The aim of this study was to evaluate the incidence, clinical data and patterns of mediastinal lymph node metastasis (pN2) in non-small-cell lung cancer patients who underwent systematic mediastinal lymph node dissection (SMLND). We retrospectively studied 140 consecutive patients [125 male and 15 female, mean ages 54.61±9.23 years (range, 21-75)], underwent SMLND and major lung resections due to non-small lung cancer (NSCLC), from January 2005 till December 2009. Preoperative clinical staging for mediastinal lymph node metastasis was negative (cN0) in all patients. SMLND was defined as a complete removal of mediastinal lymph nodes. Clinical-pathological data were compared according to the pN stage. Lymph node metastasis to the mediastinum was confirmed in 13 (9.28%) patients. In squamous cell cancer pN2 were in 8 (5.71%) cases out of 82 cases with cN0. On the other side in the adenocarcinomas pN2 were in 5 (3.57%) cases out of 48 with cN0. Unvaried analysis revealed central tumor site as predictive factor for mediastinal lymph node involvement. The upper mediastinal compartment was infiltrated in 12 (8.57%) cases, middle in 8 (5.71%) and lower in 3 (2.14%) cases. Pneumonectomy was the most performed surgical procedure in pN2 patients. We concluded that SMLND improves pTNM staging in lung cancer patients who underwent major lung resections with central location of the tumour. **Key words:** Mediastinal lymph node metastasis, clinically N0 non-small-cell lung cancer, underwent surgical resection.

1. INTRODUCTION

Lung cancer is a common cause of cancer mortality in the developed world. Despite advances in variety of therapies, surgery for NSCLC is still the most effective method of controlling the primary tumor provided it is resectable for cure. The treatment of NSCLC depends on the TNM stage and mediastinal N2 lymph nodes remain a critical part of staging lung cancer patients. For this reason many authors insist on the importance of SMLND for accurate staging (1). In this study we aimed to assess overall rate of pN2 for patients who underwent SMLND based on our experience. We evaluated all consecutive SMLND and lung cancer resections performed on our department during 5 year period.

2. MATERIAL AND METHODS

We retrospectively studied clinical records of 140 consecutive patients with mean ages 54.61±9.23 (range 21-75) who underwent complete anatomical resection for histological proven NSCLC in five years, from January 2005 till December 2009. Among this group, 125 male patients with mean age 54.45±10.91 years and 15 female patients with mean age 53.16±11.34 years were enlisted. All patients had stage T1-3N0, assessed by preoperative computer tomography (CT) imaging of the chest, brain, abdomen, bone scan and abdominal and supraclavicular ultrasound scanning. Patients with proven N2 or N3 lymph node involvement were excluded from study. None of the patients in the study received preoperative chemotherapy or radiotherapy. Patients with previous or coexisting malignant disease were excluded from the study. Pulmonary and circulatory functions were required to be eligible for radical resections. Complete resection was defined as removal of primary tumor and all accessible hilar and mediastinal lymph nodes with...
no residual tumor left behind. SMLND is defined as a radical and block mediastinal lymph node dissection. The major lung resections procedures were lobectomy and pneumonectomy with standard posterolateral thoracotomy. The three compartments included upper or superior mediastinal node (station 1-4), the middle or subcarinal and paraeosophageal node (station 7-8) and lower compartment or pulmonary ligament node (station 9). Metastasis to these compartments including either to one or multiple node regarded as positive. All tissue samples were sent to department of pathology. Three major types of carcinoma, squamous cell carcinoma, adenocarcinoma and large cell carcinoma were diagnosed and selected to analyze lymph node pattern.

2.1. Statistical analysis

Statistical analysis was performed using χ2 test (or the Fisher’s exact test as required). Values were expressed as mean ± S.D. (ranges). Univariate analysis was performed to identify factors linked to the status of nodal involvement. P-value ≤ 0.05 was regarded as significant.

3. RESULTS

All patients were treated by lobectomy or pneumonectomy with standard posterolateral thoracotomy. There were 3 postoperative deaths or 2.1%. Atrial fibrillation was observed in 12 (8.5%) patients. Wound infections, atelectasis, prolonged air leak and thoracic empyema were observed in 10 (7.1%), 8 (5.7%) 3 (2.1%), and 5 (3.6%) patients. The extent of resection was lobectomy in 89 (63.6%) patients and pneumonectomy in 51 (36.4%). The pathologist revealed 82 (58.5%) squamous cell carcinoma, 48 (34.3%) adenocarcinoma and 10 (7.1%) large cell carcinoma. Postoperative TNM and histological status is shown in Table 1.

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3.3. Postoperative TNM and histological status

Table 2. Clinicopathological characteristics of patients according to the N status

<table>
<thead>
<tr>
<th>Patients</th>
<th>NO (%)</th>
<th>N1 (%)</th>
<th>N2 (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>51</td>
<td>63</td>
<td>11</td>
<td>125 (89.3)</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>9</td>
<td>2</td>
<td>15 (10.7)</td>
</tr>
<tr>
<td>Squamous cc</td>
<td>27</td>
<td>47</td>
<td>8</td>
<td>82 (58.6)</td>
</tr>
<tr>
<td>Adeno cc</td>
<td>28</td>
<td>15</td>
<td>5</td>
<td>48 (34.3)</td>
</tr>
<tr>
<td>Central TS</td>
<td>11</td>
<td>31</td>
<td>10</td>
<td>59 (42.1)</td>
</tr>
<tr>
<td>Peripheral TS</td>
<td>44</td>
<td>41</td>
<td>3</td>
<td>81 (57.8)</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>7</td>
<td>32</td>
<td>12</td>
<td>51 (36.4)</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>48</td>
<td>40</td>
<td>1</td>
<td>89 (63.6)</td>
</tr>
</tbody>
</table>

*group of patients who underwent univariate analysis

4. DISCUSSION

This study did not reveal an increased morbidity after SMLND in patients with NSCLC compared to the findings of other reports in this respect (2). Our results in general agree with the study reported by Izbicky and associates (3), which described 2001 patients and demonstrated no increase in the rate of broncho-pleural fistula due to interruption of blood supply to the bronchial stump, phrenic and recurrent laryngeal nerve injury, chylothorax and hemothorax. We reported only relatively high incidence of arterial fibrillation (8.5%) and atelectasis (5.7%) probably due to excess denervation after hilar dissection and inadequate controlling postoperative pain. Operative mortality in lung resections reported by Allen et al. (2) was 2.0% compared with 2.1% in current study. Therefore, the fear of increased complications by performing a SMLND is unfounded.

The results of our study confirmed lymph node metastasis to the mediastinum in 13 (9.3%) patients out of 140 patients with negative preoperative mediastinal lymph node staging (cN0). There was strong similarity in the percentage of patients (11.5%) reported by Sugi et al. (4). Sioris et al. (5) also demonstrated that SMLND is necessary for accurate pN2 staging. They found 17% pN2 patients who were preoperatively diagnosed as cN0. This highly accurate staging after SMLND might allow a more precise
selection of the patient chemotherapy protocols with possible benefit in overall survival (6). It also may allow to eradicate otherwise undetected micro metastasis which might result in better local control and improved overall outcome of the patients (7).

This study also analyzed clinico-pathological factors that might be significant predictive for lymph nodal involvement in patients who underwent resections of the NSCLC. Univariate analysis revealed central tumor site as predictive factor for mediastinal lymph node involvement with p=0.04. Ketchedjian et al. also showed that central tumors have a higher incidence of lymph node metastasis (8). In their series the incidence for nodal involvement was 50% for central tumor of any size. The major contributors may be intrapulmonary lymphatic route, interlobar lymph node so-called lymph sump and tumor infiltration capability (9).

Considering our results, a lobectomy is acceptable for patients for N0-1 patients with peripheral tumor, and pneumonectomy for N1-2 patients with central tumors. The similar results are revealed by Takizawa et al. (10). In this study pneumonectomy is acceptable for patients for N0-1 disease. Factors as central location of tumor and upper mediastinal metastasis compartment involvement were highly correlated with pN2 disease. SMLND is safe procedure, and improves pTNM staging in NSCLC patients. Results confirmed that SMLND should be performed in all patients who underwent pneumonectomy with central site of the tumor.

REFERENCES

5. Sioris T, Jarvenpaa R, Kuukasjarvi P, He-