Changes in patient presentation and outcomes for major lung resection over three decades

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Abstract

Objective: Growing scrutiny of surgical results for lung cancer has prompted increased evaluation of risk factors and outcomes of resection. We determined how patient preoperative status and outcomes of resection have changed over time to identify opportunities for improving these results. Methods: We reviewed a prospectively collected database of patients undergoing major lung resection 1980–2006. Patient characteristics and immediate outcomes of resection were compared for three-decade periods (1980–1989, 1990–1999, 2000–2006). Data were compared using the Kruskal–Wallis test, chi squared analysis, and logistic regression analysis. Results: One thousand and forty-six patients underwent resection for cancer (862) and other problems. The percentage of female patients increased over time. Some elements of preoperative status worsened, with significant increases in hypertension rate, mean performance status, obesity incidence, mean risk score, and use of induction therapy. Pneumonectomy rates, immediate preoperative tobacco use, and surgery for advanced stages of disease decreased over time. Outcomes improved over time, with significant decreases in operative mortality, cardiopulmonary complications, and overall complications. Risk factors for categories of complications including operative mortality varied according to the time period studied. Conclusions: Outcomes of major lung resection have improved over time despite a worsening of some elements of preoperative status. Maintenance of surgical databases is essential to enable surgeons to provide data consonant with growing demand from payers and patients. The use of current rather than historical lung resection outcomes is vital in assessing risk. Identification of changes in surgical practice patterns helps identify opportunities for improving future outcomes.

1. Introduction

Lung cancer is the most common cause of death due to malignancy in the United States and Europe [1–3]. Mortality owing to lung cancer continues to increase in many countries [2–5]. This is especially true among women and in countries in which a reduction in tobacco use has not been evident [1,4,6]. Surgery is the primary curative treatment for early stage lung cancer and has been so since 1940s. During the last three decades there have been a number of advances in the selection and care of such patients. Examples include improvements in preoperative patient assessment, anesthetic management, intraoperative surgical management, and postoperative care including pain control. How these influence patient selection and outcomes of surgery over time is poorly understood.

Based on recent publications, some trends in surgical outcomes for lung cancer are known. A recent summary of SEER (Surveillance Epidemiology and End Results) data covering the period 1988 through 2002 demonstrated that, during this period, the average age at the time of lung surgery increased, the proportion of females in the resection population increased, and the duration of hospital stay decreased [7]. Other observed trends include a decrease in pulmonary morbidity and mortality, and a potentially confounding increase in lesser resections [8]. Most trend analyses have been observational, and few have explored preoperative variables associated with outcomes or their possible evolution over time.

It is important that we understand how characteristics of patients undergoing lung resection have changed over time and how these characteristics can influence surgical outcomes. Tracking outcomes also may aid in assessing how changes in surgical and anesthetic management have altered surgical results over time. The trends that are identified should provide an idea as to how our surgical population may change in the near future, which changes in perioperative management have provided maximum benefit to these patients, and what areas need improvement in the short term. With these objectives in mind, we reviewed our outcome data for major lung resection over three decades.
2. Materials and methods

We retrospectively reviewed information from our database for patients undergoing major lung resection (anatomic lobectomy, bilobectomy, pneumonectomy or completion pneumonectomy) 1980–2006. This protocol was approved by our Internal Review Board and an exemption was granted for specific patient consent.

We collected data including patient demographics; preoperative pulmonary function test results (FEV1 (forced expiratory volume in the first second) expressed as a percent of predicted (FEV1%)) and single breath diffusing capacity for carbon monoxide expressed as a percent of predicted (DLCO%;)); height and weight; the presence of obesity (defined as a body mass index (BMI) ≥ 30 kg/m²); the presence of comorbid factors including hypertension, diabetes, coronary artery disease, other heart disease, renal insufficiency, and protein malnutrition; and the use of induction chemotherapy and/or radiation therapy. The extent of the operation (lobe(s) and number of segments removed) was recorded. Postoperative predicted FEV1% (ppoFEV1%) and DLCO% (ppoDL-CO%) were calculated using the remaining functional segment technique or, when available, using results of quantitative perfusion scans. Postoperative complications were classified as pulmonary (pneumonia, need for prolonged initial intubation or reintubation, lobar collapse), cardiovascular (myocardial infarction, arrhythmia, transient ischemic attack, cerebrovascular accident, pulmonary embolism), other (wound infection, recurrent laryngeal nerve injury, chylothorax, empyema, etc.), overall nonfatal complications, and postoperative death, defined as death during the hospitalization during which the operation was performed or within 30 days of the operation for patients. Surgical staging was performed using the 2002 American Joint Committee on Cancer guidelines [9]. Risk scores were calculated using the expiratory volume, age, and diffusing capacity score (EVAD) system [10].

Data were assessed in aggregate and by time period, for which patients were grouped according to the decade of their operations (1980—1989; 1990—1999; 2000—2006; year of operation was not known for two patients). Comparisons among time periods were performed using the Kruskal–Wallis test for continuous variables and chi-square analysis for categorical variables. Patient characteristics associated with outcomes of surgical intervention were identified using univariate analysis for each time period and for aggregate data. Variables identified as having a possible relationship to outcomes (p < 0.15; lower cutoff values were used when the analyses were constrained by the number of events) were entered into a backwards-stepwise multivariable logistic regression analysis. Continuous data are expressed as mean ± standard deviation (SD).

3. Results

During 1980–2006 interval 1046 patients underwent major lung resection (Table 1). Important differences in patient characteristics were identified among the three time intervals, including an increase in mean age, an increase in the percentage of patients older than 70 years, and an increase in the incidence of comorbid factors including obesity, diabetes, hypertension, and preoperative chemotherapy and/or radiation therapy. In contrast, there was a decrease in the incidence of some comorbid factors such as tobacco use within 6 weeks of surgery and poor performance status. Spirometric function did not differ importantly among the time intervals, but there was a substantially higher mean DLCO% in the middle interval compared to the first and last intervals. The mean calculated risk score (EVAD score) increased moderately during the three intervals.

There was a shift towards more lobectomies and bilobectomies and away from operations on patients with stage III or IV lung cancer over time (Table 2). A substantial reduction was evident in many complication categories over time, including cardiovascular complications, nonfatal complications, and operative mortality. Interestingly, pulmonary complications decreased modestly but not significantly, whereas there was no important change in other complications. During the intervals there was a 50% decrease in postoperative length of stay.

Table 1
Characteristics of patient population

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 1046)</th>
<th>1980—1989 (n = 320)</th>
<th>1990—1999 (n = 351)</th>
<th>2000—2006 (n = 373)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>61.5 ± 11.4</td>
<td>59.5 ± 11.5</td>
<td>61.1 ± 12.3</td>
<td>63.6 ± 10.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &gt; 70 year</td>
<td>267 (25.6%)</td>
<td>64 (20.0%)</td>
<td>92 (26.2%)</td>
<td>111 (29.8%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Men</td>
<td>572 (54.8%)</td>
<td>190 (59.4%)</td>
<td>198 (56.4%)</td>
<td>184 (49.2%)</td>
<td>0.020</td>
</tr>
<tr>
<td>Current smoker</td>
<td>452 (43.5%)</td>
<td>212 (66.7%)</td>
<td>143 (41.0%)</td>
<td>97 (26.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>210 (21.3%)</td>
<td>34 (11.8%)</td>
<td>73 (22.1%)</td>
<td>103 (28.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>146 (14.1%)</td>
<td>36 (11.3%)</td>
<td>50 (14.3%)</td>
<td>59 (16.1%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Hypertension</td>
<td>407 (39.2%)</td>
<td>91 (28.6%)</td>
<td>119 (34.1%)</td>
<td>196 (52.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1%</td>
<td>82.1 ± 22.2</td>
<td>81.3 ± 22.3</td>
<td>83.2 ± 22.6</td>
<td>81.9 ± 21.9</td>
<td>0.46</td>
</tr>
<tr>
<td>ppoFEV1%</td>
<td>61.9 ± 19.7</td>
<td>59.7 ± 20.0</td>
<td>63.0 ± 20.4</td>
<td>62.9 ± 18.8</td>
<td>0.13</td>
</tr>
<tr>
<td>DLCO%</td>
<td>84.7 ± 21.9</td>
<td>84.4 ± 21.3</td>
<td>88.2 ± 23.8</td>
<td>81.3 ± 21.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ppoDL-CO%</td>
<td>63.6 ± 18.6</td>
<td>61.6 ± 17.7</td>
<td>66.6 ± 19.7</td>
<td>62.4 ± 18.0</td>
<td>0.006</td>
</tr>
<tr>
<td>EVAD score</td>
<td>6.9 ± 2.7</td>
<td>6.5 ± 2.5</td>
<td>6.6 ± 2.5</td>
<td>7.4 ± 2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PS 2—4</td>
<td>63 (16.0%)</td>
<td>64 (20.7%)</td>
<td>73 (21.2%)</td>
<td>26 (7.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Induction therapy</td>
<td>94 (10.4%)</td>
<td>16 (5.6%)</td>
<td>18 (5.6%)</td>
<td>60 (16.1%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Current smoker: any cigarette use within 6 weeks of operation; obesity: body mass index ≥ 30 kg/m²; FEV1%: forced expiratory volume in 1 s expressed as a percent of predicted; ppoFEV1%: predicted postoperative FEV1%; DLCO%: single breath diffusing capacity for carbon monoxide expressed as a percent of predicted; ppoDL-CO%: predicted postoperative DLCO%; EVAD: risk score based on weighted scores for FEV1%, DLCO%, and age (see Ref. [10]); PS: Eastern Cooperative Oncology Group performance status; induction therapy: preoperative chemotherapy and/or radiation therapy.
Tables 3 and 4 list results of univariate analyses for the pulmonary and cardiovascular complication categories performed on aggregate data and data partitioned by year interval. There were substantial differences in outcomes among the partitioned data for both complication categories. Univariate analyses were also performed using the variables listed in Tables 3 and 4 for operative mortality as an outcome (data not shown). Subset analyses by time interval were not performed for operative mortality because there were an insufficient number of events during each interval to permit logistic regression analyses.

Logistic regression analysis for the aggregate data demonstrated covariates associated with pulmonary complications to be ppoDLCO%, age, and ppoFEV1%. Similar analyses for the time intervals identified ppoDLCO% to be an important covariate for pulmonary complications during the first and last periods but not during the middle period. An analysis of expected versus actual ppoDLCO% values for aggregate data suggests that ppoDLCO% values were higher than expected during the middle period than during the first and last periods (Fig. 1). Covariates for cardiovascular complications using aggregate data were age and ppoFEV1% (Table 5). In subset analyses age was the covariate in common for all the time intervals, and ppoFEV1% was a covariate for the first two time intervals. Covariates for operative mortality were ppoDLCO% and performance status (Table 5).

### 4. Discussion

Monitoring and public reporting of surgical outcomes are becoming increasingly common in the United States, even when such outcomes have not been properly audited or risk-adjusted. These challenges require that surgeons track and evaluate their own outcomes so that reliable, objective, and appropriately risk-adjusted data are available for comparison purposes. Some prior work has demonstrated evolving outcomes for lung resection over time. However, these publications lack analysis of detailed patient characteristics, a focus on evaluating time trends, and/or an evaluation of the relationships between specific patient characteristics and outcomes over time [8,11—15].

In this study we focused on patient selection and risk assessment to identify opportunities for future improvements in our practice. We found that our lung resection population changed considerably over time. Patients were increasingly older, the percentage of female patients grew over time, and the incidences of hypertension, obesity, and diabetes increased substantially. Overall risk increased based...
on EVAD score and the incidence of preoperative chemotherapy and/or radiation therapy also increased. Opportunities for improving future outcomes that arise from these findings include bringing a geriatric focus to our patient care practices, and appropriately managing changes in lung function and performance status that often result from induction therapy but are not adequately reflected in risk assessment, which is typically based on status at the time of initial diagnosis.

Some changes that favorably influenced surgical outcomes, including improved efforts at smoking cessation and fewer pneumonectomies, reflect alterations in our practice patterns that were stimulated or reinforced by real-time tracking of information from our database. In contrast, the increasing use of induction therapy and avoidance of operating on patients with advanced disease or who had poor performance status, were influenced more by global alterations in surgical and multidisciplinary practices. Even these factors can be mitigated in an individual practice by greater emphasis on improved patient performance status through cardiopulmonary rehabilitation when necessary, and possibly greater use of minimally invasive techniques to reduce postoperative pain and induction of inflammatory mediators.

Importantly, we found that many factors were outside the influence of typical surgical practice but were instead the result of evolution of societal characteristics, including increasing incidences of obesity, hypertension, and diabetes. Identifying these changes provides an opportunity to develop algorithms for improvements in managing fluids and electrolytes, nutrition, serum glucose levels, and arterial blood pressure, clinical challenges that were heretofore much less common.

Our analyses of predictors of outcomes for different time intervals reinforce important caveats regarding interpreting clinical outcomes reports: the time period of the study and the size of the cohort can have interesting influences on the relationships between these factors and clinical outcomes. We demonstrated how predictive factors for specific complications seemed to change over time. Whether the results reflect true varying relationships among the covariates and the outcomes or are aberrations owing to a relatively small sample size is difficult to determine. Large, contemporary, uniform datasets are much more likely to provide a reliable indication of relationships among preoperative characteristics and outcomes than are long time range studies that incorporate surgical habits that have changed considerably over time.

A case in point is our evaluation of the role of DLCO in predicting pulmonary complications and mortality after major lung resection. Although DLCO in our aggregate analysis demonstrated a very strong predictive relationship to these outcomes, this was not uniformly the case for all time periods studied. The relationship between DLCO and pulmonary complications as well as operative mortality became generally known in late 1980s [16,17], leading to greater conservatism in the selection of patients for lung surgery in our institution for the ensuing 10 years (Fig. 1). As a comfort level with higher-risk DLCO levels evolved over time, the selection of patients also changed during the third time period of study to include more so-called higher risk patients.

This study demonstrates a variety of findings that are single institution based and encompass a 27-year time period. As such, specific findings we report likely cannot be generalized to risks or outcomes at other institutions. However, the main points that we illustrate are apropos of work done in other environs: patient characteristics have evolved substantially over time, outcomes are improving even though we are operating on patients with ever-

### Table 5
Logistic regression analysis outcomes for complication categories using aggregate data; covariates are listed for separate analyses for the three time intervals

<table>
<thead>
<tr>
<th>Category</th>
<th>Covariates</th>
<th>OR</th>
<th>95% CI</th>
<th>p-Value</th>
<th>Covariates for time intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary complications</td>
<td>ppoDLCO%</td>
<td>0.78*</td>
<td>0.69–0.88</td>
<td>&lt;0.001</td>
<td>1980–1989: ppoDLCO%</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>1.40**</td>
<td>1.16–1.70</td>
<td>0.0001</td>
<td>1990–1999: ppoDLCO%</td>
</tr>
<tr>
<td></td>
<td>ppoFEV1%</td>
<td>0.89</td>
<td>0.79–0.99</td>
<td>0.043</td>
<td>2000–2006: ppoDLCO%, age</td>
</tr>
<tr>
<td>Cardiovascular complications</td>
<td>Age</td>
<td>1.68**</td>
<td>1.39–2.02</td>
<td>&lt;0.001</td>
<td>1980–1989: Age, diabetes, ppoDLCO%</td>
</tr>
<tr>
<td></td>
<td>ppoFEV1%</td>
<td>0.77</td>
<td>0.70–0.85</td>
<td>&lt;0.001</td>
<td>1990–1999: ppoDLCO%, age</td>
</tr>
<tr>
<td>Operative mortality</td>
<td>ppoDLCO%</td>
<td>0.64*</td>
<td>0.53–0.77</td>
<td>&lt;0.001</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>PS 3 or 4</td>
<td>2.72</td>
<td>1.46–5.13</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: confidence interval; (*) odds ratio per 10 percentage point increase; (**) odds ratio per 10 year increase; PS: Eastern Cooperative Oncology Group performance status; N/A: insufficient number of events to permit analyses.
worsening risk profiles, and specific patterns of patient selection can have interesting and sometimes misleading effects on analyses of risk.

Maintenance of databases containing current and historical information is essential to enable surgeons to provide accurate and objective data consonant with growing demand from payers and patients. We identified a number of changes in patient characteristics, surgical practice, and lung resection outcomes over time. We conclude that the use of current rather than historical lung resection outcomes is vital in assessing risk for purposes of patient selection, outcomes modeling, and resource allocation. Identification of changes over time in practice patterns for surgical management of lung cancer helps identify opportunities for improving future surgical outcomes.

References


Appendix A. Conference discussion

Dr G. Rocco (Naples, Italy): That was an impressive series, especially showing us how you can become safer through the years and, at the same time, as you said, a little bit more conservative. As a matter of fact, looking at your data, despite taking risks on comorbidities, in the sense that you have operated on an increased number of patients with obesity, hypertension and so on, you didn't take any risk, any further risk, on the functional aspect, maybe based on the pO2, the DLCO assessment.

Now, my question to you is, what is the role of rehabilitation and what is your concept of the lung volume reduction effect?

Dr Ferguson: We're increasingly using both time and rehab to improve patient status preoperatively. So patients that we deemed to be at increased risk, who we think might benefit from cardiopulmonary rehab, we'll routinely send there for a period of 3 or 4 weeks.

Another thing that falls into this is the increasing incidence of the use of induction therapy. And we're monitoring DLCO quite carefully in these patients after their induction therapy and frequently will have to delay their operation for a month or sometimes even 2 months until the decrease that we see in diffusing capacity starts to return back towards normal to return their risk to a more normal level.

In terms of the lung volume reduction effect, we don't yet have as good a handle on how to estimate that as we would like. We certainly employ it in patients who obviously have heterogeneous disease which is the target for the lung resection. But in the majority of patients who are at increased risk, we can't count on the lung volume reduction effect. Now, we're trying to improve our predictability using quantitative CT to better estimate postoperative function in this regard.

Dr W. Klepetko (Vienna, Austria): I have two questions. The first refers to the fact that you obviously have operated more patients with obesity, hypertension and other risks factors. Does it mean that you have expanded your acceptance criteria or this simply a reflection of the normal demographic trend in the overall population in the U.S.?

Dr Ferguson: I'm afraid it's the latter. We're all getting fat and old.

Dr Klepetko: And the second question I would like to ask is, I got a little bit confused about the interpretation of your handling of Stage III patients. If I remember correctly, you showed that there were less patients Stage III in the last decade operated on. On the other hand, you showed that Stage III was a significant risk factor for the last decade only. How does that fit together? How can that be integrated? Could you comment on that.

Dr Ferguson: Well, I think it's a little confused by the fact that we're using a lot more induction therapy. And so our staging is improved, meaning we're eliminating more many Stage IV patients, so essentially zero Stage IV patients are getting surgery now, but more Stage III patients are getting surgery because we're not excluding them from surgical resection. We're operating on them after induction therapy.

Dr Klepetko: So when you showed us that there are less Stage III, and IV, patients operated, this hold true for the Stage IV but not for the Stage III patients; is that correct?

Dr Ferguson: Yes, I think so.