The risk of bilobectomy compared with lobectomy: a retrospective analysis of a series of matched cases and controls†

María Teresa Gómez, Marcelo Fernando Jiménez, José Luis Aranda, María Rodríguez, Nuria María Novoa and Gonzalo Varela*

Service of Thoracic Surgery, Salamanca University Hospital, Salamanca, Spain

* Corresponding author. Service of Thoracic Surgery, Salamanca University Hospital, Paseo de San Vicente 58, 37007 Salamanca, Spain. Tel/fax: +34-923-291383; e-mail: gvs@usal.es (G. Varela).

Received 12 July 2013; received in revised form 22 September 2013; accepted 26 September 2013

Abstract

OBJECTIVES: Bilobectomy is considered to be a risky procedure due to space mismatch between the pleural space and the remnant lung. The objective of this study was to evaluate if postoperative complications related or not to size mismatch are more frequent after bilobectomy compared with right lobectomy cases.

METHODS: Retrospective case-control study on a series of matched non-small-cell lung cancer patients. Cases were patients who underwent right bilobectomy (upper and middle or lower and middle) and controls, patients who underwent right upper or lower lobectomy. Cases and controls were matched by propensity scoring according to site, age, ppoFEV1, type of postoperative management (intensive physiotherapy or not), cardiac comorbidity and pT status. We selected two primary outcomes for comparison: occurrence of any cardiorespiratory complication and occurrence of any complication related to space discrepancies. For the latter, all complicated case records were reviewed and two blinded observers agreed on the probability of each complication to be related to space discrepancies. Agreement was measured by the $\kappa$ statistic. The overall odds ratio (OR) and 95% confidence interval (CI) for each outcome were calculated on 2 × 2 tables for the whole population and for cases with upper or lower resections.

RESULTS: The study included 689 patients: 572 right lobectomy (419 upper and 153 lower) and 117 bilobectomy cases (30 upper and lower and middle lobectomy, including 87 lower and 30 upper). The overall mortality rate of the series was 2.03% (14/689), and cardiorespiratory complications were recorded in 14.4% (99/689) and space-related complications in 19.59% (135/689) cases. Both observers agreed on space-related complications in 86% of the 135 cases ($\kappa$: 0.72). After matching, 234 cases entered the study (117 with right lobectomy, including 83 lower and 34 upper, and 117 with bilobectomy, including 87 lower and 30 upper). The prevalence of cardiorespiratory complications was higher after lower and middle lobectomy compared with lower lobectomy ($P = 0.0002$; OR: 7.96, 95% CI: 2.19–43.16). No differences were found in death rates or in space-related complications between groups of lobectomy and bilobectomy cases.

CONCLUSIONS: This study failed to demonstrate a higher space-related complication rate in bilobectomy cases but cardiorespiratory complications were statistically higher after lower and middle lobectomy compared with lower lobectomy in matched cases.

Keywords: Lung resection • Bilobectomy • Surgical risk • Operative morbidity • 30-day mortality • Postoperative morbidity

INTRODUCTION

The resection of a considerable amount of lung parenchyma in one hemithorax is expected to be followed by a high rate of the so-called space-related complications. Discrepancies between the size of the pleural cavity and the remnant lung in these patients are considered the cause of some specific complications such as prolonged air leak (PAL), atelectasis and symptomatic pneumothorax. For these reasons, several authors have recommended the practice of pneumoperitoneum [1–3] or other measures [4, 5] after bilobectomy to reduce the adverse effects of size discrepancies. This study was designed to compare the postoperative outcomes of bilobectomy and right lobectomy cases in terms of prevalence of space-related complications, cardiorespiratory complications and operative mortality.

PATIENTS AND METHODS

The investigation was designed as a retrospective study of cases and controls on a prospectively recorded database of patients...
operated on for lung carcinoma between 1994 and 2012. For this study, only records of patients who underwent right pulmonary resection different to pneumonectomy or middle lobectomy were selected. The surgical technique included a muscle-sparing posterior or axillary approach in all cases. Besides a careful technique, no standardized policy was adopted to prevent postoperative air leak and pneumothorax was never indicated as a preventive measure. One single chest tube under passive suction by gravity was left in place in all patients.

For this investigation, cases with extended surgery to the chest wall or the diaphragm were excluded. Patients with upper and middle or lower and middle lobectomy constitute the ‘case’ series, while patients with either upper or lower lobectomy are the ‘controls’. We compared the prevalence of two primary outcomes in each series of cases: the occurrence of any cardiorespiratory complication and the occurrence of any complication related to space discrepancies. All complications were defined in advance and recorded prospectively. The quality of the records was audited twice by a data manager: first at patient discharge from the hospital, and second, at the time the definitive pathological report was available, usually no more than 7 days after patient discharge.

The following cardiorespiratory complications were considered: pulmonary atelectasis requiring specific therapy, nosocomial pneumonia (according to the updated Centers for Disease Control and Prevention and National Healthcare Safety Network (CDC/NHSN) definitions [6]), respiratory or ventilatory insufficiency at discharge (PO2 under 60 mmHg or PCO2 over 45 mmHg), need of mechanical ventilation at any time after extubation in the operating theatre, pulmonary thromboembolism, brain stroke, cardiac arrhythmia, myocordial ischaemia or infarct and clinical cardiac insufficiency.

The following were considered complications potentially due to space mismatch: PAL (defined as the persistence of air leak through the chest tubes after 5 days of the operation), pulmonary atelectasis requiring aspiration bronchoscopy and pneumothorax with or without air leak requiring drainage at the criteria of the surgeon in charge of the ward. Two of the authors (Nuria María Novoa and Gonzalo Varela) independently reviewed all records and classified each of the aforementioned complications as space related or not. In case of discrepancies between both investigators, the records were reviewed again and the senior author’s opinion prevailed. The non-weighted \( \kappa \) agreement coefficient was calculated in the usual way [7].

Cases and controls were matched by propensity scores, calculated by the nearest neighbour method, descending with no replacement. The following variables entered in a non-parsimonious regression model considering the type of therapy received (bilobectomy or right lobectomy) as the dependent variable and including the following covariates: site of the resection (upper or lower), age of the patient at the time of surgery, estimated postoperative FEV1\% (ppoFEV1\%), type of postoperative management (intensive physiotherapy or not), cardiac comorbidity and tumour size.

Cardiac comorbidity was considered as a binary variable (0/1) following the European Society of Thoracic Surgeons (ESTS) risk model for prediction of cardiorespiratory morbidity after lung resection [8]. Patients were classified as ‘1’ if any of the following diseases were in the records: coronary artery disease, previous cardiac surgery, hypertension, congestive heart failure and arrhythmia requiring treatment. Tumour size was also categorized as a binary variable according to pT classification. pT0-pT1a were classified as ‘1’, and pT1b and over as ‘0’.

After matching, odds ratios (ORs) with 95% confidence intervals (CI) for cardiorespiratory and space-related morbidity were calculated twice: first for all cases and controls and then separately for upper and lower resections. If the 95% CI included the unit, the size of the sample needed for \( \alpha = 0.05 \) and \( \beta = 0.85 \) was calculated; this was done to estimate the risk of type II, or false negative error before stating the conclusions of the investigation.

Matching was performed by propensity scores using the psmatch2 module [9] for the statistical package Stata®12. Calculations of \( \kappa \) coefficient, ORs on contingency \( 2 \times 2 \) tables and number of cases were also done with Stata®12.

RESULTS

The study included 689 patients: 572 right lobectomy (419 upper and 153 lower) and 117 bilobectomy cases (30 upper and middle and 87 lower and middle). The mean hospital stay was 7 days for both series (rank 4–34 days for lobectomy and 4–40 days for bilobectomy cases). After matching, 234 cases were selected (117 with right lobectomy, including 83 lower and 34 upper, and 117 with bilobectomy, including 87 lower and 30 upper). The descriptive characteristics of the series before and after matching cases and controls are given in Table 1. In Table 2, the variables of the matched series of cases grouped by the site of lung resection are presented. Overall mortality of the series was 2.03% (14/689), cardiorespiratory complications were recorded in 14.4% (99/689) and space related complications in 19.59% (135/689) cases. Both observers agreed on space-related complications in 86% of the 135 cases (\( \kappa = 0.72 \)). The outcomes of the matched cases are given in Table 3, distributed according to the site of lung resection. The prevalence of cardiorespiratory complications was higher after lower and middle lobectomy compared with lower lobectomy (\( \beta = 0.0002; \) OR: 7.96, 95% CI: 2.19–43.16). No differences were found in death rates or in space-related complications between cases and controls. The number of cases needed for statistical differences in outcomes is given in Table 3. It is important to underline that, in upper resections, the same difference in space-related complications would have reached statistical significance only with 151 cases per arm (the current series includes 34).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (bilobectomy) (n = 117)</th>
<th>Controls (right lobectomy) (n = 572)</th>
<th>Matched controls (right lobectomy) (n = 117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median (range)</td>
<td>64.3 (27.5–83.8)</td>
<td>64.6 (24.4–84.6)</td>
</tr>
<tr>
<td>ppoFEV1%</td>
<td>n (%)</td>
<td>56.1 (27.6–96.5)</td>
<td>64.4 (29–121.6)</td>
</tr>
<tr>
<td>Cardiac risk*</td>
<td>n (%)</td>
<td>31 (26.5)</td>
<td>181 (31.6)</td>
</tr>
<tr>
<td>pT1a–pT2a</td>
<td>Physio#</td>
<td>94 (80.3)</td>
<td>492 (86)</td>
</tr>
<tr>
<td>pT1b–pT4a</td>
<td>Physio#</td>
<td>66 (56.4)</td>
<td>375 (65.6)</td>
</tr>
</tbody>
</table>

*Cases with cardiac comorbidity: coronary artery disease, previous cardiac surgery, arrhythmia, cardiac failure and hypertension.

\#Physio: cases treated under a specific programme of intensive physiotherapy.
perfect, demonstrating the differentiation. As we have shown, the interobserver agreement is not investigated in our group independently classifying correctly a postoperative event as a consequence of the lung being unable to fill up the pleural cavity. To avoid the subjective assignment of adverse postoperative events to space problems, two investigators in our group independently classified each complication. As we have shown, the interobserver agreement is not perfect, demonstrating the difficulties encountered in the task even among surgeons working in the same team; nevertheless, discrepancies were present only in 14% of the cases and the κ index, a valid and reliable measure of inter-rater agreement [11], was more than acceptable.

In our investigation, we have selected only 117 of 572 right lobectomy cases to be matched against bilobectomy patients and it could be argued that we are losing relevant information from excluded patient records. To avoid misleading comparisons, matching cases by propensity scoring has been proposed as a valid method for causal studies in the absence of randomized trials [11]. To implement matching, each case in the experimental group can be matched against one or multiple controls. Using a single comparison unit, the smallest propensity score distance between cases and controls is obtained and also the risk of biasing the population is decreased [12]. Another point to be discussed is the selection of variables to be included in the propensity score model. There is no consensus in the literature on the best variables to be selected and, in fact, the investigators can include all baseline covariates, all related to the outcome according to the literature or all covariates related to treatment assignment [13, 14].

In our study, we have decided to include all variables potentially related to the primary outcomes. For doing so, we have used covariates entering the ESTS risk model [8] (age, cardiac comorbidity and ppoFEV1) plus the site of the resection (upper or lower), the size of the tumour (which could be related to a more difficult or

### Table 2. Descriptive characteristics of the matched series grouped by site of the lung resection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (bilobectomy) (n = 117)</th>
<th>Matched controls (right lobectomy) (n = 117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Upper (n = 30)</td>
<td>Lower (n = 87)</td>
</tr>
<tr>
<td></td>
<td>Median (range)</td>
<td>Median (range)</td>
</tr>
<tr>
<td>Age</td>
<td>63.5 (35.4–76.8)</td>
<td>65.6 (27.5–83.8)</td>
</tr>
<tr>
<td>ppoFEV1%</td>
<td>58.2 (27.6–87.7)</td>
<td>55.1 (28.7–97.5)</td>
</tr>
<tr>
<td>Cardiac risk*</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Upper</td>
<td>6 (20)</td>
<td>1.2 (0.57–2.6)</td>
</tr>
<tr>
<td>Lower</td>
<td>25 (83.3)</td>
<td>5 (14.7)</td>
</tr>
<tr>
<td>pT1a-pT2a</td>
<td>25 (83.3)</td>
<td>24 (70.6)</td>
</tr>
<tr>
<td>Physio*</td>
<td>15 (50)</td>
<td>17 (50)</td>
</tr>
<tr>
<td>Upper</td>
<td>55 (66.3)</td>
<td>51 (58.6)</td>
</tr>
</tbody>
</table>

*Cases with cardiac comorbidity: coronary artery disease, previous cardiac surgery, arrhythmia, cardiac failure, hypertension.

**Physio**: cases treated under a specific programme of intensive physiotherapy.

### Table 3. Prevalence of 30-day death, cardiorespiratory complications and space-related complications in matched cases. Overall data and grouped by site of lung resection

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Site</th>
<th>Lobectomy cases/total (%)</th>
<th>Bilobectomy cases/total (%)</th>
<th>OR (95% CI)</th>
<th>Cases needed*</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day death</td>
<td>All</td>
<td>2/117 (1.7)</td>
<td>3/117 (2.5)</td>
<td>1.51 (0.17–8.39)</td>
<td>6015</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>2/34 (5.9)</td>
<td>1/30 (3.3)</td>
<td>0.55 (0.01–1.22)</td>
<td>1240</td>
</tr>
<tr>
<td></td>
<td>Lower</td>
<td>0/83 (0)</td>
<td>2/87 (2.3)</td>
<td>NA</td>
<td>468</td>
</tr>
<tr>
<td>Cardiorespiratory morbidity</td>
<td>All</td>
<td>11/117 (9.4)</td>
<td>26/117 (22.2)</td>
<td>2.75 (1.23–6.51)*</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>8/34 (23.5)</td>
<td>6/30 (20)</td>
<td>0.81 (0.2–3.14)</td>
<td>2551</td>
</tr>
<tr>
<td></td>
<td>Lower</td>
<td>3/83 (3.6)</td>
<td>20/87 (22.9)</td>
<td>7.96 (2.19–43.16)**</td>
<td>-</td>
</tr>
<tr>
<td>Space-related morbidity</td>
<td>All</td>
<td>18/117 (15.4)</td>
<td>21/117 (17.9)</td>
<td>1.2 (0.57–2.55)</td>
<td>4066</td>
</tr>
<tr>
<td></td>
<td>Upper</td>
<td>8/34 (23.5)</td>
<td>3/30 (10)</td>
<td>0.36 (0.07–1.75)</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>Lower</td>
<td>10/83 (12)</td>
<td>18/87 (20.7)</td>
<td>1.9 (0.77–4.8)</td>
<td>346</td>
</tr>
</tbody>
</table>

*Number of cases needed for two-sided α = 0.05 and β = 0.85.

P = 0.0002 and **P = 0.0072.

### DISCUSSION

Bilobectomy is a good therapeutic option for patients with lung cancer invading both superior and middle or lower and middle lobes. Long-term survival after bilobectomy is comparable with lobectomy [10]. Nevertheless, bilobectomy encompasses a higher immediate risk for the patient, as has been reported previously [4, 5, 10]. Current overall morbidity for bilobectomy is around 50% and some authors have also found that middle–lower bilobectomy is followed by a higher rate of complications, as it happened in our series [10].

Immediately after bilobectomy, an evident mismatch between the size of the pleural cavity and the lung is produced. This space problem has been considered responsible for several types of pleural and pulmonary complications; but, although frequently quoted, the risk of these complications has not been quantified in the literature and this is why our report could be considered complementary to previously published ones. The first problem when talking on space-related complications is classifying correctly a postoperative adverse event as a consequence of the lung being unable to fill up the pleural cavity. To avoid the subjective assignment of adverse postoperative events to space problems, two investigators in our group independently classified each complication. As we have shown, the interobserver agreement is not perfect, demonstrating the difficulties encountered in the task...
prolonged procedure) and, finally, the type of postoperative management since we have previously demonstrated lower postoperative risk in cases under an intensive programme of perioperative physiotherapy [15].

Some limitations to our study have to be commented upon, the first one being the type of complications we have included in the analysis. As we have shown, both observers agreed on atelectasis as one of the space-related complications in some patients, but it could be argued that bronchial obstruction leading to atelectasis is not a space-related problem. Our understanding when we agreed on atelectasis was that, in specific cases, the lack of negative pleural pressure and residual pneumothorax was the first step leading to partial lung collapse. Also, the readmission rate could be investigated as a delayed complication. Unfortunately, we lack complete information on the causes for readmission in some patients and so we could not investigate this problem.

To conclude, we have not found a higher risk of postoperative complications related to space mismatch after bilobectomy. This finding could be biased by non-recorded especially vigorous postoperative physical therapy by the nursing team in bilobectomy patients, but this confounding factor is non-controllable. It is relevant to underline the risk of type II error in our conclusions since the difference in the rates of space-related complications in upper resections would be statistically different studying a series of around 150 cases per arm. Owing to the low rates of bilobectomy in single institutional reports, our findings could be tested in multi-institutional databases.

Conflict of interest: none declared.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr M. Refai (Ancona, Italy): A very interesting topic. I want to ask you one question. Did you include the patients who received induction treatment in your study?

Dr Gómez-Hernández: This is a good point to discuss. In fact, several authors have published that the performance of a bilobectomy in the setting of sleeve resection or induction therapy can be considered a risk factor that increases morbidity and mortality. But other authors more recently, such as Galetta et al. and Kim et al., have published in their series that sleeve resection and induction chemotherapy are not associated with a higher incidence of complications in the setting of a bilobectomy.

In our series, the induction therapy rate in bilobectomy patients was around 10% or 11% and in right lobectomy patients it was around 5%. So we didn’t have enough patients to achieve a significant conclusion, but maybe it will be a good point to investigate in future studies.

Dr H. Fernando (Boston, MA, USA): You demonstrated a difference in cardiorespiratory complications but not in space-related complications. So that begs the question, how did you define a space-related complication? And did you also measure prolonged air leak as well as prolonged duration of chest tubes, because that could be something potentially related?

Dr Gómez-Hernández: As I said before, two observers on our team defined the space-related complications. They reviewed all the records and they classified all complications as space-related or not. At the end, persistent air leak through the chest tube over five days was considered a space-related complication, as well as atelectasis requiring bronchoscopy, and pneumothorax. We maintained the chest tube over five days in case of persistent air leak.

Dr Fernando: Can you repeat that? What were the factors that you specifically used to define space problems, atelectasis and prolonged air leak?

Dr Gómez-Hernández: Air leak over five days.

Dr A. Torna (İstanbul, Turkey): It is very surprising to see that the rate of space-related complications was not higher in the bilobectomy patients. Did you take any preventive measures during bilobectomy, such as pneumoperitoneum or pleural tenting?

Dr Gómez-Hernández: No.

Dr Torna: Otherwise, did you free the pulmonary ligament during right upper lobectomy?

Dr Gómez-Hernández: In general, we didn’t use a special technique to reduce chest cavity volume. We do the the same in lobectomy and bilobectomy cases. We don’t perform pleural tent, pneumoperitoneum or phrenic nerve paralysis. In relation to the ligament, we never free the ligament to allow the lung to move.

Dr E. Lim (London, UK): I have two brief questions. One is, when we do matching or propensity score matching in general, we normally account for differences in which a patient can have two different treatments. Say, for example, you have a right upper lobe cancer, some people get VATS lobectomy, some people get open lobectomy. In this case, whether you have a bilobectomy or lobectomy, it cannot be controlled. You either need a bilobectomy or you need a lobectomy. So I don’t understand why you then had to match the patients, because, after all, you are looking at a volume/space discrepancy which will be applicable for two populations which don’t need to be matched.

Dr Gómez-Hernández: In the matching process, we selected all variables that we considered could be potentially related with the outcomes, and for that reason we chose the age, the site of the tumour, and so on. The aim of the matching was avoiding all variables that could be related to the outcomes that we were analysing.

Dr Lim: And my second question is, because you have introduced matching in circumstances where matching may not be required, sometimes as a process of matching you reduce the group size into a smaller group and sometimes you introduce bias. So, for example, I would be interested to see if you repeat your analysis without matching whether your cardiopulmonary complications still remain the same or is it because you have actually inadvertently matched a small population with a high burden of cardiopulmonary complications?

Dr Gómez-Hernández: I don’t know. We will have to redo the analysis without matching. Otherwise we tried it with other matching methods, and the conclusions were similar.