Cardiac comorbidity is not a risk factor for mortality and morbidity following surgery for primary non-small cell lung cancer

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Abstract

Objective: We examined the effect of cardiac comorbidity on mortality and postoperative complications following surgery for primary non-small cell lung cancer.

Methods: Between October 2001 to December 2005, 1067 consecutive patients underwent lung resection for primary cancer within a single centre; patient data was collected prospectively. Two hundred and seventy-one patients had a history of cardiac comorbidity, which included 196 angina, 118 myocardial infarction, 36 revascularisation, 10 congestive cardiac failure and 19 rhythm disorders (numbers not mutually exclusive). To account for differences in case-mix we used logistic regression to develop a propensity score for cardiac comorbidity group membership and then performed a propensity-matched analysis. Kaplan—Meier curves were used to assess follow-up mortality.

Results: Patients with cardiac comorbidity were more likely to be hypertensive, have severe dyspnoea, diabetes, current or ex-smokers and were older. After performing propensity matching to account for these differences we successfully matched 199 patients with cardiac comorbidity to 398 patients with no cardiac history. There was no difference in in-hospital mortality (2.5% vs 3%, \( p = 0.73 \)), myocardial infarction (0.5% vs 0.3%, \( p > 0.99 \)), arrhythmia (15.6% vs 14.1%, \( p = 0.62 \)), renal failure (2% vs 1.5%, \( p = 0.65 \)), stroke (0.5% vs 0.3%, \( p > 0.99 \)), respiratory insufficiency (4% vs 3.3%, \( p = 0.64 \)), reintubation (1% vs 2.5%, \( p = 0.35 \)), tracheostomy (4% vs 7.8%, \( p = 0.08 \)), intensive care readmission (8.5% vs 6.5%, \( p = 0.37 \)) and length of stay (8 days vs 8 days, \( p = 0.98 \)). Three-year survival was similar (61.4% vs 56.2%, \( p = 0.39 \)). No differences in outcomes existed with different cardiac conditions.

Conclusion: With careful assessment and patient selection, patients with cardiac comorbidity were not found to be at increased risk of mortality and morbidity following lung resection for primary non-small cell lung cancer in a propensity-matched population.

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Keywords: Cardiac comorbidity; Lung resection; Lung cancer; Mortality; Morbidity

1. Introduction

The incidence of associated cardiovascular morbidity in patients with lung cancer is reported to be between 13% and 23% [1,2]. This relatively high incidence is not surprising since the two conditions share common risk factors such as older age and smoking [3,4]. Patients with atherosclerotic vascular disease also have higher incidence of chronic respiratory disease which in turn is also another risk factor associated with carcinoma of the lung [3—5].

One would expect that these comorbidities would impact adversely on the postoperative outcome after lung resection. However previous reports are conflicting and show either a minimal impact [6,7] or a marked adverse impact [4,8] of cardiac comorbidities on postoperative outcome after lung resection.

In this study we analyse the relationship between cardiac comorbidity and outcome of patients undergoing surgery for primary lung cancer, using propensity matching of populations.

2. Patients and methods

Between 1st October 2001 and 31st December 2005, 1067 consecutive patients underwent lung resection for primary non-small cell lung cancer in our institution. All data was collected prospectively at patient admission as part of routine clinical practice and entered into an electronic database. Associated cardiac comorbidities and in-hospital outcomes chosen for analysis are shown in Tables 1 and 2, respectively. The definitions of these variables are as described in the Society of Cardiothoracic Surgeons of Great Britain and Ireland (SCTS) database [http://www.scts.org/].
Table 1
Patient characteristics prior to propensity matching.

<table>
<thead>
<tr>
<th>Cardiac comorbidity</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes ($n=271$)</td>
<td>No ($n=796$)</td>
</tr>
<tr>
<td>Age at operation (years)</td>
<td>70.5 (64.6—75.5)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.6 (22.8—28.5)</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>76.2 (63.1—91.5)</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>57.6</td>
</tr>
<tr>
<td>Previous cancer (%)</td>
<td>16.9</td>
</tr>
<tr>
<td>Previous thoracic surgery (%)</td>
<td>6.6</td>
</tr>
<tr>
<td>COAD (%)</td>
<td>28.8</td>
</tr>
<tr>
<td>Emphysema (%)</td>
<td>5.9</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>25.5</td>
</tr>
<tr>
<td>Ex-smoker (%)</td>
<td>70.5</td>
</tr>
<tr>
<td>NYHA class &gt;2 (%)</td>
<td>12.6</td>
</tr>
<tr>
<td>NYHA class &lt;2 (%)</td>
<td>45.4</td>
</tr>
<tr>
<td>High alcohol consumption (%)</td>
<td>40.9</td>
</tr>
<tr>
<td>Gastrointestinal history (%)</td>
<td>21.8</td>
</tr>
<tr>
<td>Peripheral vascular disease (%)</td>
<td>8.1</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>47.2</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>13.3</td>
</tr>
<tr>
<td>Renal dysfunction (%)</td>
<td>1.8</td>
</tr>
<tr>
<td>Stage of lung cancer</td>
<td></td>
</tr>
<tr>
<td>III or IV</td>
<td>13.3</td>
</tr>
<tr>
<td>II or I</td>
<td>21.0</td>
</tr>
</tbody>
</table>

FEV1, forced expiratory volume in 1 s; COAD, chronic obstructive airways disease; NYHA, New York Heart Association.

3. Surgical and anaesthetic technique

All patients are admitted a day before the operation after being fully evaluated in the surgical outpatient clinic. The preoperative evaluation is performed in accordance with the British Thoracic Surgery guidelines for selection of patients for resection of lung cancer [9]. Patients with cardiac history who are taking aspirin do not stop it. Patients taking clopidogrel are advised to stop it 7 days before the operation. However, clopidogrel is continued in patients who have drug eluting stents implanted in their coronary arteries until the day of the operation because of the risk of stent blockage. All patients have an arterial cannula inserted for monitoring postoperative blood gases. An epidural catheter is inserted in the majority of patients for postoperative pain control; this is continued until after the intercostal drains are removed. In patients in whom inserting the epidural catheter is not technically feasible, a paravertebral catheter and patient controlled morphine infusion is used.

Postoperatively, all patients receive unfractionated heparin subcutaneously 8 hourly for prevention of deep vein thrombosis while the epidural catheter is in-situ. After the epidural catheter is removed the heparin is changed to once daily dosage of low molecular weight heparin subcutaneously.

Long-term patient survival was investigated using the National Strategic Tracing Service (NSTS), which records all patient deaths occurring in the United Kingdom.

4. Statistical analysis

Continuous variables are shown as median with 25th and 75th percentiles. Categorical data is shown as percentages. Univariate comparisons were made with Wilcoxon rank sum tests and chi-square tests as appropriate. Deaths occurring over time were described using Kaplan–Meier survival curves and associated log-rank tests for significance [10].

To account for differences in case-mix we developed a propensity score for cardiac comorbidity group membership [11]. The propensity for cardiac comorbidity group membership was determined using multivariable logistic regression analysis [12]. A full non-parsimonious model was developed which yielded a C statistic of 0.79. This process matched two patients without cardiac comorbidity for every one patient with cardiac comorbidity using an identical 8-digit propensity score. If this could not be done we proceeded to a 7-, 6-, 5-, 4-, 3-, 2-, or 1-digit match. This resulted in 199 patients with cardiac comorbidity being propensity-matched to 398 patients without cardiac comorbidity (Table 3).

In all cases a $p$ value $<0.05$ was considered significant. All statistical analysis was performed using SAS for Windows Version 8.2.

5. Results

Prior to propensity matching, patients with cardiac comorbidity were found to be significantly older, had more severe dyspnoea, and were more likely to have other comorbidities (peripheral vascular disease, hypertension and diabetes) (Table 1). Significantly more patients with cardiac comorbidity were ex-smokers. The type of resection performed was the same in both groups (Table 4).

Outcome analysis between the groups prior to propensity matching showed a significantly higher incidence of renal failure and intensive care readmission in patients with cardiac comorbidity (Table 2). After propensity matching, the differences in both patient characteristics and in-hospital events between the patient groups disappeared (Tables 3 and 5).

No difference existed in 3-year survival before or after propensity matching. Freedom from death for patients with cardiac comorbidity at 12 months, 24 months, and 36 months...
was 80.8%, 67.1%, and 59.2%, respectively compared to 83.7%, 70.4%, and 60.3% for patients without cardiac comorbidity in the un-matched groups \( \text{log-rank} = 0.48 \).

Following matching, freedom from death for patients with cardiac comorbidity at 12 months, 24 months, and 36 months was 82.4%, 70.2%, and 61.4%, respectively compared to 81.2%, 68.3%, and 56.2% for patients without cardiac comorbidity \( \text{log-rank} = 0.39 \) (Fig. 1).

6. Discussion

Although cancer stage is the most important predictor of survival overall in patients with lung cancer, between 19% and 30% of stage I lung cancer who undergo surgery die because of other diseases [13,14]. The Charlson comorbidity index is the sum of weighted score allocated to individual comorbidities [15]. This score allocates a weighted score of one to cardiac comorbidities. In studies done by Moro-Sibilot the postoperative outcome of patient with score 1—2 is not significantly different from that of patients with score 0, implying that cardiac comorbidities did not have a negative postoperative impact on outcome [6]. Our results are in concordance with this report.

The incidence of cardiac comorbidities in patients undergoing surgery for NSCLC varies with age, with an incidence of 6% in those below 60 years to 21% in those above 60 years [16]. Since age is an independent prognostic factor for mortality [17,18], the negative impact on survival in patients with cardiac disease may well be a reflection of a patient’s older age rather than associated cardiac disease. The lack of consensus regarding the impact of associated cardiac comorbidity on the postoperative outcome is likely to be due to variation in the selection of patients for surgery and different definitions of cardiac comorbidity. Propensity matching is one of the ways of reducing these variations in the selection of patients for surgery.

We follow the guidelines laid out by the British Thoracic Society stringently to assess the patients preoperatively [9]. All those patients requiring cardiac assessment are investigated and referred to cardiology as appropriate. The best evidence does not support a management strategy of preventive preoperative coronary revascularisation before noncardiac surgery in patients with chronic stable angina [19]. In our practice coronary revascularisation is limited to those patients who have a well defined need for the procedure independent of need of non cardiac surgery. Therefore the indications for operative or percutaneous procedures would be based on current clinical needs and patient’s suitability for coronary revascularisation [9].
revascularisation in our patients presenting with lung cancer are similar to those outlined in the American Heart Association guidelines for revascularisation for coronary artery disease [20]. In patients in whom there is a clear need for revascularisation lung cancer surgery is usually performed after the revascularisation, although care of these patients should be individualised.

The reported risk of perioperative MI after thoracic surgery is between 2.8% and 17% [21]. Our incidence of perioperative MI is less than reported in the literature. In addition to an effective preoperative work-up strategy all our patients are invasively monitored at least for the first 24 h. This enables prompt treatment in case of any physiological derangement. Invasive monitoring and keeping all parameters within physiological limits has been shown to reduce the risk of cardiac complications [5].

Excessive activation of the cardiac (T1—T5) sympathetic nervous system by surgical stress has been demonstrated to increase myocardial oxygen demand, while inducing coronary artery vasoconstriction [22]. Thoracic epidural anaesthesia (TEA) by selectively blocking cardiac sympathetic nerve fibres, blunts these adverse effects of surgical stress. By blocking sympathetically mediated coronary constriction, endocardial to epicardial blood flow ratio is improved, thus optimizing the regional distribution of myocardial blood flow. Thoracic sympathetic blockade also reduces the major determinants of myocardial oxygen demand, such as blood pressure, heart rate, and contractility. TEA thus improves the balance between cardiac supply and demand. A meta-analysis of epidural analgesia has shown a diminished risk of perioperative myocardial infarction in patients who receive it [22]. The majority of our patients had a thoracic epidural.

The reported incidence of arrhythmias is 12–87% depending upon the type of arrhythmia [17,18]. There is a correlation between incidence of postoperative arrhythmia and history of congestive cardiac failure and history of previous arrhythmia [18]. However, peripheral vascular disease, hypertension, older age and pneumonectomy also contribute to the occurrence of postoperative arrhythmias [18]. Our incidence of arrhythmias in this supposed high-risk group is towards the lower end of that reported in the literature. This again can be attributed to invasive monitoring and the use of epidural analgesia which by sympathetic blockade reduces the stress as well as tachycardia induced by it. The institute also has a low threshold for prophylactic mini-tracheostomy for bronchial clearance to prevent sputum retention atelectasis and hypoxia which contribute to tachycardia and arrhythmia.

7. Study limitations

This is a retrospective study involving a single institution. Due to the nature of cardiac disease there is a certain amount of surgical preselection in the population. The propensity score only analyses data captured on the surgical database. It has its own limitations and the findings are never as robust as a randomised controlled trial. We also have not included the patients with valvular heart disease in the study due to inadequate data.

8. Conclusions

In our experience, in-hospital mortality and morbidity after lung resection for NSCLC in patients with cardiac comorbidity is not significantly different from those patients without cardiac comorbidity in a propensity-matched population. This is presumably due to appropriate selection and perioperative care of those patients with IHD who undergo surgery. The 3-year survival for both the groups is the same. Patients should therefore not be denied surgery for cardiovascular comorbidities alone.

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References


