Completeness of lung cancer surgery: is mediastinal dissection common practice?

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Abstract

OBJECTIVES: In patients with early-stage non-small cell lung cancer, surgery offers the best chance of cure when a complete resection, including mediastinal lymph node dissection, is performed. A definition for complete resection and guidelines for intra-operative lymph node staging have been published, but it is unclear whether these guidelines are followed in daily practice. The goal of this study was to evaluate the extent of mediastinal lymph node dissection routinely performed during lung cancer surgery, and hereby the completeness of resection according to the guidelines of the European Society of Thoracic Surgery (ESTS) for intra-operative lymph node staging.

METHODS: In a retrospective cohort study, the extent of mediastinal lymph node dissection was evaluated in 216 patients who underwent surgery for lung cancer with a curative intent in four different hospitals, three community hospitals and one university hospital. Data regarding clinical staging, the type of resection and extent of lymph node dissection were collected from both the patient’s medical record and the surgical and pathology report. Based on histology, location and side of the primary tumour, the extent of mediastinal dissection was compared with the ESTS guidelines for intra-operative lymph node staging.

RESULTS: According to the surgical report interlobar and hilar lymph nodes were dissected in one-third of patients. A mediastinal lymph node exploration was performed in 75% of patients; however, subcarinal lymph nodes were dissected in <50% of patients and at least three mediastinal lymph node stations were investigated in 36% of patients. In 35% of the mediastinal stations explored, lymph nodes were sampled instead of a complete dissection of the entire station. A complete lymph node dissection according to the guidelines of the ESTS was performed in 4% of patients. Despite an incomplete dissection unexpected mediastinal lymph nodes were found in 5% of patients.

CONCLUSIONS: In daily practice, the intended curative resection for lung cancer cannot be considered complete in the majority of patients, because of an incomplete lymph node dissection according to the current guidelines of the ESTS.

Keywords: Lung cancer surgery • Staging • Lymph node dissection

INTRODUCTION

In early-stage non-small cell lung cancer (NSCLC), surgery offers the best chance of cure when a complete resection is performed and a 5-year survival rate up to 75% may be expected [1]. The completeness of a resection is based on both pathological assessment of the bronchial, vascular and parenchymal resection margin of the surgical specimen, and the extent of a mediastinal lymph node dissection [2].

Already in the sixth, but also in the seventh edition of the TNM system for staging lung cancer [1, 3], a different survival was observed for patients after clinical versus pathologic staging, favouring the second in the same stage group. Thus, although progress has been made in pre-operative staging by the use of FDG-PET and EUS- or EBUS-FNA eventually followed by mediastinoscopy, a dissection of both peripheral, hilar and mediastinal lymph nodes is mandatory for accurate staging and optimizing therapy [4]. However, in a large survey of >11.000 NSCLC patients treated surgically, only 57.8% of patients underwent any kind of mediastinal lymph node dissection [5]. Furthermore, the extent, with regard to the number of mediastinal stations explored, remains unclear.
and different techniques were used in removing lymph nodes.

In 2006, guidelines for intra-operative lymph node staging in lung cancer surgery have been published by the European Society of Thoracic Surgery (ESTS) [6], but it is unclear if these guidelines have been implemented in daily practice.

The goal of our study was to evaluate the extent of mediastinal lymph node dissection routinely performed during lung cancer surgery, and hereby the completeness of resection according to the Guidelines of the ESTS for intra-operative lymph node staging.

MATERIALS AND METHODS

In a retrospective cohort study, the extent of mediastinal lymph node dissection was evaluated in patients who underwent an intended curative resection for early-stage NSCLC. Patients from four different hospitals were included, three community and one university hospital. Operations were performed by general surgeons with an additional certification for thoracic surgery, and cardio-thoracic surgeons, each in two hospitals, which is representative for the general practice in the Netherlands. In three hospitals a training programme in thoracic surgery is provided.

All patients who underwent a lung resection for NSCLC in 2007 were extracted from the surgical database of each hospital. Only patients who were judged to be candidates for a curative resection after clinical staging were included in this study.

Data regarding clinical staging by means of CT-scan, FDG-PET, EUS-/EBUS-FNA and mediastinoscopy were collected from the patient’s medical record. Mediastinal lymph nodes with a short axis of >1 cm on CT-scan were considered enlarged, mediastinal FDG-PET was considered positive if noted by nuclear medicine.

The surgical report was used for collecting data about the type of resection and extent of lymph node dissection. Finally, the pathology report was used to check the presence of lymph nodes in each dissected station, as well as the result of histological assessment.

In patients who had undergone induction chemo-radiotherapy, data concerning restaging were used.

Based on histology, location and side of the primary tumour, the extent of mediastinal dissection was compared with the ESTS guidelines for intra-operative lymph node staging [6]. For a tumour on the right the upper- and lower-paratracheal lymph nodes (station 2R and 4R), and visible nodes anterior of the superior caval vein or posterior to the trachea (station 3), are supposed to be resected, as well as the inferior mediastinal lymph nodes which are located subcarinal (station 7), paraeosophageal (station 8) and in the pulmonary ligament (station 9). For a tumour on the left, the same inferior mediastinal lymph nodes should be removed, in addition to the subaortic, para-aortic and lower-paratracheal lymph nodes (station 5, 6 and 4L). A systematical dissection of all the mediastinal tissue containing lymph nodes is recommended and the highest mediastinal node should be labelled.

In case of a peripheral squamous cell carcinoma, <3 cm, a lobe-specific lymph node dissection is justified when the interlobar and hilar lymph nodes appear to contain no metasteses. Three mediastinal lymph node stations have to be dissected, depending on the lobar location of the tumour, but always the subcarinal nodes. At least six lymph nodes have to be removed.

Since the surgical procedures were performed in 2007, lymph node mapping was performed according to the Mountain-Dresler lymph node classification [7].

RESULTS

In a combined series, from 4 hospitals 216 patients underwent an intended complete resection for NSCLC in 2007, representing 14% of all lung cancer resections in the Netherlands in 1 year.

Clinical staging

Pre-operatively all patients had undergone a CT-scan of the chest, as well as a whole body FDG-PET. By imaging 85 patients (39%) appeared to have suspicious mediastinal lymph nodes: in 25 patients (11%) enlarged mediastinal lymph nodes, were seen on CT-scan only, in 15 patients (7%) at least one mediastinal lymph node station appeared to be positive on FDG-PET without lymph node enlargement on CT, while both modalities were positive in 45 patients (21%). Of all patients with suspicious lymph nodes by imaging, 28 patients underwent EUS- or EBUS-FNA, but these procedures weren’t standard of care at that time.

A cervical mediastinoscopy was performed in 84 patients (39%), because of enlarged and/or PET positive mediastinal lymph nodes in 72 patients (33%) and due to a centrally located tumour in 12 patients (6%).

Twenty-four patients had undergone induction chemo-radiotherapy due to positive mediastinal lymph nodes at initial staging.

Surgery

A lobectomy was the standard procedure and was performed in 182 out of 216 patients (84%), in 179 patients by means of a thoracotomy. Three patients underwent a video-assisted lobectomy. In 27 patients (13%) a pneumonectomy had to be performed and 7 patients (3%) underwent a sublobar resection due to poor pulmonary function: a segmentectomy in 2 patients and a wedge resection in 5 patients.

According to the surgical report, interlobar lymph nodes were dissected in 74 patients (34%) and hilar lymph nodes in 67 patients (31%). Any kind of mediastinal lymph node dissection was performed in 161 patients (75%).

In total 414, mediastinal lymph node stations were explored during surgery in 216 patients, a mean of 1.9 station per patient, ranging from zero to six. No mediastinal lymph node station at all was dissected in 55 patients, whereas 6 stations were dissected in only 4 patients (Fig. 1). There were clear differences between the participating hospitals, the number of patients without any mediastinal dissection ranged from 3% in one clinic to 44% in another. Accordingly, the mean number of dissected mediastinal lymph node stations per patient ranged from 0.8 to 3.9 per clinic.

However, no difference could be found depending on the surgeon specialty. In 83 patients operated by additionally certified general surgeons, the mean yield was 2.0 mediastinal stations dissected per patient, which was comparable with a mean yield of 1.8 mediastinal stations per patient in 133 patients operated by cardio-thoracic surgeons.
Of all 216 patients, according to the ESTS guidelines, a complete lymph node dissection should have been performed in 189 patients: because of a resection on the right in 101 patients and on the left in 88 patients. In 27 patients a peripheral squamous cell carcinoma of <3 cm was present for which a lobe-specific lymph node dissection is thought to be sufficient, in 9 patients on the right and in 18 patients on the left side.

Of patients with a right-sided tumour, the lower-paratracheal lymph nodes were dissected most frequently, in 55 out of 101 patients (54%), followed by the subcarinal lymph nodes, in 48 out of 101 patients (47%) (Fig. 2). Lymph nodes in front of the superior caval vein or behind the trachea were dissected in only one patient. On the left the subaortic nodes were dissected most frequently, in 48 out of 88 patients (54%), followed again by the subcarinal lymph nodes in 33 out of 88 patients (38%) (Fig. 3). The upper-paratracheal lymph nodes were dissected in four patients. In patients with a lobe-specific dissection, the subcarinal lymph nodes were dissected in just more than half of patients, in 5 out of 9 patients (56%) on the right and in 10 out of 18 patients (56%) on the left side (Fig. 4).

Of 85 patients with suspicious mediastinal lymph nodes on CT-scan and/or FDG-PET, no mediastinal dissection was performed in 21 patients (25%).

Pathologic assessment

Histological examination of the resected tumours revealed an adenocarcinoma in 117 patients, a squamous cell carcinoma in
79 patients, an undifferentiated large cell carcinoma in 9 patients, a carcinoid in 10 patients and a small cell carcinoma in 1 patient.

Assessment of the resection margins revealed a microscopic incomplete resection in five patients.

In 169 patients (78%) the peripheral, intrapulmonary lymph nodes were described in the pathology report.

With regard to the mediastinal lymph node stations, based on the pathology report no distinction could be made between sampling and dissection; however, multiple fragments of lymphatic tissue or an unidentified number of lymph nodes were found in 144 of 414 mediastinal stations, suggesting sampling rather than dissection.

Based on pathologic assessment, 31 patients (14%) were upstaged because of lymph node involvement that was not identified during pre-operative work-up. In 20 patients (9%), clinically staged N0, positive interlobar- or hilar lymph nodes were found and 11 patients (5%) appeared to have unexpected mediastinal metastases.

Ultimately, in only eight patients (4%) a complete lymph node dissection of interlobar, hilar and all mediastinal stations according to the recommendations of the ESTS guidelines was performed.

**DISCUSSION**

In this study, we show that a vast difference exists between a complete mediastinal lymph node dissection as recommended in the current ESTS guidelines and performance in daily practice.

The number of patients that underwent any form of mediastinal lymph node dissection in our study is higher than has been reported in two large surveys concerning surgical care in lung cancer patients [5, 8]. Adherence to the guidelines, however, appears far from ideal: in only 4% of patients a complete lymph node dissection was performed.

Preceding the ESTS guidelines a proposed definition of complete resection has been published [2], which has been adopted by the International Union Against Cancer in the seventh edition of the *TNM Classification of Malignant Tumors* [9]. Based on this definition a resection can be considered complete when only six lymph nodes are removed, three from mediastinal stations, but always including the subcarinal lymph nodes, and three from hilar, interlobar or peripheral stations. But even by these criteria the resection in >50% of patients in our study was not complete, but should be qualified as ‘uncertain’, since the subcarinal lymph nodes were not removed in these patients. Moreover, in only 36% of the patients at least three mediastinal lymph node stations were explored.

The extent of mediastinal staging is considered a process measure of quality [10] that may be dependent of the surgeon specialty [11]. In contrast to a recently presented study [12], we did not find a different yield of mediastinal dissection between patients operated by general surgeons, with an additional certification for thoracic surgery, and cardio-thoracic surgeons. However, the extent of mediastinal dissection varied considerably between the participating hospitals in this study. Although we did not intend to make a comparison, it is illustrative of the controversy that still remains with regard to a mediastinal dissection.

A survival benefit for patients undergoing a complete mediastinal dissection would be the strongest argument in favour of this procedure. Yet, apart from several observational studies [13–15], only one randomized controlled trial demonstrates a better prognosis for patients after a systematic mediastinal lymph node dissection when compared with lymph node sampling [16].

In contrast, two other randomized trials [17, 18] have been published which did not show a prognostic advantage, but finally a meta-analysis concerning these three studies still reports a survival benefit after a follow-up of 4 years, when a complete dissection was performed [19].

Despite this report, it is questionable whether a survival benefit in the future will ever be proved [4]. Also in the recently published ACOSOG Z0030 trial, a complete dissection of mediastinal lymph nodes did not improve survival in comparison with systematic sampling, despite an additional yield of mediastinal lymph node metastases of 4% [20, 21]. Therefore improving staging should be considered the merit of a lymph node dissection and hereby identifying patients who may benefit from adjuvant therapy.

Clinical staging has already improved over the last decade by the implementation of FDG-PET, and a widespread availability of EUS- and EBUS-FNA will probably lead to a further reduction in futile thoracotomies. Since the yield of a mediastinal dissection, of course, is dependent of the pre-operative evaluation, this may diminish the need for an additional evaluation. But even after precise clinical staging, including mediastinoscopy in case of a negative result of EUS- and/or EBUS-FNA performed in dedicated centres, positive mediastinal lymph nodes can be identified in 7% of patients who have undergone a systematic lymph node dissection [22]. Moreover, in general practice the accuracy of pre-operative evaluation will probably be less than reported by dedicated centres.

In our study, all patients underwent FDG-PET in addition to a CT-scan and a mediastinoscopy was performed in 72 out of 85 patients with enlarged and/or PET positive lymph nodes. Despite an incomplete lymph node dissection, positive mediastinal lymph nodes were found in 5% of patients, emphasizing the need for a complete dissection in every patient.

From the surgical report, it remained unclear which criteria were used to perform or omit a mediastinal lymph node dissection in our entire patient cohort, as well as in the group of patients with clinically suspicious lymph nodes. Also the reason to explore a certain lymph node station was rarely described. Of the 75% of patients in whom any mediastinal dissection was performed, on the right side the lower-paratracheal lymph nodes were dissected most frequently and on the left side the subaortic lymph nodes, followed on both sides by the subcarinal lymph nodes. The reason for this may be that both the lower-paratracheal and the subaortic lymph nodes are most easily accessible and under direct vision of the surgeon, whereas for the other mediastinal stations additional exploration is needed. Furthermore, the border with adjacent lymph node stations is not always clear during surgery, despite their definition in the latest edition of the current staging manual [9], so that dissected lymph nodes may not always have been labelled as separate stations. For example, the border between the lower- and upper-paratracheal lymph nodes on the right and on both sides the border between the pulmonary ligament and paraoesophageal lymph nodes can be difficult to identify. Since no differences in survival seem to exist among patients with lymph node metastases to separate stations confined to a single zone [23, 24], this may be an argument to define a complete resection based on exploration of mediastinal zones instead of distinct stations.
In the guidelines of the ESTS, different techniques are described concerning intra-operative lymph node assessment. In a large part of the patients in our study, lymph node sampling instead of a dissection seems to have been performed, since only lymph node fragments were found by pathology rather than mediastinal fat tissue containing lymph nodes. A lymph node dissection is often considered time consuming and causing additional morbidity, but the impact of both aspects appeared to be modest in the randomized ACOSOG Z0030 trial and not responsible for a prolonged length of stay [25].

The question can be raised whether the participating hospitals in this study are representative for the real-world, but patients were included from the four largest hospitals from a national cancer registry in the centre and eastern part of our country. In the Netherlands, on average only 25 lung cancer resections are performed per clinic per year, while the number of operations in the participating hospitals ranged from 35 to 72 in 1 year. Also in the USA the median number of lobectomies for lung cancer performed per year per participant was only 31, according to the Society of Thoracic Surgeons database [8]. Furthermore, three out of the four hospitals in this study are approved as a training facility, what makes it unlikely to perform worse than average.

In conclusion, despite an exploration of the mediastinal lymph nodes in 75% of patients who underwent an intended curative resection for lung cancer, based on the current guidelines resection was far from complete in the majority of patients, both with regard to the surgical technique and the extent of lymph node dissection, as well as the reporting.

Efforts should be made to increase the implementation of guidelines in general practice, to improve the quality of surgical care in lung cancer patients.

Conflict of interest: none declared.

REFERENCES