Alternative paratracheal lymph node dissection in left-sided hilar lung cancer patients: comparing the number of lymph nodes dissected to the number of lymph nodes dissected in right-sided mediastinal dissections

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Abstract

Objective: Removing or sampling lymph nodes from the bilateral paratracheal area through a left thoracotomy is not a standard procedure in patients with lung cancer. The aim of this study was to evaluate the feasibility of a technique without ductus arteriosus division and mobilization of the aortic arch and to compare the number of lymph nodes resected in left-sided dissections to the number of lymph nodes removed in right-sided mediastinal dissections that are routinely performed in clinical practice.

Methods: A total of 93 patients with hilar lung cancer were evaluated. A prospective study was conducted on 51 patients with primary left-sided hilar lung cancer, who underwent left thoracotomy and paratracheal lymphadenectomy between January 2008 and January 2010. The number of nodes dissected in these patients was compared with the number of nodes dissected in 42 patients with right-sided hilar lung cancer by right-sided mediastinal dissection within the same period.

Results: The mean number of resected nodes in the bilateral paratracheal area via left thoracotomy was 8.4 (2—18 nodes). The distribution from 4R—4L—2L—2R was as follows: 3.3—2.5—0.5—2.1, respectively. Six patients (11.7%) were diagnosed with occult N2, and two (3.9%) of these patients also had N3 disease concomitantly. The number of dissected nodes from the ipsilateral station 2 via right-sided versus left-sided thoracotomy was 1.6 versus 0.5 (p = 0.000), whereas the number of dissected nodes from ipsilateral station 4 via right-sided versus left-sided thoracotomy was 3.3 versus 2.5, respectively (p = 0.1). The number of dissected nodes from the contralateral station 2 via right-sided versus left-sided thoracotomy was 0.2 versus 2.1 (p = 0.000), whereas those numbers from the contralateral station 4 via right-sided versus left-sided thoracotomy were 1.0 versus 3.3, respectively (p = 0.000).

Conclusions: Lymphadenectomy of the paratracheal area via left thoracotomy without ductus arteriosus division and mobilization of the aortic arch is technically feasible. From these data, regardless of approach, more lymph nodes are obtained from the right paratracheal space; this appears to be due to the fact that there are more right-sided paratracheal lymph nodes.

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Keywords: Lung cancer; Mediastinal dissection; Left thoracotomy

1. Introduction

The most important prognostic factor in operable non-small-cell lung cancer (NSCLC) is the presence or absence of lymph node metastases. Thus, systematic mediastinal nodal dissection or sampling of N2 and N1 nodes during thoracotomy is essential for the accurate evaluation of pathological N (node) stage. It is clear that lymph node sampling is useful for staging and prognostic purposes. However, the optimal extent of lymph node dissection is controversial, and the benefits of systematic sampling versus complete mediastinal lymph node dissection or extended lymph node dissection are still under investigation [1—6]. A meta-analysis of three randomized trials found a significant survival benefit of dissection compared with sampling [5].

There is a major discordance between the approaches to paratracheal compartment dissection for tumors of the right and left lung. For a right-sided NSCLC, tumor resection could be accompanied by systematic mediastinal lymph node dissection or extended lymph node dissection, according to the surgeon’s preference [7,8]. The bilateral paratracheal area including the azygos vein, superior vena cava, and ascending aorta can be completely dissected during right-sided resections (level 1—4). Dissection of the bilateral paratracheal area through left-sided thoracotomy is not a standard procedure [9].

To date, lymphadenectomy of the bilateral paratracheal area for left-sided tumors has been performed using median
The inclusion/exclusion criteria for the study were as follows:

- usefulness of an alternative paratracheal lymph node dissection technique for patients with left-sided hilar NSCLC.
- The latter two techniques were described as a preoperative work-up, but they allow for complete adenectomy [16].

The aim of this study was to use pathology reports from the same surgical team to evaluate bilateral paratracheal dissection, compare the number of lymph nodes resected during left-sided versus the standard right-sided paratracheal dissection, and discuss the possible risks and benefits of the left-sided approach.

2. Materials and methods

2.1. Study group

From 31 December 2007 to 31 December 2009, we conducted a prospective study to evaluate the feasibility and usefulness of an alternative paratracheal lymph node dissection technique for patients with left-sided hilar NSCLC. The inclusion/exclusion criteria for the study were as follows:

(a) diagnosed with NSCLC in clinical stage T2—T4 (left-sided hilar location and T4 due to left atrial invasion);
(b) negative cervical mediastinoscopy: a standard cervical mediastinoscopy was performed on all patients, and five stations in the mediastinum (2R—2L—4R—4L and 7) were sampled. None of these patients had extended mediastinoscopy or anterior mediastinotomy to evaluate stations 5 and 6.
(c) general performance status enabling a major resection;
(d) informed consent of patients (all patients received detailed information regarding the procedure, and potential risks and benefits were discussed); and
(e) patients, who received neoadjuvant treatment, underwent a previous operation for lung cancer or cardiac pathology or those with stents or a calcified aorta were excluded.

The basic preoperative work-up included a medical history, physical examination, chest computerized tomography, fiberoptic bronchoscopy, cranial magnetic resonant imaging and positron emission tomography—computed tomography (PET—CT). All patients with hilar NSCLC underwent cervical mediastinoscopy, even if the mediastinal lymph nodes did not show increased uptake during PET—CT. Patients with N2—3 disease underwent oncological treatment and were further evaluated for surgery. None of these patients underwent an extended mediastinoscopy or anterior mediastinotomy to evaluate stations 5 and 6. We performed left-sided paratracheal dissection only in patients with hilar lung cancer and excluded those of T1 and peripherally located T2 and T3 lesions. Although performing this study in patients with a low probability of lymph node involvement may be helpful in confirming the other tests or finding the positive nodes that passed unnoticed, we aimed not to perform an extra dissection in these patients due to the lower possibility of mediastinal lymph node metastases to prevent the possible side effects of this technique.

2.2. Data collection

All preoperative data (age, gender, histology, and clinical tumor, node, metastasis (cTNM)), operative data (type of resection and duration of paratracheal dissection) and postoperative data (length of stay, morbidity, mortality, number of nodes dissected from each station, and pathological TNM (pTNM)) were recorded prospectively. Each node particle that was removed was counted toward the total only if the capsule was intact and the lymph node was removed in its entirety. If the node was removed in pieces, the lengths of the longest side of the pieces were added. If the lengths reached 1 cm, the node was counted as one node toward the total. If the lengths of pieces did not add up to 1 cm, the node was not counted. Mediastinoscopically removed nodes and nodes less than 1 cm in the greater dimension, but fragmented, were also not counted.

2.3. Control group (patients with right-sided hilar lung cancer)

During this period, 288 patients with NSCLC underwent operations by the same team. Data were collected prospectively from the department’s electronic medical record database. Matching was performed based on the anatomical location of the resected tumors. Patients, who had a right-sided pneumonectomy, upper sleeve resection, or upper bilobectomy for a tumor located in the hilum of the right lung, formed the control group. Patients who underwent neoadjuvant treatment were excluded. Patients with right-sided lung cancer underwent either systematic sampling or systematic lymph node dissection, as determined by European Society of Thoracic Surgeons (ESTS) [16]. According to this nomenclature system, systematic sampling refers to a predetermined selection of the lymph node stations specified by the surgeon [16]. This technique was chosen by our department for mediastinal dissection in patients without lymph node metastases identified by PET—CT or histological examination of frozen sections. Systematic lymph node dissection is the dissection and removal of all mediastinal tissue containing lymph nodes within anatomical landmarks [16]. This technique was employed when frozen-section examination revealed a positive lymph node in the mediastinum or in a hilar location. Extended mediastinal dissection, including the contralateral and cervical lymph nodes, is performed through a median sternotomy and cervicotomy [16]. This technique was not employed at all during this study. All the patients had pathological stage T2—T3 tumors except for six patients, who had T4 tumors due to the invasion of the superior vena cava or the left atrium.

Demographic, clinical, surgical, and pathological data from right-sided hilar lung cancer patients were prospectively recorded in an electronic database, and the data were retrieved from our unit’s database. We evaluated the subjects’ pathology reports. The number of nodes dissected from stations 2R, 2L, 4R, and 4L were counted and noted.
2.4. Technique of paratracheal area dissection from left thoracotomy without ductus arteriosus division and aortic arch mobilization

The pulmonary hilum on the left side is exposed after dissection of the mediastinal pleura along the lower edge of the aortic arch, anterior and posterior to the vagus nerve, and posterior to the phrenic nerve. Subaortic, paraaortic, subcarinal, hilar, and interlobar lymph nodes (level 5—11) are resected in the standard manner. After complete removal of number 5 nodes, blunt dissection is performed toward the superior and contralateral mediastinum through an opening posterior to the left main pulmonary artery (LMPA) and anterosuperior to the left main bronchus (LMB). The ductus arteriosus, LMPA and LMB are the borders of the inlet to the superior mediastinum via left thoracotomy (Fig. 1). Endopeanuts are used to retract the descending aorta to dissect the 4L station while retracting the LMB caudally. After complete dissection of the 4L station with standard equipment, further dissection with sponge sticks and endopeanuts enables sampling/dissection of the 4R nodes with large forceps. The borders of the 4R dissection zone are as follows: the left border is the posterior wall of the main pulmonary artery and ascending aorta, the superior border is the inferior wall of the aortic arch, the right border is the anterolateral wall of the trachea and the anterior border is the medial wall of the superior vena cava (Fig. 2). To reduce the potential for vessel damage, extreme caution should be taken. Small branches coming from bronchial arteries or mediastinal veins can be managed with clipping and cautery. Sharp dissections are required to divide trachea—broncho—pericardial ligaments. Blunt dissection with an aspiration cannula is a good way to release the number 4R station, and these nodes are resected by retracting the trachea posteriorly with endoscopic peanuts and the main pulmonary truncus with another retractor (Video 1).

By dissecting the mediastinum superiorly and retracting the trachea caudally and posteriorly, the surgeon can sample the 2R station (Video 1). Complete clearance of the medial sides of the superior vena cava and the azygos vein, both sides of the trachea and the inferomedial side of the aortic arch are accepted standards of this surgical technique.

Dissection of 2L is not feasible from this approach due to the angulation of the aortic arch. Finger dissection under the aortic arch and above the trachea is performed, such that the index finger can be seen behind the left subclavian artery. A longitudinal incision posterior to the left subclavian artery is performed, and dissection of the artery posteriorly helps to reach station 2L (Fig. 3). Finally, a complete systematic dissection of the bilateral paratracheal area is performed.

2.5. Morbidity

Subjects experienced complications as a result of resections of hilar tumors combined with mediastinal dissection; hence, morbidity cannot be attributed to mediastinal dissection alone. Postoperative morbidity was defined as respiratory (atelectasis, pneumonia, postpneumonectomy edema, adult respiratory distress syndrome, or pulmonary embolism), cardiac (arrhythmia, myocardial infarction, cardiac failure, deep vein thrombosis, transient ischemic attack (TIA), or stroke), surgical (hemothorax,
bronchopleural fistula, empyema, or chylothorax), or neurological (nerve injuries to the recurrent laryngeal nerve and phrenic nerve). The length of time that subjects’ required chest tubes was evaluated in addition to the morbidity and mortality in both groups.

2.6. Analyses

Groups were compared in terms of epidemiologic (mean age and gender), oncological (pT and histology), and surgical (number of nodes dissected from each station, type of resection, complications, and mortality) data. Statistical analyses were performed with Fisher’s exact tests, Pearson chi-square tests and independent samples t-tests.

3. Results

Because patients were matched only by the anatomical locations of their tumors, both groups’ epidemiological, oncological, and surgical data were compared to assess any differences. No significant differences were found between groups with regard to mean age ($p = 0.28$), gender ($p = 0.40$), pT ($p = 0.54$), type of resection ($p = 0.06$), complications ($p = 0.95$), duration of chest tube placement ($p = 0.69$), mortality ($p = 0.59$), or histology ($p = 0.81$), as shown in Table 1.

3.1. Number of nodes dissected from each station

The lymph-node-dissection techniques used for patients with right-sided hilar lung cancer were systematic sampling in 21 patients and systematic lymph node dissection in 21. In all patients with left-sided hilar lung cancer, we performed bilateral paratracheal lymph node dissection in addition to systematic mediastinal lymph node dissection, according to the ESTS proposal [17]. The number of nodes dissected from each station in the bilateral paratracheal area and mean number of nodes are shown in Table 2.

No significant differences were found between groups with regard to the total number of paratracheal nodes dissected (left: 8.4 and right: 6.1). The number of nodes dissected in ipsilateral nodal stations 2 (2L: 0.5 ± 0.8 (0–3) vs 2R: 1.6 ± 1.3 (1–6) ($p = 0.000$)) and 4 (4L: 2.5 ± 1.8 (1–10) vs 4R: 3.3 ± 2.4 (1–11) ($p = 0.1$)), and contralateral stations 2 (2R: 2.1 ± 2.1 (0–10) vs 2L: 0.2 ± 0.6 (0–3) ($p = 0.000$)) and 4 (4R: 3.3 ± 2.7 (0–13) vs 4L: 1.0 ± 1.3 (0–6) ($p = 0.000$)) showed a trend toward more extensive ipsilateral lymph node removal in the right-sided resections and contralateral removal in the left-sided resections (Table 2).

There were six and four patients with N2 disease in the left-sided and right-sided groups, respectively ($p = 0.73$).

3.2. Mortality and morbidity

The number of patients that died after right-sided and left-sided resections was two (4.7%) and one (1.9%), respectively. The number of patients with major complications was 13 (30.9%) and 14 (27.4%) for the right-sided and left-sided patients, respectively. Respiratory and surgical complications were more commonly seen in patients who underwent right-sided resections, whereas left recurrent laryngeal nerve palsies were more commonly seen in patients who underwent left-sided resection. Most of these palsies were transient (60%), and patients recovered spontaneously within 2 months (Table 3).

4. Discussion

No significant differences were found between groups with regard to morbidity and mortality when bilateral
paratracheal lymph node dissection in patients with left-sided hilar lung cancer was employed. Although the patients with right-sided dissections were not balanced for age, gender, histology, and co-morbidity, both groups demonstrated similar durations of chest-tube drainage, similar numbers of complications, and similar incidences of mortality.

The potential hazards of this technique included transient recurrent laryngeal nerve palsy and chylothorax, which were also seen more often in left-sided resections. The percentage of patients, who had recurrent laryngeal nerve palsy, could be considered high although most of them recovered spontaneously. Because all of the patients had hilar lung cancer requiring hilum dissection, and all of them had a preoperative mediastinoscopy, especially for a search of possible 4L metastases, we could not claim the technique only for the occurrence of this complication. Patients who underwent right-sided resections experienced more surgical and pulmonary complications, and these findings are consistent with the nature of the lung surgery.

Of note, only 50% of the patients with right-sided resections underwent 2L and 4L dissection, whereas all of them had 2R and 4R dissections. This situation might have created a difference between the number of lymph nodes dissected in the paratracheal area via left- and right-sided dissections. In addition, fewer lymph nodes were able to be removed via the dissection of the left chest in the ipsilateral paratracheal area. Based on these findings, two questions arise: (1) Are there fewer lymph nodes in the left paratracheal area than in the right? And (2) Could the current techniques to dissect the left paratracheal area be insufficient either from the left or right chest? We could have compared systematic dissections on both sides; however, we aimed to have a specific group of patients with hilar location, non-neoadjuvant, with a preoperative mediastinoscopy. These criteria restricted our number and we decided to have our routine practice in this group. In systematic sampling performed in half of the right-sided lung cancer patients, stations 2R–4R and 7 are removed mostly.

We believe that dissection of the left paratracheal area is sufficient and effective. This inequality could be an effect of less lymph node potential of the left side, as originally described by Sukienikow in 1903 [18]. Glazer et al. [19] reported on the size and the number of normal lymph nodes located in the mediastinum. The largest normal mediastinal nodes were found in the subcarinal and right paratracheal regions. The nodes were demonstrated to be larger on the right side than on the left side. Station, percentage with nodes present, and minimum number of nodes were presented as follows: (2R, 80%, 2.5), (2L, 68%, 2.1), (4R, 98%, 4.8), and (4L, 98%, 4.5) [19] Another interesting finding was that the number of nodes dissected in stations 2R and 4R was similar in both groups, suggesting that this technique is effective for contralateral paratracheal node dissection. It could be speculated that the dissection and complete removal of the 2R station from left thoracotomy is difficult and the chance of the entire removal of a lymph node is low. The risk of fragmentation could be high, which could cause uncertainty as regards the actual number of nodes in this location. Dissection of this area could be necessary when number 7 nodes are found to be positive during a resection of a left-lower-lobe tumor. These tumors have a tendency to metastasize to contralateral paratracheal nodes [20]. Other authors also suggested that the normal short-axis diameter of the lymph nodes in station 2 is 8 mm and in station 4 is 10 mm [21].

Although mediastinal dissection techniques and nomenclature are still not standardized, the most significant step in nomenclature regarding systematic nodal dissection was performed in 1996 and published in 1997 by Goldstraw [22]. This was an international consensus meeting during which nomenclature and minimal requirements were agreed upon [22]. To define a systematic nodal dissection, at least 3 stations from the mediastinum, including station 7, should be resected along with all lymph nodes and fatty tissue.

The side of the primary tumor, technical variables, intra-operative results of frozen section analysis from specific stations, intra-operative events such as hemodynamic deteriorations or hemorrhagic events, and surgeons' personal preferences affect the type and amount of anatomical hilar, interlobar, and mediastinal lymph node dissections performed. From the oncological point of view, a very important question is whether, and to what extent, a systematic mediastinal lymph node dissection is feasible.

### Table 3. Complications in left and right-sided dissections and resections.

<table>
<thead>
<tr>
<th>Side</th>
<th>Right side</th>
<th>Left side</th>
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<tr>
<td><strong>Nerve</strong></td>
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<tr>
<td>Respiratory</td>
<td>1 patient atelectasis</td>
<td>5 patients (3 recovered)</td>
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<tr>
<td></td>
<td>1 patient pulmonary embolism</td>
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<td></td>
<td>1 patient ARDS</td>
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<tr>
<td></td>
<td>3 patients pneumonia</td>
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<tr>
<td><strong>Cardiac</strong></td>
<td>1 patient stroke</td>
<td>1 patient atrial fibrillation</td>
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<tr>
<td><strong>Surgical</strong></td>
<td>2 patients prolonged airleak</td>
<td>2 patients prolonged airleak</td>
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<tr>
<td></td>
<td>1 patient empyema</td>
<td>2 patients chylothorax</td>
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<td></td>
<td>1 patient hemorhage</td>
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<td></td>
<td>1 patient bronchopleural fistula</td>
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<td>1 patient dehiscence of thoracotomy</td>
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<tr>
<td><strong>Other</strong></td>
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<tr>
<td>Nerve 5 patients (3 recovered)</td>
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</tr>
<tr>
<td>Respiratory 13 patients (30%)</td>
<td>14 patients (27%)</td>
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"p: 0 > 0.05" * Pearson chi-square test.
There is still no consensus in the field, but there has been a trend, at least among the European chest surgeons, toward performing a systematic node dissection or systematic sampling of the right side, including at least stations 2R—4R—7—8 and 9 [17]. The frequency of occurrence of skip metastasis and absence of a reliable sentinel lymph node in lung cancer could make systematic lymph node dissection in anatomical compartments as a standard procedure for the evaluation of the exact N stage [6]. However, more extensive dissection, including the contralateral and the cervical lymph nodes, has not been a common a practice in Europe and North America. In the left chest, systematic dissection or sampling included dissection of level 5—9 nodes [17]. The ipsilateral dissection of stations 2L and 4L from a left thoracotomy for a complete nodal dissection of the left upper mediastinum could be done after division of the ductus arteriosus and mobilization of the aortic arch [17]. Although contralateral paratracheal lymph node drainage of the left lower lobe has been widely considered, it has not become a part of a standard practice to dissect the contralateral paratracheal nodes of the left side. To date, surgeons have only performed this procedure in extended dissections including cervical dissection techniques. In this study, we show that dissection of the contralateral paratracheal lymph nodes is possible without undertaking more extensive surgical dissection.

The potential benefits of this technique are as follows:

- complete and correct staging of the bilateral paratracheal area (staging procedures similar to right-sided resections);
- for high-risk patients, frozen section analysis may help to avoid potential morbidity and mortality of the resection; and
- lymphadenectomy through the primary surgical approach may take less time per patient when compared with alternative techniques such as VAMLA and TEMLA due to repositioning and reorganization of the operation room.

Employing this procedure in every patient with left-sided lung cancer is not recommended. This technique is strongly suggested for patients with left-lower-lobe lung cancers with a positive number 7 station and patients with upper-lobe lung cancers with positive number 5 and/or 6 stations. In addition, this technique should be considered prior to a decision for a major resection if station 10 positivity was diagnosed and a mediastinoscopy was not performed. Further, when an exploratory thoracotomy for an undiagnosed mass turns out to be an NSCLC, dissection of the mediastinum may be considered prior to resection.

These findings suggest that paratracheal dissection from the left thoracotomy without ductus arteriosus division was as effective in detecting mediastinal node metastases in NSCLC patients as systematic nodal dissection for the right side. More extensive prospective studies are required to establish the clinical usefulness of this technique.

We believe that this simple technique facilitates successful contralateral and ipsilateral paratracheal lymph node dissection. Major morbidity events were not observed during or after this procedure, although there was a tendency toward a common and mostly transient recurrent laryngeal nerve palsy. This new technique could be a part of routine practice when systematic nodal dissection is considered in patients with left-sided lung cancer.

References


Appendix A. Supplementary data

Supplementary data associated with this article (video 1) can be found, in the online version, at doi:10.1016/j.ejcts.2010.09.013.