Inhalation with Tobramycin® to improve healing of tracheobronchial reconstruction

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Abstract

Objective: Sleeve resections were introduced to preserve lung function in patients with limited pulmonary reserve. Ischaemia and infection of the distal part of the anastomosis is the leading cause of bronchial anastomotic leakage. We have learned from our experience in lung transplantation that inhalation with Tobramycin® helps prevent anastomotic insufficiency. We would like to present our experience in patients with tracheobronchial sleeve and prophylactic Tobramycin® inhalation. Patients and methods: Retrospective analysis of 114 patient records, between 01.01.2005 and 31.12.2006, where a bronchial anastomosis (patients with tracheal resection were excluded) was performed. All patients received Tobramycin® inhalation (2 × 80 mg) for 7 days. Data analysed were; length of chest tube drainage in days, complications, morbidity and hospital mortality.

Results: In 694 patients, an anatomic resection was performed. Of these, 114 (16%) were sleeve resections and 63 (9%) pneumonectomies. In 21 women and 93 men, between 25 and 84 years old, sleeve lobectomy was performed 104 times and carinal resection 10 times. A preoperative neoadjuvant therapy had been given in 26%. Radical (R0) resection was possible in 94%. The duration of the operation was between 83 and 225 min (median: 127 min). Chest tubes were removed on average after 6 days. Patients were discharged after 11 days. The rate of bronchial anastomotic leakage was 4.4%. There were two patients with postoperative respiratory insufficiency and mechanical ventilation, two patients with technical failure required early correction of the suture and one patient with a necrosis of the anastomosis. Thirty-day hospital mortality was 2.6% (3/114).

Conclusions: Increasing experience with sleeve resection has reduced the rate of pneumonectomy below 10%, although a number of the patients had received neoadjuvant therapy and the carinal resection rate of necrosis and infection of the anastomosis was low. We therefore recommend use of local antibiotic inhalation after sleeve resection.

Keywords: Lung cancer surgery; Nebulised antibiotics; Sleeve resection

1. Introduction

Sleeve lobectomy has become a leading method suitable in terms of radicality for resection of bronchial carcinoma in all patients regardless of their lung function [1–3]. Initially, compared with pneumonectomy, it was proven to have a better long-term survival and quality of life [2]. We have therefore increased our percentage of sleeve lobectomies and reduced the total number of pneumonectomies. Anastomotic insufficiency remains a major concern, which may compromise successful treatment. Ischaemia and infection of the distal part of the anastomosis is the leading cause of bronchial anastomotic leakage. Revascularisation occurs within 4 and 5 days from the surrounding tissue [4,5]. We have learned from our experience in lung transplantation that inhalation with Tobramycin® helps prevent anastomotic insufficiency. Protection of the ischaemic tissue during this time may prevent infection and be the clue to reducing the rate of anastomotic insufficiency after sleeve resection. We would like to present our experience in patients with tracheobronchial sleeve and prophylactic Tobramycin® inhalation.

2. Patients and methods

Between January 2005 and December 2006, 694 patients underwent pulmonary anatomic resections with curative intent for bronchial carcinoma. The pneumonectomy rate was 63 (9%) and the total number of sleeve resection was 114 (16%) (Fig. 1). The data was collected retrospectively and analysed from the patient records.

Preoperative staging included a chest X-ray, computed tomography of the chest and upper abdomen, lung function test, arterial blood gases and perfusion scintigraphy of the lung when FEV1 was below 80%. Patients at a high risk of
coronary heart disease were screened by echocardiography, stress testing or coronary arteriography if appropriate. Bronchoscopy was performed for endobronchial staging and selection of the potential candidates for sleeve lobectomy.

All patients underwent double lumen endotracheal intubation. The routine approach was an anterolateral thoracotomy in the bed of the fifth rib. After complete exposure of the pulmonary artery, bronchus and vein, the final decision was taken as to whether sleeve lobectomy was feasible oncologically and technically. Care was taken to manipulate the tumour as little as possible and to preserve the bronchial blood supply. Resection of the main bronchus was performed proximally and distally to the lobar orifice for sleeve resection. A tension free bronchial anastomosis was performed with a continuous suture using absorbable 4/0 material (PDS®, Polydioxanon, Ethicon Products, GmbH) over the complete circumference. Suture lines were checked for air leaks with an airway pressure of 30 mmHg. The anastomosis was not covered. Systematic lymphadenectomy was performed for lymph node staging. Two chest tubes were placed, one anterolaterally and the second posterobasally. After sleeve resection routine prophylactic Tobramycin inhalation (2 × 80 mg) was given for 7 days. Routine postoperative bronchoscopy was performed in all patients on day 8 as a quality control.

Histological classification according to the TNM classification (1997) [6] was used to determine the stage of the disease. All patients were discussed in a tumour board to decide whether adjuvant chemotherapy or radiotherapy was indicated.

### 3. Results

Between 01.01.2005 and 31.12.2006 we performed sleeve resection in 114 patients, there being 93 (82%) men and 21 women. The overall median age was 63 years (range: 25—84 years). The sleeve resection was performed on the right side in 81 (71%) and on the left side in 33 patients. Histological spread is demonstrated in Table 1. In a quarter of the patients, neoadjuvant therapy had been administered (29/114) prior to surgery. The type of sleeve resection that was performed is listed in Fig. 1. R0-resection was achieved in 106 (94%) patients. Positive resection margins (R1) in the final histological examination were found in five patients. These patients had microscopic tumour cells in the peribronchial lymphatic vessels. In three patients, localised parietal pleura disease (R2) was discovered at thoracotomy, making radical resection impossible. In these cases, we performed sleeve resection to reduce tumour load. An enlargement of the procedure with combined resection of pulmonary artery, pericardium, atrium chest wall or diaphragm was required in 40%. Angioplastic procedures were necessary in 28/114 (25%). Operation duration was 83—225 min (median: 127 min). Chest tubes were removed in median after 6 days and hospital stay was 11 days.

All patients received Tobramycin inhalation (2 × 80 mg) for 7 days. There were no side effects documented. The rate of anastomotic insufficiency was 4.4% (5/114). There were

<table>
<thead>
<tr>
<th>Resection (114)</th>
<th>Number</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Lobectomy</td>
<td>90</td>
<td>79%</td>
</tr>
<tr>
<td>Bilobectomy</td>
<td>10</td>
<td>8%</td>
</tr>
<tr>
<td>Pneumonectomy + carina</td>
<td>6</td>
<td>5%</td>
</tr>
<tr>
<td>Lobectomy + carina</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Segmental</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Bronchial sleeve</td>
<td></td>
<td>2%</td>
</tr>
<tr>
<td>Carina</td>
<td>1</td>
<td>1%</td>
</tr>
</tbody>
</table>

Fig. 1. Overall sleeve resections performed between 2005 and 2006.

<table>
<thead>
<tr>
<th>Histology</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC (60%)</td>
<td>59</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>36</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>SCLC</td>
<td>14</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 1

Histological spread.
two patients with postoperative respiratory failure requiring mechanical ventilation, and two patients had a technical failure of the anastomosis that was immediately corrected on the following day after the operation. Only one patient had a true infection with necrosis of the anastomosis. The 30-day mortality was 2.6% (3/114). Two patients died of postoperative ARDS and one patient of pneumonia.

4. Conclusions

Tracheobronchial sleeve resection should be considered whenever possible for resection of malignant pulmonary tumours without loss in radicality to preserve lung function [7]. Sleeve lobectomy has been compared to pneumonectomy and proven to be favourable in terms of 30-day mortality [1,8,9], long-term survival and quality of life [2,7,10,11]. This has led us to a continuous decrease in the number of pneumonectomies at our institution below 10%, whereas the number of sleeve resections is steadily increasing (16%).

Anastomotic insufficiency after sleeve resection remains a major complication. Healing of the anastomosis is dependant on the early revascularisation of the anastomosis by surrounding tissue [4,5]. Ischaemia and infection of the distal end of the sleeve cause anastomotic insufficiency. In a previous study, our anastomotic insufficiency and 30-day mortality rate was 6.9% and 4.3%, respectively [12]. In the attempt to improve our results, we learnt from our experience in lung transplantation where all patients receive nebulised antibiotics [13]. Patients with cystic fibrosis or end-stage lung disease have chronic colonisation of the airways and therefore a high risk of postoperative infection. Nebulised antibiotics are safe and efficient in these patients [13—16]. We introduced prophylactic Tobramycin™ inhalation (2 × 80 mg) for 7 days. No treatment-related side effects were noted. To document endobronchial healing, all patients received a control bronchoscopy on the eighth postoperative day. As of 2006, we developed a classification of the anastomosis (Table 2) to facilitate description and documentation.

However, a number of the patients had received neoadjuvant therapy and with carinal resection the rate of insufficiency of the anastomosis was as low as 4.4% (5/114) and 30-day mortality fell to 2.6% (3/114). More detailed analysis of patient data showed that two patients had a postoperative respiratory failure with mechanical ventilation, two patients had technical failure of the anastomosis and only one patient had a true infection and necrosis of the anastomosis.

It can be argued that the increasing experience of the surgeons performing the intervention is the reason for the better results. We believe that on the contrary the increasing experience has led us to enlarge the indication for sleeve lobectomy for patients at higher risk (26% patients with neoadjuvant therapy). Only one patient had a true infection and necrosis of the anastomosis, even then a conservative treatment was possible. In our previous study there was a secondary pneumonectomy rate of 6% (7/116); since introduction of local antibiotics our secondary pneumonectomy rate is zero. We believe that prophylactic inhalation of Tobramycin™ protects the anastomosis from deep infections and destruction of the bronchial wall in the early fragile period of ischaemia.

To reduce the rate of anastomotic insufficiency and 30-day mortality after sleeve resection, we recommend use of local antibiotic inhalation.

References


Appendix A. Conference discussion

Dr P. Rajesh (Birmingham, United Kingdom): Can I start the questions by asking how you differentiate between an ischaemia-related complication and infection-related complication? You’re using a continuous running suture, so this may be interrelated.

Dr Stoelben: No, we think that all patients had some kind of ischaemia in the distal part of the anastomosis or rather in the distal bronchus. That’s the reason why we cut the distal bronchus always very short.

The problem appears when ischaemia becomes complicated by infection. We know from studies about transplantation that revascularisation needs about 4 to 5 days before you can see the first capillaries filled with red blood cells. That’s the reason why we use antibiotic treatment for 7 days to protect the bronchus until revascularisation. Afterwards the bronchus is protected against infection.