demographic variables were incorporated into all models. Because of the significance of the presence of 2 or more comorbid illnesses and religiosity in our previous work,[6] these measures were also included in the regressions. Coronary artery disease and diabetes were prevalent but did not impact mortality or physical function scores in either bivariate or regression analyses, and so these variables were dropped from the final models. Therefore, for the purpose of this analysis, exactly as per our previous work, significant comorbidities included chronic obstructive lung disease, renal insufficiency, poor mobility, congestive heart failure, cerebrovascular disease, obstructive sleep apnea and oxygen dependence.[6] The modeling approach fitted a maximum model using main effects only; however, we did assess the effect of several interactions including race and comorbid illnesses, comorbid illnesses and surgery and age and surgery without detecting additional significance beyond the main effects.

All statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc, Cary, NC). A priori statistical significance for independent variables and the primary outcomes was set at ≤ 0.05 based on a 2-sided test for bivariate and multivariate associations.

RESULTS

As previously described, 386 patients remained eligible in this early-stage lung cancer prospective cohort.[6] All patients with absolute contraindications to surgery as defined by pulmonary function results were excluded. Fifty-nine patients (15.3%) died before 1-year follow-up. Thirty-seven patients either refused or were unable to complete the SF-12 survey 1 year after diagnosis. Therefore, 290 baseline and 1-year surveys were available for paired analyses and 349 were available to assess the combined outcome of significant physical function decline or death.

Demographic characteristics, religiosity, comorbid conditions and baseline SF-12 scores plus surgical rates according to these characteristics are summarized in Table 1. Gender, educational attainment and marital status are similar to previous reports.[4,13] Because the cited reports are based on combined Surveillance, Epidemiology and End Results-Medicare data, the age of our population is marginally younger. We oversampled African Americans because of initial sample size calculations that allowed enough statistical power to make valid comparisons according to race.[6] Note that 13% of participants had 2 or more of the designated comorbidities. The prevalence of each individual comorbidity included in the summary variable was as follows: Chronic Obstructive Pulmonary Disease (COPD): 40%; congestive heart failure: 10%; history of cerebrovascular accident (CVA): 6.2%; renal failure: 5.5%; poor mobility (walking limited to a room): 4.7%; oxygen dependence: 2.6%; and obstructive sleep apnea: 1.8%.

Bivariate analyses for all 3 outcomes are shown in Table 2. Age above the median (age, 66 years) is strongly associated with death (1-year survivors averaged 65.8 years of age at enrollment compared with 69.5 years in the group who died [$P = 0.01$]), significant physical decline and the combined 1-year outcome of death plus physical decline. Patients who placed in the lowest quartile MCS on the baseline SF-12 experienced twice the mortality within a year compared with those with higher MCS scores. There is no relationship between MCS and physical decline or the composite outcome.

The age-old conundrum between surgical benefit and the risk of comorbid conditions remained in the bivariate results. One-year mortality in the surgical group was 10.8% compared with 22.8% in the nonsurgical group ($P = 0.002$), but patients with 2 or more significant comorbidities at diagnosis had a 27.5% 1-year mortality compared with 13.5% in the group with <2 ($P = 0.01$). However, when comorbidity was stratified by surgical status, we found that the 2 or more comorbidity surgical group had a 1-year mortality rate of 19% compared with 10% for the group with <2 (P = NS); in the no surgery group, these 1-year mortality rates were 31% and 20%, respectively (P = NS). There was no difference in 1-year mortality according to race (African Americans = 15.0 and whites = 15.4; $P = 0.9$), but African Americans who died were 4 years younger than white patients (66.6 versus 70.6 years; $P = 0.05$).

The physical function analysis was limited to the 290 patients who survived 1 year and answered the baseline and