The influence of open-heart surgery on survival of patients with co-existent surgically amenable lung cancer (stages I and II)

A.J. Voets a, K. Sheik Joesoef b,*, M.E.J.M. van Teeffelen a

a Department of Pulmonology, Thoraxcentrum, Medisch Centrum de Klokkenberg, Galdersweg 81, 4836 AE Breda, The Netherlands
b Department of Cardiology, Thoraxcentrum, Medisch Centrum de Klokkenberg, Galdersweg 81, 4836 AE Breda, The Netherlands

Received 28 January 1997; received in revised form 30 June 1997; accepted 30 July 1997

Abstract

Objective: The evaluation of the influence of open-heart surgery on the survival of patients with co-existent surgically amenable lung cancer stages I and II. Methods: A retrospective, observational study was conducted in a tertiary centre for cardiothoracic surgery. From 1988 to 1995, 121 consecutive patients underwent pulmonary resection for stages I–II primary non-small cell bronchogenic carcinoma. Eighty seven of them had merely a lung carcinoma necessitating resection, 34 had in addition defined coronary-artery disease and consequently were also subjected to open-heart surgery. Results were statistically computed. Results: Follow-up was complete in 117:121 patients, 96.7% (83:87, 95.4% and 34:34, 100% in respective groups). Both groups were matched with regard to preoperative features possibly influencing survival. Median long term survival time was 4.3 years overall, 5.8 years for patients merely undergoing lung resection and 4.2 years for them undergoing open-heart surgery as well; this difference was not statistically significant (log-rank test: $\chi^2 = 0.92$, df = 1, $P = 0.34$), indicating no or limited influence of open-heart surgery on survival of patients with surgically amenable co-existent lung carcinoma. No relationship was found between survival and age, tumour stage, and histopathology. However, metastatic disease as cause of death was significantly increased in patients undergoing open-heart surgery (5:8 vs. 10:33, $P = 0.0898$), indicating a possible promotion of metastatic spread of co-existent lung carcinoma by this procedure. Overall perioperative mortality rate was 10:121, 8.3%, for the greater part the result of a relatively high mortality rate in the group of patients undergoing heart as well as lung surgery (6:34, 17.6%), underscoring the great risks involved in these patients, the mortality rate for lung resection alone being comparably low 4:87, 4.6% ($P = 0.0191$). Conclusion: Open-heart surgery for defined coronary-artery disease in patients with surgically amenable lung carcinoma carries a substantially higher perioperative risk, but has no influence on long term results. Metastatic spread is possibly promoted by open-heart surgery. Optimal treatment, consisting of complete revascularization and appropriate lung resection, is therefore sufficiently justified by these results. © 1997 Elsevier Science B.V.

Keywords: Lung resection; Primary bronchogenic carcinoma; Open-heart surgery; Coronary artery disease

1. Introduction

Coronary-artery disease constitutes a major operative risk factor in patients undergoing non-cardiac surgery [1,9]. Prior revascularization seems to confer a protective effect and therefore, ‘prophylactic’ bypass surgery has been advocated [7,11]. In patients with synchronously occurring heart disease and another ailment, for which surgery is indicated, at the same time, surgical treatment can be achieved in either a staged or a concomitant procedure. The feasibility of concomitantly performed coronary-artery bypass grafting and lung resection for carcinoma has also been repeatedly reported, with overall satisfying results [2,26]. We have already reported our experience with this group of patients in a separate paper in this journal [24].
The influence of coronary vascular disease on the prospects of patients with lung cancer has also been studied before [14,21,23]. These studies, however, do not take into account the possible role of open-heart surgery itself, where promotion of growth and spread of the synchronously present carcinoma caused by the extracorporeal circulation is postulated [2,19,26]. This could show not only by worse long term results, but also by an increase of metastatic disease in the group of patients undergoing open-heart surgery with co-existent carcinoma. Yet, if such a role would exist and extracorporeal circulation would have such a deleterious effect, this will have major implications for treatment and prognosis of this particular subset of patients.

We therefore examined our experience, with special reference to this subject, on which we like to report here.

2. Materials and methods

From 1 January, 1988, to 1 March, 1995, a total of 121 consecutive patients with lung carcinoma stages I and II underwent lung resection. In 87 of them there was no suspicion of coronary-artery disease, so these patients were only subjected to lung resection; 34 of them, however, did have defined coronary-artery disease (2 of them had valvular problems), so they consequently underwent CABG (or valvuloplasty) and lung resection. In almost all of them an asymptomatic pulmonary nodule was discovered during preoperative examination; laboratory studies including liver function tests, chest X-ray and computed tomography were normal. Two patients had a history of recurrent chest pain, indicating possible coronary-artery disease.

Preoperative assessment included: history; physical examination; laboratory studies including liver function tests; twelve-lead electrocardiography; X-ray of thorax; spirometry, excluding patients with FEV1 < 2.0 l; endoscopic bronchoscopy; mediastinoscopy or CT-scanning of mediastinum; ultrasonography of the upper abdomen (if indicated); skeletal scintigraphy (if indicated); and coronary angiography (if indicated). Operative procedures were standard; open-heart surgery was performed either concomitantly (n = 24), or in a staged procedure (n = 10) with lung resection (mean interval 33.9 ± 34.7 days). Postoperatively all patients were initially taken care of in the intensive care unit, until their clinical condition had stabilized sufficiently to warrant transfer to the regular ward. Eventual hospital discharge was also primarily guided by clinical parameters.

By reviewing medical files the following features were recorded: age; gender; location of tumour; extent of lung resection; pTNM (using standard TNM-classification [12]); histopathology (squamous cell carcinoma, adenocarcinoma, or other); perioperative complications (none, minor complications like supraventricular arrhythmias or respiratory infections, or major complications like rebleeding necessitating reoperation, and pulmonary embolism or myocardial infarction causing death); postoperative hospital stay; perioperative mortality (defined as within 30 days after operation or in the same hospitalization period); and long term follow-up. Any features missing were, if possible, supplied by the primary responsible general practitioner, or the referring institute, or the Registry Office. Long term follow-up could be obtained in 117 of 121 patients, 96.7% (83/87, 95.4% in group A; 34/34, 100% in group B). Zero time was the date of lung resection, the final censoring date regarding survival was 1 July, 1995.

The results were statistically computed. Comparisons were made using \( \chi^2 \)-test, Student’s t-test, or Wilcoxon signed-rank test. Actuarial survival curves were plotted according to Kaplan and Meier, with the perioperative deaths included in the analysis. Survival curves of various groups of patients were compared using the log-rank test. Statistical significance is \( p < 0.05 \), unless stated otherwise.

3. Results

A total of 117 patients was eligible for analysis, 83 undergoing merely lung resection because of stage I–II bronchogenic carcinoma and 34, having defined coronary-artery disease at the same time, being subjected to open-heart surgery in addition. Patients were randomly distributed throughout the entire study period. The characteristics of these patients are listed in the table. The patients in these two distinct groups were preoperatively fully comparable with respect to age, gender, histopathology, tumour extent, and tumour location (Table 1). Perioperatively there existed, however, major differences in type of resection (lesser resections in the group with combined heart–lung surgery, \( P < 0.025 \)) and complication rate (more in this same group, \( P < 0.001 \)).

The overall median survival time is 4.3 years, the actuarial survival curve is depicted in Fig. 1. The survival curves for the two distinct patient groups (merely lung resection, median survival time 5.9 years vs. combined heart–lung surgery, median survival time 4.2 years) are depicted in Fig. 2. A comparison between the survival curves of these two groups showed no statistical significant difference (log-rank test: \( \chi^2 = 0.92, \text{df} = 1, P = 0.34 \)). Late deaths were in a vast majority of cases attributable to the lung cancer (patients undergoing merely lung resection: 30/33, 10 patients died of metastases, 20 of recurrent disease; 1 patient died after a cerebrovascular accident, cause of death in the remaining 2 patients is unknown; patients subjected to combined heart–lung surgery: 6/8, 5 patients had metastatic disease, 1 recurrent, in 2 patients cause of death is unknown). The rate of occurrence of metastatic disease was significantly higher in this latter group of patients (5/8 vs. 10/33, \( P = 0.0898 \)).
The overall perioperative mortality was 10/121, 8.3%. There is, however, a major, statistically significant, difference in mortality rates between the group of patients merely undergoing lung resection, 4/87, 4.6%, and the group with patients who underwent combined heart–lung surgery, 6/34, 17.6% (P = 0.0191). This latter figure is mainly caused by the high perioperative mortality rate in the subset of patients undergoing a concomitant heart–lung surgical procedure (5/24, 20.8%). Causes of death were in the group of patients merely undergoing lung resection myocardial infarction in three and multiple organ failure related to empyema in 1 patient; in the group of patients undergoing combined heart–lung surgery heart failure in 1, myocardial infarction in 1, hypovolemic shock after rebleeding in 1, and multiple organ failure, possibly related to sepsis in 3 patients.

An analysis was made of a possible relationship between survival and age (≤ 66.5 vs. > 66.5 years—this being the median age of the patients, $\chi^2$ 0.10, df = 1, $P = 0.75$); survival and histopathology (squamous cell carcinoma vs. adenocarcinoma, $\chi^2$ 2.57, df = 1, $P = 0.11$; adenocarcinoma vs. squamous and other carcinoma, $\chi^2$ 2.63, df = 1, $P = 0.11$); survival and gender (male vs. female, $\chi^2$ 3.26, df = 1, $P = 0.07$); and survival and extent of tumour (stage I vs. stage II, $\chi^2$ 0.05, df = 1, $P = 0.82$). Such a relationship could not be demonstrated, although an association between survival and gender is suggested.

### Table 1
Pre- and perioperative characteristics of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Merely lung resection</th>
<th>Combined heart–lung surgery</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>83</td>
<td>34</td>
<td>—</td>
</tr>
<tr>
<td>Mean (± S.D.)</td>
<td>65.2 ± 8.3</td>
<td>67.1 ± 6.7</td>
<td>ns</td>
</tr>
<tr>
<td>Gender male/female</td>
<td>75/8</td>
<td>31/3</td>
<td>ns</td>
</tr>
<tr>
<td>T 1/2</td>
<td>34/49</td>
<td>17/17</td>
<td>ns</td>
</tr>
<tr>
<td>N 0/1</td>
<td>53/30</td>
<td>27/7</td>
<td>ns</td>
</tr>
<tr>
<td>Lung left/right</td>
<td>41/42</td>
<td>13/21</td>
<td>ns</td>
</tr>
<tr>
<td>Lobectomy/bilobectomy/pneumonectomy</td>
<td>45/15/24$^a$</td>
<td>27/4/2$^b$</td>
<td>0.0069/0.0071</td>
</tr>
<tr>
<td>Squamous cell carcinoma/adenocarcinoma/other</td>
<td>57/18/8</td>
<td>19/9/6</td>
<td>ns</td>
</tr>
<tr>
<td>Complications none/minor/major</td>
<td>47/32/4</td>
<td>9/16/9</td>
<td>0.0030/0.0007</td>
</tr>
<tr>
<td>Postoperative hospitalstay (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>14</td>
<td>16.5</td>
<td>ns</td>
</tr>
<tr>
<td>Range</td>
<td>(1–100)</td>
<td>(1–172)</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ One patient underwent a wedge resection.

$^b$ One patient died before undergoing lung resection.

4. Discussion

The results of surgical treatment of lung carcinoma have been extensively discussed after the introduction of the new international TNM-classification, now about a decade ago [12]. This classification is thoroughly...
artery disease in addition to co-existent lung carcinoma, substantially higher in patients with defined coronary-artery disease [23]. Even though we can not show any difference in survival between stages I and II, possibly because of the relatively limited number of patients, our results are nevertheless in a comparable range as reported in these studies, as well as with others [6]. Our findings with regard to perioperative mortality rate are in keeping with those reported from academic centers elsewhere [6,8,18], and even better compared to those from community hospitals [17]. In view of the sometimes conflicting results in the literature, it is by no means surprising that no influence on survival could be demonstrated of patient age [5,10,18,22,25], histopathology of tumour [10,15,16,20], patient gender [10,25], or type of resection [10,25].

The influence of coronary-artery disease on the prognosis of patients with lung carcinoma has already been the subject of study before [14,21,23]. Nataf et al. reported on a series of 51 patients undergoing lung resection for lung cancer with coronary disease. Forty-nine of them had lung surgery alone, in 5 preceded by PTCA, and only 2 patients underwent open-heart surgery. Follow-up was limited to only 3 months, but the results were excellent [14]. Thomas et al. describe out of a total of 462 patients, who underwent lung resection, 80 patients with concomitant atherosclerosis, in 32 of them involving mainly the coronary arteries. The mortality rate was significantly higher (10% in those with vs. 4.7% in those without atherosclerosis), but the long term survival was not negatively influenced by the presence of the vascular disease [21]. In a later study the same group of investigators report on a smaller group of 21 patients, with resectable non-small cell lung cancer and defined coronary-artery disease, of which only 3 underwent open-heart surgery. The overall results are satisfying, and, as before, it is concluded that they justify the surgical treatment of the lung carcinoma in patients with coronary-artery disease [23].

However, our study addresses another important aspect of this problem. It reports on the influence not only of the disease process itself, but also on the influence of open-heart surgery on the prognosis of these patients. The retrospective observational character of our study poses of course strong limitations to the interpretation of results and the conclusions to be drawn. One could even argue that the patients in our study undergoing a combined heart–lung operation should have done better, since they mostly had asymptomatic nodules necessitating lesser resections than the other group of patients, suggesting earlier detection of the carcinoma, although this was not reflected in the eventual pTNM-classification. Nevertheless our results still do point in the same direction as indicated by previous studies. Perioperative mortality rates are substantially higher in patients with defined coronary-artery disease in addition to co-existent lung carcinoma, especially in those undergoing a concomitant heart–lung procedure. This underscores the much greater risks involved in these patients not just because their clinical condition may be worse as a consequence of this extra disease, but also as a result of the combined heart–lung operation itself. This is also reflected in the significantly higher complication rate. On the other hand, long term survival, which is mainly determined by the lung carcinoma, does not seem to be negatively influenced by heart surgery. Therefore, coronary bypass surgery, which is of course essentially palliative in nature, is well justified in these patients. A point of major concern is the increase in metastatic disease as cause of death, presumably related to the extracorporeal circulation used during the open-heart surgery [2,19,26]. Further studies, confirming this association, are needed for a definitive statement in this regard, and perhaps in the future in selected patients bypass surgery without the use of extracorporeal circulation will have to be taken into consideration.

It is therefore concluded that optimal treatment for patients with synchronously occurring coronary-artery disease and surgically amenable lung carcinoma—and that should consist of complete revascularization and appropriate lung resection for the two conditions, respectively—is fully warranted by these results. This combined approach carries, however, a greater perioperative risk, and possibly promotes metastatic spread of the co-existent lung carcinoma. Further study is needed to clarify this last issue.

Acknowledgements

We express our thanks to W. Devillé, M.D., for his help in preparing this manuscript.

References


