Extended cervical mediastinoscopy revisited

Birutė Witte, Michael Wolf, Hubertus Hillebrand, Elke Kriegel and Martin Huertgen*

Department of Thoracic Surgery, Katholisches Klinikum Koblenz-Montabaur, Koblenz, Germany

* Corresponding author. Department of Thoracic Surgery, Katholisches Klinikum Koblenz-Montabaur, Rudolf-Virchowstraße 7, 56073 Koblenz, Germany. Tel.: +49-261-4963590; fax: +49-261-4963599; e-mail: m.huertgen@kk-km.de, martinhuertgen@yahoo.de (M. Huertgen).

Received 8 February 2013; received in revised form 25 April 2013; accepted 30 April 2013

Abstract

OBJECTIVES: To describe the diagnostic value of selective extended cervical mediastinoscopy (ECM) in combination with video-assisted mediastinoscopic lymphadenectomy (VAML) in mediastinal staging of potentially resectable left-sided lung carcinoma.

METHODS: Institutional report on 110 ECM procedures indicated for enlarged lymph nodes within the aorto-pulmonary (AP) zone on computed tomography. Staging sensitivity, negative predictive value (NPV) and specificity of ECM, combined VAML and ECM, VAML alone and systematic dissection for lung resection via left-sided video-assisted thoracoscopic surgery (VATS) or thoracotomy were calculated from a subset of 92 patients with left-sided lung carcinoma.

RESULTS: Selective ECM was performed in 12.6% of all video-mediastinoscopic procedures, and added, except for one vascular complication, there was no morbidity. ECM had an impact on mediastinal staging in 78.0% of the lung cancer cases. Sensitivity, NPV and specificity were 0.94, 0.96 and 1 for ECM to detect nodal involvement within the AP zone. Sensitivity, NPV and specificity to detect any mediastinal diseases were 0.94, 0.96 and 1 for the combination of ECM and VAML; 0.64, 0.80 and 1 for VAML alone and 0.76, 0.84 and 1 for systematic mediastinal dissection via left-sided VATS or thoracotomy approach.

CONCLUSIONS: ECM complements VAML in comprehensive mediastinal dissection. Selective ECM is a valuable addendum to mediastinoscopic staging procedures for left-sided tumours, as it enhances sensitivity and NPV. Precaution and experience are required to circumvent the rare risk of potentially fatal vascular accidents.

Keywords: Extended cervical mediastinoscopy • Lung carcinoma • Mediastinal staging • Mediastinoscopy • Video-assisted mediastinoscopic lymphadenectomy

INTRODUCTION

Standard cervical mediastinoscopy first described by Carlens in 1959 is restricted to the pretracheal, paratracheal, tracheobronchial and sub-carinal, and thus central, nodal stations of the middle mediastinum. This limitation was overcome by extended cervical mediastinoscopy (ECM) reaching the sub- and para-aortic nodes (aorto-pulmonary; AP zone [1]), first described by Specht in 1965 [2, 3]. Mediastinoscopy and ECM were introduced at an age when imaging was restricted to chest X-ray and tomography, and multimodality oncological treatment was not available. Pearson [4] and Ginsberg et al. [5] introduced standard and ECM into the diagnostic work-up of lung carcinoma in order to detect mediastinal nodal disease and to exclude affected patients from surgery. At that point of time, doing so was reasonable, as surgery alone was unable to control the high risk both of local recurrence and systemic progression associated with mediastinal disease [6]. In the meanwhile, a growing number of sophisticated diagnostic and therapeutic possibilities became available and allowed a differentiated approach to locally advanced lung carcinoma with mediastinal involvement. Imaging by fused positron emission and computed tomography (PET-CT), harvesting of cytological samples by endoscopic fine-needle aspiration and minimally invasive mediastinal dissection techniques have shifted the diagnostic objective from mere confirmation of mediastinal disease towards its exact localization and quantification, at comparatively higher levels of accuracy. This kind of detailed investigation of mediastinal disease revealed its prognostic heterogeneity, and translated into adopted multimodality treatment strategies [7, 8]. It is particularly helpful in identifying candidates with low risk for multimodality treatment including surgery. Recent guidelines for mediastinal staging are still recommending conventional mediastinoscopy, but do not refer to ECM or its left-sided extension to the AP zone—surprisingly, for two reasons [9, 10]. First, the diagnostic accuracy of extended mediastinoscopy was reported to be 97.8% [11]. Secondly, further development of standard mediastinoscopy into video-assisted mediastinoscopic lymphadenectomy (VAML) created a new interest in extending this otherwise complete mediastinal dissection tool into the AP zone [12, 13]. Therefore, the role of extended mediastinoscopy has to be re-evaluated five decades after its first description. To contribute to the re-evaluation process incited by Rami-Porta and co-workers [14, 15], we analysed our institutional experience, the cornerstone of which is one decade of personal experience of the senior author (M.H.), who
performed 72 of the reported procedures and assisted in 38 more to teach younger colleagues.

**METHODS**

In our institution, ECM is a common diagnostic approach to enlarged para- and sub-aortic lymph nodes at stations 5 and 6 of the Naruke map, referred to as AP zone of the IASLC map proposed by Rusch et al. [1]. It is performed immediately after dissection of the central middle mediastinum by VAML or video-assisted mediastinoscopy (VAM) through the same jugular incision. As already described by Specht and Ginsberg, a tunnel connecting the jugular pretracheal space and the AP zone is created [2, 5]. First, the tunnel follows an antero-lateral direction dorsal behind the left sternoclavicular junction and the innominate vein; secondly, between the innominate and left carotid artery and thirdly, on the left side of the aortic arch downwards to the left para-aortic region and the AP window to finally stop at the upper aspect of the left pulmonary artery. The first two steps are prepared by blunt digital dissection, and the further completion is achieved under direct mediastinoscopic vision by advancing a small spreadable (Wolf, Knittlingen, Germany) or tubular (Storz, Tuttingen, Germany) video-mediastinoscope. For systematic sampling, the adipose tissue within the AP zone is dissected carefully, and all detected nodes are removed by means of a grasper and mainly blunt dissection. Aliquots of fatty tissue are taken in case no nodes are present. Haemostasis is achieved by temporary compression or clipping. The specimen was weighted, dissected for node count and sent for routine pathological examination. Among the patients with a resectable left-sided lung carcinoma, the nodal-negative ones were scheduled for consecutive lung resection via left-sided thoracotomy or video-assisted thoracoscopic surgery (VATS). During this procedure, the AP zone was revisited and completely dissected in the course of systematic nodal dissection [16]. All patients had given informed consent. As they followed an institutional routine algorithm based on established procedures, a votum of the regional ethics committee was waived. All cases and data were extracted from a prospectively collected institutional database dedicated to video-assisted mediastinoscopic surgery. Categorical and continuous clinical variables were expressed by frequency, and median and inter-quartile range, respectively. Accuracy calculations refer to the subpopulation of 92 patients with left-sided lung carcinoma. They were performed according to the customary formulae describing sensitivity, negative predictive value (NPV) and specificity provided in [11]. Negative ECM results were considered to be false-negative, if lymph node metastases were detected by histopathological examination in specimens removed from the AP zone at lung resection. Accuracy measures of ECM refer to the para- and sub-aortic lymph nodes (stations 5 and 6). Accuracy measures of combined VAML and ECM refer to the entire central mediastinum (stations 4R, 4L, 5, 6 and 7). Accuracy measures of VAML alone, and systematic dissection at lung resection via left-sided VATS or thoracotomy referring to the entire mediastinum, were estimated on the basis of the local prevalences of

![Figure 1: Patient flow chart starting above at the clinical baseline situation in which selective ECM was indicated, then descending to the definitive histopathological diagnoses, mediastinal staging, therapy and accuracy analysis (shaded grey).](image-url)
Among 92 lung carcinoma patients, VAML A and ECM combined identified 21 cases, and complementary ECM additional 10 cases of mediastinal involvement. VAML A was positive in 21, and ECM in 17 cases. Among these, both ECM and VAML A were positive in 7 cases. Thus, ti

Figure 2: Among 92 lung carcinoma patients, VAML A and ECM combined identified 31 cases of mediastinal involvement. VAML A was positive in 21, and ECM in 17 cases. Among these, both ECM and VAML A were positive in 7 cases. Thus, VAML A identified 21 cases, and complementary ECM additional 10 cases of mediastinal disease. Surgical re-exploration revealed one false-negative VAML A result (black diamond), and one false-negative ECM result (black dot) at upfront resection. Another false-negative ECM result was observed in a VAML A-positive patient after neoadjuvant treatment (chequered dot), that had to be excluded from accuracy calculation.

mediastinal disease at the different nodal stations observed within our cohort, and the known yield of the video-mediastinoscopic and left-sided access to the mediastinum. Patients resected after neoadjuvant therapy were reported, but excluded from accuracy calculations. Concurrent with the anglophone literature, the term ‘extended cervical mediastinoscopy’ was applied not for the entire mediastinoscopic procedure, but for its extension to the AP zone.

RESULTS

One hundred and ten of 873 (12.6%) patients, who underwent a video-mediastinoscopic procedure in our institution from 2001 to 2010, received 110 ECMs. Their median age was 63 (Q3–Q1; 55.5–67) years, and 24 (21.8%) of them were female. Their initial clinical and definitive tissue diagnoses are shown in Fig. 1.

The para- and sub-aortic regions were accessed in all cases. For its exploration and dissection, the spreadable Linder-Dahan video-mediastinoscope was feasible in 77.3% of the procedures. In the remaining cases, tubular scopes of smaller diameters were used. The central mediastinum underwent VAML A in 71.8%, and a less radical nodal dissection in 28.2% of the cases. The median duration of the entire procedure including ECM and VAM (LA) was 70 (Q3–Q1; 45–85) min. Six perioperative adverse events were observed in 5 patients. The most severe, occurring during the 19th procedure, was a circumscribed laceration of the aortic arc between the offsprings of the innominate and left carotid artery, requiring immediate open repair and resulting in a prolonged ischaemic neurological deficit. It became apparent as major bleed-

In the remaining cases, tubular scopes of smaller diameters were used. The central mediastinum underwent VAML A in 71.8%, and a less radical nodal dissection in 28.2% of the cases. The median duration of the entire procedure including ECM and VAM (LA) was 70 (Q3–Q1; 45–85) min. Six perioperative adverse events were observed in 5 patients. The most severe, occurring during the 19th procedure, was a circumscribed laceration of the aortic arc between the offsprings of the innominate and left carotid artery, requiring immediate open repair and resulting in a prolonged ischaemic neurological deficit. It became apparent as major bleed-

The specimen retrieved from the left AP zone had a median weight of 0.54 (Q3–Q1; 0.3–1.2) g and contained a median number of two lymph nodes: 1–3 lymph nodes in 42.7% of the cases, >3 nodes in 24.4% and no lymph nodes in 32.9%.

Definitive tissue diagnosis identified 92 lung carcinoma patients. Fifty patients with nodal-negative mediastinum were resected upfront, whereas 13 nodal-positive patients underwent resection after neoadjuvant treatment (Fig. 1). Prevalence and distribution of mediastinal involvement are summarized in Table 1. The prevalences of mediastinal disease and station 5/6 involvement were 35.9, and 20.7%, respectively, resulting in 16 pN2a, 4 pN2b and 13 pN3 situations. ECM and VAML A identified 31 of the 33 nodal-positive patients, and 17 of 19 cases with positive station 5/6. Station 5/6 was the only involved station in 10, and skipped in 17 cases. The false-negative findings (Fig. 2) were due to sampling error and overlooked minimal disease: No. 15, a case of microscopic disease in one node left over in the AP zone, ex-post confirmed in the EMC specimen as well by immunohistochemistry; No. 29, a case of microscopic disease at stations 4L and 7 and No. 92, a case of residual tumour in the AP zone after neoadjuvant chemotherapy for multilevel disease, whose ECM had not yielded any lymph nodes. Sensitivity and NPV calculated for the
performance of ECM in the AP zone were 0.94 and 0.96; and for ECM combined with VAMLA in the entire mediastinum 0.94 and 0.96. Specificity and positive predictive value, relying on histology-based tissue diagnosis, were assumed to be 1.00. As the systematic bilateral mediastinal dissection by combined VAMLA and left-sided approach provided accurate information on the presence, magnitude and distribution of mediastinal involvement, we were able to estimate sensitivity and NPV calculations for two other situations we did not observe, but which are common in clinical practice: surgical mediastinal staging by VAMLA without ECM; and systematic mediastinal dissection of station 5, 6 and 7 via a left-sided VATS or open approach, as often done together with lung resection. A survey on all accuracy calculation is given in Table 2.

**DISCUSSION**

From the surgical point of view, ECM provides both a practical and elegant access to the sub- and para-aortic lymph nodes, sparing additional anterior mediastinotomy or thoracoscopy in patients scheduled for staging mediastinoscopy for left-sided lung carcinoma [17]. However, ECM contains the risk of rare but potentially lethal vascular accidents. Besides one aortic laceration described in our series, two previously reported cases, one of aortic laceration communicated by Ginsberg himself, and one case of perioperative stroke, have obviously discouraged surgeons from adopting this otherwise valuable, safe and accurate staging procedure [11, 18]. So, it is not surprising to find only few publications on extended mediastinoscopy (Table 3). Despite different technical preconditions, selection criteria and prevalences of nodal disease, these studies document consistently high NPVs. Their results suggest a steady increase of sensitivity over time, which is probably due to patient selection based on advanced imaging techniques, and improved intraoperative visualization by video-mediastinoscopy. So far, our results confirm these observations. In contrast to previous studies, we combined ECM not with standard mediastinoscopy, but with complete mediastinal dissection by means of VAMLA. This resulted in a comparatively high sensitivity and NPV for the presence of any mediastinal disease of 0.94 and 0.96, respectively. We did not see a substantial

<table>
<thead>
<tr>
<th>Method of mediastinal dissection</th>
<th>Status</th>
<th>Sensitivity</th>
<th>NPV</th>
<th>Clinical result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECM</td>
<td>Involvement of station 5/6</td>
<td>Observed</td>
<td>0.94</td>
<td>0.96</td>
</tr>
<tr>
<td>VAMLA + ECM</td>
<td>Mediastinal involvement</td>
<td>Observed</td>
<td>0.94</td>
<td>0.96</td>
</tr>
<tr>
<td>VAMLA only</td>
<td>Mediastinal involvement</td>
<td>Estimated</td>
<td>0.64</td>
<td>0.80</td>
</tr>
<tr>
<td>Systematic mediastinal dissection via left-sided approach</td>
<td>Mediastinal involvement</td>
<td>Estimated</td>
<td>0.76</td>
<td>0.85</td>
</tr>
</tbody>
</table>

**Table 2:** Survey on observed and estimated accuracy data, based on systematic bilateral mediastinal dissection by combined VAMLA and left-sided VATS or thoracotomy approach

<table>
<thead>
<tr>
<th>Report</th>
<th>Cohort</th>
<th>Adverse events</th>
<th>Prevalence</th>
<th>Para-and sub-aortic zone</th>
<th>Any mediastinal involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginsberg et al. [5]</td>
<td>100 Consecutive</td>
<td>1 Superficial infection</td>
<td>0.29</td>
<td>Sensitivity 0.69</td>
<td>NPV 0.89 Sensitivity 0.75</td>
</tr>
<tr>
<td>Lopez et al. [11]</td>
<td>50 Consecutive</td>
<td>Not reported</td>
<td>0.18</td>
<td>Sensitivity 0.83</td>
<td>NPV 0.98 Sensitivity 0.75</td>
</tr>
<tr>
<td>Urschel et al [18]</td>
<td>6</td>
<td>1 Embolic stroke</td>
<td>0.34</td>
<td>Sensitivity 0.81</td>
<td>NPV 0.91 Sensitivity 0.75</td>
</tr>
<tr>
<td>Freixinet et al. [24]</td>
<td>106 Selected (CT)</td>
<td>2 Mediastinitis</td>
<td>0.10</td>
<td>Sensitivity 0.44</td>
<td>NPV 0.94 Sensitivity 0.75</td>
</tr>
<tr>
<td>Call et al. [14]</td>
<td>89 Selected (CT)</td>
<td>1 Ventricular fibrillation</td>
<td>0.24</td>
<td>Sensitivity 0.69</td>
<td>NPV 0.89 Sensitivity 0.75</td>
</tr>
<tr>
<td>Metin et al. [25]</td>
<td>55 Selected (PET)</td>
<td>1 superficial infection</td>
<td>0.24</td>
<td>Sensitivity 0.69</td>
<td>NPV 0.89 Sensitivity 0.75</td>
</tr>
<tr>
<td>Obiols et al. [15]</td>
<td>132 Selected (PET)</td>
<td>1 Intraoperative haemorrhage</td>
<td>0.19</td>
<td>Sensitivity 0.94</td>
<td>NPV 0.96 Sensitivity 0.75</td>
</tr>
<tr>
<td>Current series</td>
<td>110 Selected (CT)</td>
<td>1 Aortic laceration</td>
<td>0.21</td>
<td>Sensitivity 0.94</td>
<td>NPV 0.96 Sensitivity 0.75</td>
</tr>
</tbody>
</table>

**Table 3:** Extended mediastinoscopy: synopsis of published series and reported adverse events, prevalence of mediastinal disease in the para- and sub-aortic zone and parameters describing staging accuracy
rise in the overall complication rate, which was 4% in VAMLA, and 4.5% in the combination of VAMLA and ECM [13]. However, this good rate conceals one nearly catastrophic vascular accident. Therefore, we have to advise against any forceful use or even opening up of spreadable video-mediastinoscopes during dissection of the para- and sub-aortic zone, the routine use of ECM in unselected cases. Case selection by imaging, regardless of whether it was based on PET-CT scan [15] or CT scan like in the presented series, resulted in equally high accuracy values (Table 3).

Beyond accurate data, we intended to describe the impact of ECM on mediastinal staging, as it is an adjunct to standard mediastinoscopy, or, in our series, VAMLA, and therefore always associated with some status information concerning other nodal stations. For left-sided tumours, the result of ECM is irrelevant in the presence of other mediastinoscopically detected positive stations, and the ECM result is relevant if all other stations are mediastinoscopically negative. So, in our cohort, 78.0% of ECM findings had an impact on mediastinal staging (Fig. 2). In accordance with earlier studies of lymphatic spread, we observed considerable rates of mediastinal disease either skipping the para- and sub-aortic zone (42.4%), or being confined to it (30.3%) (Table 1) [19, 20]. So, every third case of mediastinal disease would have been missed without ECM, and about a quarter of nodal-positive cases would have been missed without dissection of the central and contralateral parts of the mediastinum by VAMLA (Table 1). Translated into surgical practice, this implies that, in similar subsets of patients, there is a considerable risk of false-negative mediastinoscopies if ECM is not performed, and of overlooked mediastinal disease if nodal staging is confined to the AP zone and station 7, as is often the case at the time of lung resection [21]. The resulting loss of sensitivity and NPV, and the clinical consequences, are illustrated and quantified by simulated calculations based on the known mediastinal status of the investigated patients (Table 2). In seven of our nodal-positive patients, the information of VAMLA and ECM was redundant due to multilevel mediastinal diseases. This finding suggests intraoperative frozen section of macroscopically suspicious nodes detected at VAMLA in order to reduce unnecessary ECM procedures.

However, the most important question is not how to select and dissect patients, but for which purposes. On this meta-level of clinical consequences, the relevance of ECM is dependent on how single-station mediastinal disease, a subgroup with comparatively favourable prognosis, is perceived and treated, either by upfront resection with intraoperative mediastinal dissection and adjuvant therapy, or by resection after neoadjuvant treatment [7, 8, 22, 23]. In this context, two points should be considered. First, cases selected for ECM by CT- or PET-CT imaging are different from those described as occult or unforeseen mediastinal disease; so, at upfront resection, neither single-station involvement nor acceptable outcome can be taken for granted. Secondly, complete central and contralateral mediastinal dissection that is consequently mandatory in any case of left-sided occult or unforeseen mediastinal disease is rarely part of clinical routine, as it requires extensive vascular mobilization or sternotomy [22].

To conclude, selective extended mediastinoscopy is a valuable addendum to mediastinoscopic staging procedures for left-sided tumours, as it enhances sensitivity and NPV and complements VAMLA in comprehensive mediastinal dissection. Precaution and experience are required to circumvent the rare risk of potentially fatal vascular accidents.

Conflict of interest: none declared.

REFERENCES


