Factors affecting survival after bronchoplasty and broncho-angioplasty for lung cancer: single institutional review of 147 patients

Takeshi Nagayasu*, Keitaro Matsumoto, Tsutomu Tagawa, Akihiro Nakamura, Naoya Yamasaki, Atsushi Nanashima

Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan

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Abstract

Objective: We compared the results of bronchoplasty and bronchoplasty with pulmonary angioplasty (broncho-angioplasty). Multivariate analysis was done to determine potential prognostic factors for both procedures based on our 20-year single-center experience.

Methods: Between January 1985 and December 2004, 163 bronchoplastic procedures were done in 1405 patients who underwent lung resections for lung cancer at Nagasaki University Hospital. After excluding 16 carino-plasty patients, 147 patients (118 bronchoplasty and 29 broncho-angioplasty) were included.

Results: In the bronchoplasty group, the postoperative morbidity was 22.9% (27/118) and the 90-day postoperative mortality was 5.9% (7/118), while in the broncho-angioplasty group the postoperative morbidity was 27.6% (8/29) and the postoperative mortality was 17.2% (5/29). The 5-year survival for all patients was 56.0%. Among patients with stage I or II, the 5-year survival was 76.2% in the bronchoplasty group and 51.9% in the broncho-angioplasty group (p = 0.1791). On the other hand, among patients with stage III or IV, 5-year survival was 43.5% in the bronchoplasty group and 7.9% in the broncho-angioplasty group (p = 0.0192). Multivariate analysis indicated that the type of operation, postoperative complications, histologic type, and pN status were significant factors affecting survival.

Conclusions: Both bronchoplasty and broncho-angioplasty are useful for the treatment of patients with lung cancer and should be performed in stage I or II. However, careful patient selection is mandatory in patients with advanced tumor stages and in those with nonsquamous cell carcinoma, especially if broncho-angioplasty is being considered.

Keywords: Bronchoplasty; Broncho-angioplasty; Lung cancer

1. Introduction

Ever since Thomas [1] performed the first sleeve resection in a patient with a carcinoid tumor, bronchoplasty has become widely accepted as a reliable and safe lung-saving procedure for lung cancer patients [2,3]. Several reports have shown that sleeve lobectomy has several advantages over pneumonectomy, including preservation of lung function and lower morbidity and mortality [4–6]. Given the progress that has been made in vascular surgery, bronchoplasty with pulmonary artery (PA) reconstruction (broncho-angioplasty) has become feasible in cases of cancer invading the pulmonary artery [7]. However, there have been only a few reports that have dealt with the outcomes following broncho-angioplasty [8–10]. The aim of this study was to compare the outcomes after bronchoplasty and broncho-angioplasty for the treatment of lung cancer. A multivariate analysis was done to identify potential prognostic factors for both procedures based on our 20-year single-center experience.

2. Patients and methods

Between January 1985 and December 2004, 1405 patients underwent lung resections for lung cancer at Nagasaki University Hospital. During this period, 163 bronchoplastic procedures were performed. Sixteen patients with carino-plasty (lobectomy, n = 7; pneumonectomy, n = 6; without parenchymal resection, n = 2; bilobectomy, n = 1) were excluded, and the remaining 147 patients were evaluated in this study. The data were collected retrospectively from the patient records and analyzed. There were 135 male and 12 female patients, with a mean age of 63.4 ± 9.7 years (range, 8–78 years). Thirty-two (21.8%) patients had a preoperative respiratory risk (chronic obstructive pulmonary disease, defined as a preoperative forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) ≤60% of predicted value)
2.2. Surgical technique

Single-lung ventilation was established through a double-lumen endotracheal tube. A routine posterolateral thoracotomy in the fifth intercostal space was done. Mediastinal and hilar lymph node dissection was routinely performed, and frozen sections of all bronchial margins were carefully examined. The bronchial anastomoses were done using an interrupted suture technique with monofilament absorbable 4-0 sutures and were wrapped with a pericardial fat pad, omentum, or mediastinal pleura, as described elsewhere [12]. Suturing of the pulmonary artery was done using a running suture technique with monofilament nonabsorbable 5-0 sutures. Ringed or patchy expanded polytetrafluoroethylene grafts (Gore-Tex, USA) were used for the sleeve or patch plasty procedures. We washed the anastomosis sites with diluted heparin to prevent intraluminal thrombosis, but systemic heparin was not used intraoperatively or postoperatively.

2.3. Perioperative evaluation

Preoperative staging routinely included chest X-rays, computed tomography of the chest and upper abdomen, bronchoscopy, upper abdominal ultrasonography, magnetic resonance imaging of the cerebrum, and bone scintigraphy. A pulmonary angiogram was performed in selected cases. After the anastomoses were completed, postoperative bronchoscopy was performed routinely in the operating room, as well as 2 weeks following surgery, 3–6 months after discharge, and whenever anastomotic complications were suspected. Patients were followed up by routine chest X-rays and chest computed tomography after discharge. Operative morbidity or mortality was defined as the occurrence of complications or death within 90 days of the operation.

2.4. Statistical analysis

All results are expressed as mean ± standard error. Categorical data were calculated as percentages and compared using the χ²-test. Patient survival rates were calculated by life-table analysis. Kaplan–Meier curves were plotted and compared using the log-rank test for univariate analysis. Multivariate analyses of independent prognostic factors were assessed by the Cox proportional hazards stepwise model using StatView V (SAS Institute Inc., Cary, NC, USA). Statistical significance was set at p < 0.05. Results are presented as the estimated relative risk with corresponding 95% confidence intervals. The study protocol was approved by the Human Ethics Review Committee of Nagasaki University School of Medicine and a signed consent form was obtained from each subject.

3. Results

TNM staging based on the recent International Union against Cancer (UICC) classification is given in Table 1. In the bronchoplasty group, 49 (41.5%) patients were stage I (27 IA and 22 IB), 23 (19.5%) were stage II (4 IIa and 19 IIb), 25 (21.2%) were stage IIIA, 18 (15.3%) were stage IIIB, and 3 (2.5%) were stage IV. Two patients with stage IV disease had cerebral metastases, and one patient had a single metastasis in another lobe. T4 disease included involvement of the left atrium (n = 6), superior vena cava (n = 2), esophagus (n = 1),...
and trachea (n = 1), as well as a malignant pleural effusion (n = 1) and a separate tumor nodule in the same lobe (n = 5). Tumor histology was squamous cell carcinoma in 74.6% (88/118) and nonsquamous cell carcinoma in 25.4% (30/118). The nonsquamous cell carcinoma included adenocarcinoma (n = 15), large cell carcinoma (n = 8), adenosquamous carcinoma (n = 2), and other (n = 5).

In the broncho-angioplasty group, 4 (13.8%) patients were stage I (1 IA and 3 IB), 6 (20.7%) were stage II (6 IIB), 12 (41.4%) were stage IIIA, and 7 (24.1%) were stage IIIB. T4 disease involved the superior vena cava (n = 4) and aorta (n = 1), as well as a separate tumor nodule in the same lobe (n = 2). The nonsquamous cell carcinoma included adenocarcinoma (n = 6) and large cell carcinoma (n = 1).

Of the 147 patients, a preoperative respiratory risk was present in 32 (21.8%), of whom 26 (22.0%) were in the bronchoplasty group and 6 (20.7%) in the broncho-angioplasty group.

Overall, 31 patients had adjuvant or neoadjuvant therapy. In the bronchoplasty group, of the 23 (19.5%) patients who had adjuvant or neoadjuvant therapy, 11 had neoadjuvant chemotheraphy, 8 had adjuvant chemotherapy, 2 had adjuvant radiotherapy, and 2 had adjuvant chemo-radiotherapy. In the broncho-angioplasty group, of the 8 (27.6%) patients who had adjuvant or neoadjuvant therapy, 1 had neoadjuvant chemotherapy, 3 had adjuvant chemotherapy, 3 had adjuvant radiotherapy, and 1 had adjuvant chemo-radiotherapy.

The 90-day postoperative morbidity rate was 23.8% (35 of 147 patients) overall, 22.9% (27 of 118 patients) in the bronchoplasty group, and 27.6% (8 of 29 patients) in the broncho-angioplasty group (p = 0.5953). The 90-day postoperative mortality rate was 8.2% (12/147) overall, 5.9% (7/118) in the bronchoplasty group, and 17.2% (5/29) in the broncho-angioplasty group (p = 0.047) (Table 2).

In the bronchoplasty group, four patients with pneumonia died on postoperative days 8, 21, 25, and 35, respectively. In five patients with a bronchopleural fistula, one patient was suspected of having a minor bronchopleural fistula on day 15. This patient had undergone a right lower sleeve lobectomy with wedge resection of the left atrium and was successfully treated with fibrin glue administered by bronchoscopy, but died on day 21 from unexpected duodenal bleeding. Another patient with a bronchopleural fistula who had undergone left lower-lingular sleeve lobectomy died on day 55 after a completion pneumonectomy. Among the remaining three patients with a bronchopleural fistula, there were two reanastomoses with omentopexy and one completion pneumonectomy. The patient who had a right middle—lower sleeve lobectomy with partial esophagectomy died on postoperative day 10 from an unexpected bronchovascular fistula.

In the broncho-angioplasty group, two patients were suspected of having minor bronchopleural fistulas based on chest X-rays and bronchoscopy. Both of these patients with a bronchopleural fistula were observed and improved, but one patient who had undergone right upper—middle sleeve lobectomy with S6 segmentectomy and PA sleeve plasty died from contralateral pneumonia on day 46. The other patient who had undergone left upper sleeve lobectomy with shaving of aortic adventitia and PA sleeve plasty died from perforation of the aorta on day 65. A patient who had a right upper sleeve lobectomy with resection of the chest wall and PA sleeve plasty died on postoperative day 8 from an unexpected bronchovascular fistula. The two cases from both groups who died from a bronchovascular fistula had surgery in 1986 and did not undergo wrapping for their bronchial anastomoses. Since 1990, all patients in the bronchoangioplasty group had wrapping for their anastomoses, mainly using the pericardial fat pad. Pulmonary artery occlusion occurred in one patient who had undergone left upper sleeve lobectomy with PA sleeve plasty. Left completion pneumonectomy was performed on the fourth postoperative day, but the patient died as a result of a bronchopleural fistula on day 58. Another patient who had undergone right upper sleeve lobectomy with PA patch plasty died from pulmonary embolism on day 62. Other complications were managed conservatively in most cases.

### 3.1. Factors affecting survival

The median follow-up for all patients was 26.6 months (8 days to 174.8 months). The overall 5-year survival for all patients was 56.0%. There was a significant difference in the 5-year survival between the bronchoplasty group (63.4%) and the broncho-angioplasty group (24.2%, p = 0.0003). Among patients with stage I or II, the 5-year survival was 76.2% for the bronchoplasty group and 51.9% for the broncho-angioplasty group (p = 0.1791; Fig. 1). Among patients with stage IIIA, IIIB, or IV, there was a significant difference in 5-year survival between the bronchoplasty group (43.5%) and the broncho-angioplasty group (7.9%, p = 0.0192; Fig. 2).

The 5-year survivals for pT1 (n = 36), pT2 (n = 67), pT3 (n = 21), and pT4 (n = 23) were 96.2%, 53.7%, 38.5%, and 22.2%, respectively. The survival rates with different pT lesions differed considerably (p < 0.0001). The 5-year survivals for pN0 (n = 67), pN1 (n = 30), pN2 (n = 46), and pN3 (n = 4) were 73.8%, 53.3%, 34.7%, and 25.0%, respectively. The survival rates with different pN lesions also differed considerably (p < 0.0001). Univariate analysis was done to identify risk factors associated with poor survival (Table 3). The independent factors analyzed were age (age < 70 years vs ≥70 years), gender, preoperative respiratory risk, type of operation (bronchoplasty vs broncho-angioplasty), adjuvant or

### Table 2
Postoperative complications occurring within 90 days after bronchoplasty and broncho-angioplasty

<table>
<thead>
<tr>
<th>Complications</th>
<th>Bronchoplasty (n = 118)</th>
<th>Broncho-angioplasty (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morbidity</td>
<td>Mortality</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Bronchopleural fistula</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Prolonged air leakage</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Sputum retention</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>ARDS</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bronchovascular fistula</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Empyema</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PA occlusion</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27 (22.9%)</td>
<td>7 (5.9%)</td>
</tr>
</tbody>
</table>
neoadjuvant therapy, postoperative complications, histologic type (squamous cell carcinoma vs nonsquamous cell carcinoma), pT status (pT1 or T2 vs T3 or T4), and pN status (pN0 or N1 vs N2 or N3). Significant risk factors associated with poor survival included use of the broncho-angioplastic procedure, the incidence of postoperative complications, nonsquamous cell histologic type, pT3 or T4, and pN2 or N3. Table 3 shows the results of the multivariate analysis of the independent prognostic factors. The data indicate that the type of operation, postoperative complications, histologic type, and pN status are significant factors affecting survival. The pT status showed a trend, but it was not statistically significant.

4. Discussion

Today, bronchoplasty for lung cancer has been widely accepted and is performed by many surgeons worldwide. Many reports have compared survival rates after sleeve lobectomy and after pneumonectomy [4,5,13—15]. It has been found that sleeve lobectomy, when performed in selected patients, provides at least similar or superior long-term survival to that seen after pneumonectomy. Thus, whenever possible, sleeve lobectomy is recommended.

Ever since early 1980, when our institution reported a small series of lung cancer patients who had undergone bronchoplasty, we have been performing bronchoplasties in lung cancer patients to effectively preserve pulmonary parenchyma and control the disease [16]. In this paper covering the period from 1985 to 2004, 11.6% (163/1405) of the patients who underwent lung resections for primary lung cancer had bronchoplastic procedures. Compared to other reports [6,14,15], this rate is relatively high, as our data includes 29 cases with combined PA reconstruction. Despite data that support the use of bronchoplasty as compared to pneumonectomy, so far there have been only a few small series that have evaluated broncho-angioplasty [8—10]. In our series, the overall survival rate for bronchoplasty patients was 63.4%, which is higher than that in other recent reports [4—6,10,15,17]. In contrast, the overall survival rate

Table 3

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Characteristics</th>
<th>Unfavorable</th>
<th>Favorable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p value</td>
<td>Hazard risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>95% CI a p value</td>
</tr>
<tr>
<td>Age</td>
<td>&gt;70</td>
<td>&lt;70</td>
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<td>0.3687</td>
<td>2.416</td>
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<tr>
<td></td>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td>0.7836</td>
<td>1.310—4.457</td>
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<tr>
<td></td>
<td>Respiratory risk</td>
<td>Yes</td>
<td>No</td>
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<td></td>
<td>Adjuvant therapy</td>
<td>Yes</td>
<td>No</td>
<td>0.1791</td>
<td>2.446</td>
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<tr>
<td></td>
<td>Type of operation</td>
<td>Broncho-angioplasty</td>
<td>Bronchoplasty</td>
<td>0.0003</td>
<td>2.176</td>
</tr>
<tr>
<td></td>
<td>Postoperative complications</td>
<td>Yes</td>
<td>No</td>
<td>0.0003</td>
<td>1.794</td>
</tr>
<tr>
<td></td>
<td>Histologic type</td>
<td>Non-SQ</td>
<td>SQ</td>
<td>0.0008</td>
<td>0.997—3.225</td>
</tr>
<tr>
<td></td>
<td>pN status</td>
<td>N2, 3</td>
<td>N1, 2</td>
<td>&lt;0.0001</td>
<td>2.124—3.866</td>
</tr>
</tbody>
</table>

SQ: squamous cell carcinoma; non-SQ: nonsquamous cell carcinoma.

a CI, confidence interval.

b Including 11 cases of neoadjuvant chemotherapy.
for patients undergoing broncho-angioplasty was not satisfactory, as it was similar to the rate reported in pneumonectomy patients [4–6]. However, when the results of broncho-angioplastic resection are examined in patients with stage I or II disease, it is seen that long-term survival is similar or superior to that after bronchoplasty [4–6,13–15]. This result indicates that broncho-angioplasty can be a valuable alternative to pneumonectomy in stage I or II, and may be considered as an alternative to pneumonectomy in stage III or IV only when pneumonectomy is contraindicated due to poor cardiopulmonary function.

The overall 30-day postoperative mortality was 4.1% (6/147), which was lower or similar to that of previous reports [2,6]. However, the overall 90-day postoperative mortality rate increased to 8.2% (12/147); 17.2% (5/29) in the bronchoangioplasty group and 6% (7/118) in the bronchoplasty group. Six of the 12 cases of 90-day postoperative deaths related to insufficient anastomoses (four with a bronchopleural fistula and two with a bronchovascular fistula) and occurred early in the time period of this series. Wada et al. [9] demonstrated that, in the postoperative management of broncho-angioplasty, there was a high incidence of severe postoperative complications; therefore, utmost caution is required in the postoperative management of such patients. In the present series since 1996, no 30- or 90-day postoperative deaths occurred after sleeve lobectomy with or without angioplasty. It should be emphasized that the improvement in the healing process of the bronchial anastomosis contributed more than postoperative management to the prevention of fatal anastomotic insufficiency. Therefore, to promote healing, we have been combining several individual techniques, such as tissue coverage of the bronchial anastomoses with the pedunculated pericardial fat pad or omentum [12], telescope anastomosis [18], simple interrupted suture combined with figure-of-eight suture [19], and preserving the bronchial arterial branches [20].

Despite intraoperative confirmation of the safety margin by frozen sections, local tumor recurrence always has to be considered as a major postoperative complication after bronchoplasty or broncho-angioplasty. In their review, Tedder et al. [2] found that the local recurrence rate for sleeve lobectomy was 13%, and in other recent series, the local recurrence rate has ranged from 8% to 22% [4,5,17]. During the follow-up period in our series, the incidence of local recurrence at the site of first occurrence was 17.2% (5/29) in the broncho-angioplasty group and 7% (8/118) in the bronchoplasty group. Local recurrence was more frequent in the broncho-angioplasty group; however, three of the five patients in this group had pN2 disease. Thus, it was difficult to determine whether local recurrence truly occurred from the site of bronchoplasty or whether the patient had regional lymph nodal involvement.

In most of the other series, multivariate analysis has shown that long-term survival in patients treated with bronchoplasty or broncho-angioplasty was influenced mainly by the nodal stage or advanced tumor stage [10,11,17]. End et al. [11] showed that the presence of respiratory or cardiovascular risk was associated with a poor outcome along with advanced tumor stage and the type of bronchoplastic procedure; however, their data included a small number of sleeve pneumonectomy cases with a 25% 1-year survival. In the current series, the presence of nonsquamous cell carcinoma on histology, advanced nodal status, broncho-angioplasty, and postoperative complications were all risk factors for a poor outcome, whereas the preoperative respiratory risk and adjuvant therapy were not significant risk factors. We suspect that one possible reason for this is that the rate of pN2 or N3 disease was higher in patients with nonsquamous cell carcinoma (20/37) than in patients with squamous cell carcinoma (30/110).

In conclusion, both bronchoplasty and broncho-angioplasty are useful in the treatment of lung cancer and should be performed as an alternative to pneumonectomy in patients with stage I or II disease. However, careful patient selection is mandatory in patients with an advanced tumor stage and with nonsquamous cell carcinoma. As well, utmost caution is needed in broncho-angioplasty cases, as postoperative complications tend to be fatal.

Acknowledgment

The authors wish to honor the memory of Hiroyoshi Ayabe, MD, PhD, the late Professor of the First Department of Surgery, Nagasaki University School of Medicine, who passed away on August 17, 2002, during his tenure.

References


