Sleeve Pneumonectomy for Central Non-Small Cell Lung Cancer: Indications, Complications, and Survival

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Background. Sleeve pneumonectomy is a challenging therapeutic strategy for patients with non-small cell lung cancer (NSCLC) invading the carina. The aim of this study was to illustrate common indications and individual concepts for surgery and to investigate oncologic outcomes and complications.

Methods. Sixty-four consecutive sleeve pneumonectomies were performed between September 2000 and November 2011. All patients had histologically proven central NSCLC. Data were retrospectively reviewed for indications, complications, and factors influencing long-term survival.

Results. Sixty-four patients underwent sleeve pneumonectomy for curative (n = 50, 78%) or palliative therapy (n = 14, 22%). Complete resection was achieved in 83%. Pathologic N2 disease was found in 41%. Complications occurred in 41%, with severe anastomotic problems in 8% of cases. Thirty-day mortality was 3% (n = 2). Outcome was significantly influenced by pathologic nodal status with 5-year survival rates of 70%, 35%, and 9% for N0, N1, and N2 subgroups, respectively. Patients with multilevel N2 disease and contraindications for chemotherapy or radiotherapy had a mean survival of 13 months after palliative surgery.

Conclusions. Sleeve pneumonectomy for central NSCLC invading the carina or proximal main bronchus can be performed with tolerable risk and encouraging survival rates in selected cases. Palliative sleeve pneumonectomy displays an option in the absence of alternative therapeutic strategies.

ultrasound (EBUS) with transbronchial needle aspiration (TBNA). Mismatches between EBUS-TBNA and radiologic findings were examined by standard diagnostic mediastinoscopy.

Clinical and pathologic staging referred to the then-current 6th and 7th editions of the TNM Classification of Malignant Tumors [8, 9]. All cases were discussed in our multidisciplinary tumor board. The option of sleeve pneumonectomy was considered either for NSCLC close to or invading the main carina (T3/4) and/or subcarinal N2-disease with intraoperative findings of local infiltration. All patients were closely involved in the decisions regarding the therapeutic process and its treatment alternatives. The indications for surgery at our department were as follows.

1) Curative intent. (A) Primary surgery in M0 patients who were fit for surgery, presenting with resectable tumor and nodal disease N2 or less single level. Adjuvant chemotherapy or radiotherapy was indicated based on postoperative nodal status and clearance of resection margins. (B) Subsequent surgery: surgery as part of a multimodal concept after good response to neoadjuvant treatment.

2) Palliative intent. Surgery was offered to patients who were fit for surgery, presenting with resectable tumor, less than bulky N2 disease and with urgent palliative indication (e.g., hemoptysis or retention pneumonia) that was not manageable by endoscopic intervention.

Surgical Procedure
Sixty-four pneumonectomies were performed under general anesthesia with endobronchial double lumen tubes and epidural catheter placement for perioperative and postoperative pain management. High-frequency jet ventilation (HFJV) was used during carinal resection and anastomotic reconstruction [10]. Cross-field ventilation was routinely available but seldom used as high-frequency jet ventilation has been established at our institution for years as a safe means for ventilatory management during surgery with only minimal hindrance to the surgeon. Flexible bronchoscopy was routinely used for confirmation of tube placement and for reevaluation of endobronchial tumor. All procedures were done through a standard anterolateral thoracotomy in the fourth intercostal space. Extensions to the hemi-clamshell procedure or bilateral thoracotomy were not necessary in our series. For right-sided procedures, transection of the azygos vein facilitated the approach to the right main bronchus. For left-sided tumors, the main carina was exposed by dissection of the ductus Botalli and careful mobilization of the aortic arch. The tracheobronchial sleeve is finally resected after adequate mobilization of the distal trachea and main carina. If tumor-free margins at the bronchial site were not confirmed by frozen section, a wider resection was performed if technically feasible. Telescoping the main bronchus into the distal trachea was frequently done to overcome size differences. The anastomosis was created using running 3-0 sutures (PDS) for the membranous portion and interrupted 3-0 sutures (PDS) for the cartilaginous portion. The anastomosis was covered using pleura, pericardial fat pads, diaphragm strips, or intercostal muscles. Complete radical en bloc dissection of the ipsilateral hilar and mediastinal lymph node compartments was integral part of each procedure [11]. Extubation was intended immediately after restoring spontaneous respiration. The single chest tube was removed after 24 hours. Standard monitoring time on the intensive care unit was 48 hours. Bronchoscopy was performed at least twice during the hospital stay to evaluate anastomotic healing.

Complications, Adjuvant Therapy, and Follow-Up
Postoperative complications were regarded as “minor” if manageable conservatively and as “major” if surgical interventions were needed, respectively. All cases were finally debated in the multidisciplinary board for postoperative therapy before discharge. Adjuvant chemotherapy was discussed for patients with pathologically proven N1 or N2 disease. Irradiation as the only adjuvant therapy was advised for non-radical resections (R1) or single-level N2 disease. Individual treatment protocols were defined for patients with contraindications to immediate chemotherapy or radiotherapy. Follow-up visits were scheduled at our outpatient service after 3, 6, and 12 months, including at least 1 endoscopy, chest X-ray, and CT scan of the chest. Recurrence of disease resulted in whole-body restaging and interdisciplinary discussion.

Statistical Methods
The Kaplan-Meier method was used to calculate survival curves. Factors associated with survival were assessed by multivariate analysis (Cox model) [12]. A p value of less than 0.05 was considered statistically significant.

Results
The series comprised 50 males (78%) and 14 females, with a mean age of 58 years. Most common clinical nodal stages were N0 (18 patients, 28%) and N2 (38 patients, 60%). The curative group comprised 50 patients, of whom 42 (84%) underwent primary surgery. Inductive chemotherapy was given in 5 patients and inductive chemotherapy and radiotherapy in 3 cases. Subsequent surgery was recommended for good tumor and nodal response (n = 5) or only local tumor progression (n = 3). Palliative surgery was indicated in 14 patients with multilevel N2 diseases and hemoptysis or tumor-associated infection as a contraindication for inductive treatment (group 2, palliative).

Sixty-one patients had tumor extension intrapericardially. Atrial partial resection was necessary in 17 patients. The superior vena cava was resected tangentially in 4 patients, the pulmonary artery in 2 patients. In 1 patient the pulmonary artery was simultaneously reconstructed (double sleeve pneumonectomy), and a Gore-Tex graft (W.L. Gore & Associates, Inc Medical
Products Division, Flagstaff, AZ) for the superior vena cava was used in 5 patients (8%). Overall morbidity was 41% (26 patients). Major complications occurred in 16 patients (25%) (Table 1). Uncomplicated empyema cases (n = 7) were treated by thoracoscopic lavage and chest-tube placement. Two secondary hemothoraces (n = 2) underwent thoracoscopic revision. Relevant anastomotic insufficiency that required redo thoracotomy was observed in 8% (n = 5) of patients. Treatment was open window thoracostomy and subsequent thoracoplasty in 4 cases, secondary suturing and wrapping of the anastomosis using a diaphragm flap without the need of a thoracostomy in 1 case (Table 2).

Two patients died within 30 days (3%). One patient developed contralateral lung gangrene caused by fulminating pneumonia. Another patient died after cardiac herniation due to a ruptured pericardial patch during cardiopulmonary resuscitation for ventricular fibrillation.

Minor complications (cardiac, respiratory, surgical) were detected in 10 patients (16%) (Table 1).

**Histopathology and Staging**

There were 48 squamous cell carcinomas (75%), 12 adenocarcinomas (19%), 1 large-cell carcinoma (2%), and 3 with a mixed subtype (5%). Complete resection (R0) was achieved in 53 patients (83%). Microscopic positive resection margins (R1) were noted in 10 cases (16%). Tumor residuals were as follows: pulmonary artery or vein or perivascular (n = 4), peribronchial lymphatic tissue (n = 3), and bronchial sleeve (n = 3). In any case a wider resection was regarded as not feasible by the surgeon. Macroscopic residual carcinoma (R2, lateral trachea) was tolerated in 1 palliative case.

Postoperative nodal status was classified as pN0 in 10 (16%), pN1 in 28 (44%), and pN2 in 26 patients (41%) (Table 1). Five of the 26 pN2 patients had multilevel N2 disease, 3 of whom (3 of 5) underwent palliative surgery for retention or hemoptysis. The remaining 2 cases with postoperative multilevel N2 were staged false negative as clinical N0 and single level N2, respectively. Accordance of clinical and pathologic N status was found in 28 cases (44%) and clinical nodal overrating (cN > pN) in 19 patients (30%). The remaining 17 patients had a higher pathologic N status than clinically expected (pN > cN).

Two patients (3%) were stage IV postoperative. One had a newly detected single osteolysis (11th rib). The second patient underwent carinal surgery, assuming to suffer from a simultaneous renal cell carcinoma that subsequently turned out to be a distant metastasis of his concurrent NSCLC.

**Adjuvant Therapy**

Eighteen patients received adjuvant chemotherapy; 12 for pathologic N1 and 6 for multilevel N2 disease. Thirteen patients received radiotherapy alone, for single level N2 disease (n = 7), positive resection margins (n = 3), or both (n = 3). Two patients with excellent physical status received adjuvant radiochemotherapy. The remaining

<table>
<thead>
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<th>No.</th>
<th>Endoscopic Findings</th>
<th>Revision</th>
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</thead>
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<tr>
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<td>2</td>
<td>Ulcer</td>
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<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>Ulcer</td>
<td>No</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
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<td>Omentum majus</td>
<td>Yes/Yes</td>
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<td>Yes</td>
<td>Diaphragm</td>
<td>No/Yes</td>
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<tr>
<td>6</td>
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<td>Musculus subscapularis</td>
<td>Yes/Yes</td>
</tr>
<tr>
<td>7</td>
<td>Insufficiency</td>
<td>Yes</td>
<td>Omentum majus</td>
<td>Yes/Yes</td>
</tr>
</tbody>
</table>
patients with a formal indication for chemotherapy (or radiotherapy) had either a poor physical status or a systemic progressive disease.

**Long-Term Survival and Affecting Factors**

Mean survival of the entire cohort was 31 months. Actuarial 3- and 5-year survival rates were 40% and 31%, respectively (Fig 1). Five-year survival was 70% for pN0, 35% for pN1, and 9% for pN2 patients. Nodal status was identified as the only factor with a significant impact on long-term survival (N0 vs N2: $p = 0.001$; Fig 2). Mean survival was 13 months for pathologic multilevel N2 disease and 21 months for single level N2 disease ($p = 0.03$). Survival was not significantly affected by patient’s sex, age, or induction treatment. Residual tumor (R1 vs R0) correlated with a shorter 5-year survival (32% vs 25%, $p = 0.06$). Adjuvant chemotherapy (AC) had no significant effect on survival within the pN1 (3-year survival: 44% [AC] vs 38.5%; $p = 0.15$) or pN2 subgroups (3-year survival: 25% [AC] vs 24%, $p = 0.3$). Postoperative irradiation for pathologic single level N2 disease improved survival rates (3-year survival 30% with irradiation vs 10% without irradiation, $p = 0.06$), although this difference was not statistically significant.

**Comment**

We retrospectively reviewed 64 lung cancer patients who underwent sleeve pneumonectomy for curative or palliative intent. Severe anastomotic complications occurred in less than 10%. Long-term survival was influenced only by pathologic nodal status and not by patient’s age, sex, or presurgical and postsurgical oncologic treatment. Surgery for curative and palliative intent resulted in a mean survival of 21 months and 13 months, respectively, with N2-disease included.

Sleeve pneumonectomy is an extensive surgical treatment option for a small number of patients suffering from central NSCLC (approximately 1% of all surgical lung cancer cases at our institution). Carinal involvement is often co-associated with mediastinal nodal metastasis that significantly influences prognosis [6, 13, 14]. Poor survival for progressive nodal affection has also been observed in our series with 5-year survival rates of 70%, 35%, and 9% for pN0, pN1, and pN2, respectively (Table 4). Regarding preoperatively proven N2 as a contraindication for extensive surgery, most authors claim for routine invasive mediastinal staging in all lung cancer patients [3, 5, 7, 14]. We did not routinely perform mediastinoscopy but explored the mediastinal space using EBUS-TBNA. In experienced hands, both procedures may result in a similar hit ratio of up to 90%, especially for non-subcarinal N2 [15]. The role of the PET scan, in addition to standard computed tomography for noninvasive staging, has been discussed frequently. In fact, PET-CT scans show higher sensitivity in nodal staging than standard computed tomography chest scan does and furthermore display an excellent modality to exclude distant metastasis [16, 17]. However, there may be limitations for the diagnostic value of PET-CT scans, especially for mediastinal nodal staging in potentially resectable central NSCLC. First, due to frequent concomitant retention pneumonia in tumors affecting central airways, the rate of false positive findings is high [18]. Second, some reports revealed the subcarinal N station (that was co-responsible for sleeve resection in 12 of 20 patients in our series) to have the highest incidence of both false negative and false positive results in mediastinal staging [19, 20]. In our series, patients with single level N2
disease (in particular single level subcarinal N2 disease) were not being denied primary surgery. However, rigorous invasive mediastinal staging was performed in non-palliative cases to exclude suspected multilevel N2 or N3 disease. The benefit of inductive treatment for potentially resectable NSCLC with single level N2 disease has been a subject of great controversy as discussed by Tada and colleagues [21] and Depierre and colleagues [22]. Both studies could not show significant survival benefits for completely resected single level N2 disease with neoadjuvant or adjuvant therapy compared with observation alone. However, higher mortality rates after induction therapy have been frequently reported [3, 14, 23] as well as a negative impact on anastomotic healing [24, 25]. Independent of perioperative systemic treatment, reported complication rates for sleeve pneumonectomy vary between 30% and 60% [5, 6, 13]; especially, anastomotic insufficiencies occur in up to 14% and are associated with a high mortality rate of up to 50% [26, 27] (Table 3). In our series the overall complication rate was 41%, with severe anastomotic problems in 5 patients (8%). Concerning

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patients with central tumors frequently experience significant tumor-related complications such as hemoptysis or retention pneumonia. Our series comprises 14 patients with multilevel but not bulky N2 disease and contraindications for systemic treatment due to hemoptysis, post-stenotic pneumonia, or renal dysfunction. These 14 patients represent a highly select group in whom the tumor-related complications were not manageable by endoscopic intervention but who were otherwise generally fit for surgery, and in whom the tumor was deemed operable. Surgery was offered to these patients in the light of the only alternative treatment being palliative radiotherapy. This treatment may result in 3-year survival rates of 5% to 10% for patients without hemoptysis or relevant infection [28]. The decision to pursue surgery in these cases is based on the idea of not to refuse the chance of tumor-specific therapy only because of tumor-associated complications. A concept of palliative sleeve pneumonectomy has been reported previously in only a few cases [2, 29]. Complete resection in our palliative group was achieved in 10 of 14 cases, anastomotic problems occurred in 1 patient (1 of 14). Mean survival was 13 months, with no significant difference regardless of whether adjuvant systemic treatment was given or not. Thus, regarding the lack of true alternative options, we consider sleeve pneumonectomy for palliative indication as an acceptable option in selected patients.

Regarding the feasibility of adjuvant therapy, we found 7 patients with N2 disease who had poor physical recovery that prohibited any kind of tumor-directed adjuvant treatment. Four of them had multilevel N2 diseases and potentially would have been elected for standard radiotherapy or chemotherapy. However, 5 of these 7 patients underwent surgery in a palliative setting and presented with contraindications for systemic

### Table 3. Mortality and Complication Rates in Sleeve Pneumonectomy

<table>
<thead>
<tr>
<th>Author</th>
<th>Case Number</th>
<th>Operative Mortality (%)</th>
<th>Operative Morbidity (%)</th>
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<tbody>
<tr>
<td>Roviaro et al, 2001 [50]</td>
<td>48</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Macchiarini et al, 2006 [31]</td>
<td>34</td>
<td>2</td>
<td>16</td>
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<td>Subotich et al, 2007 [26]</td>
<td>42</td>
<td>16</td>
<td>35</td>
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<tr>
<td>This study, 2013</td>
<td>64</td>
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<td>41</td>
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</tbody>
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### Table 4. Pathologic Nodal Status and 5-Year Survival; Own Data and Literature Survey

<table>
<thead>
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<th>Author</th>
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<th>Nodal Status</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N0 (%)</td>
<td>N1 (%)</td>
</tr>
<tr>
<td>Porhanov et al, 2002 [27]</td>
<td>101</td>
<td>32a</td>
</tr>
<tr>
<td>Mitchell et al, 2001 [5]</td>
<td>60</td>
<td>51</td>
</tr>
<tr>
<td>Regnard et al, 2005 [13]</td>
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<td>38a</td>
</tr>
<tr>
<td>De Perrot et al, 2006 [14]</td>
<td>100</td>
<td>53a</td>
</tr>
<tr>
<td>This study, 2013</td>
<td>64</td>
<td>70</td>
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a N0 and N1. b N0/N1 vs N2. c N2 and N3. d N0 vs N2. e N1 vs N2.
chemotherapy. Analyzing our other patients with proper admittance of stage-related inductive or adjuvant therapies, we did not find any impact on survival. Only adjuvant irradiation resulted in slightly longer survival for the subgroup of patients with N2 disease. However, the number of patients receiving additional treatment in our series was too small to draw any conclusions.

In conclusion, sleeve pneumonectomy for central non-small cell lung cancer invading the carina or proximal main bronchus can be performed with tolerable risk and encouraging survival rates in selected cases. Five-year survival rate for completely resected nodal negative patients was 70% in this retrospective single-institution series. The number of patients receiving additional treatment in our series was too small to draw any conclusions. Sleeve pneumonectomy may also be an option for palliative indication in highly selected cases with complications from a central tumor not manageable by endoscopic intervention.

References