Review Article

Present indications of surgical exploration of the mediastinum

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Abstract: Preoperative mediastinal staging is crucial in the management of patients with non-small cell lung cancer (NSCLC), especially to define prognosis and the most proper treatment. To obtain the highest certainty level before lung resection, the current American and European guidelines for preoperative mediastinal nodal staging for NSCLC recommend getting tissue confirmation of regional nodal spread in all cases except in patients with small (≤3 cm) peripheral carcinomas with no evidence of nodal involvement on computed tomography (CT) and positron emission tomography (PET). We have a wide variety of surgical methods for mediastinal staging that are well integrated in the current preoperative algorithms. Their main indication is the validation of negative results obtained by minimally invasive endoscopic techniques. However, recent studies have reported the superiority of mediastinoscopy over endosonography methods in terms of accuracy for those tumours classified as clinical (c) N0-1 by CT and PET or with intermediate risk of N2 disease (cN1 and central tumours). Apart from the exploration of the mediastinum, other surgical procedures [parasternal mediastinotomy, extended cervical mediastinoscopy (ECM) and video-assisted thoracoscopic surgery (VATS)] allow the completion of the staging process with the assessment of the primary tumour and metastasis, exploring the lung, pleural cavity, and pericardium when it is required. Transcervical lymphadenectomies represent the evolution of mediastinoscopy and they are already considered the most reliable method for mediastinal staging, mainly in the subgroup of patients in whom endosonography methods have a low sensitivity: tumours with normal mediastinum by CT and PET. In addition to their indication for staging, these procedures have also demonstrated to be feasible as preresectional lymphadenectomy in VATS lobectomy, improving the radicality of the number of lymph nodes and lymph node stations explored, mostly for left-sided tumours for which a complete mediastinal nodal dissection is not always possible by VATS approach.

Keywords: Lung cancer; invasive mediastinal staging; mediastinoscopy; transcervical lymphadenectomies

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Introduction

The current American and European guidelines for preoperative mediastinal nodal staging for non-small cell lung cancer (NSCLC) (1,2) are in agreement in obtaining the highest certainty level before lung resection. For this reason, their recommendation is to get tissue confirmation of regional nodal spread in all cases except in those patients with small (≤3 cm) peripheral carcinomas with no evidence of nodal involvement on computed tomography (CT) and positron emission tomography (PET). Tissue confirmation can be performed with endoscopic or surgical

techniques. When both modalities are available, it is recommended to start with endobronchial ultrasonographic fine-needle aspiration (EBUS-FNA) or with esophageal ultrasonographic FNA (EUS-FNA) or with their combination. Nevertheless, their negative results should be validated with a mediastinoscopy, technique that still remains the gold standard for preresection mediastinal assessment. Other surgical procedures [such as extended cervical mediastinoscopy (ECM), parasternal mediastinotomy or thoracoscopy] can be chosen depending on the location of suspicious nodes, the surgeon's preference or the policy of each surgical team.

The aim of this review is to describe the present indications of the classical and most innovative surgical techniques for staging NSCLC, and their integration in the current staging algorithms according on their accuracy in the different clinical scenarios.

Mediastinoscopy

Carlens described his first report on mediastinoscopy in 1959 after performing more than 100 procedures without any complications (3). For more than a half a century, this procedure was considered the gold standard for mediastinal nodal assessment. At the present time, despite the introduction of other less invasive procedures that provide cyto-histological evidence of nodal status, mediastinoscopy still has an important role in invasive staging of mediastinal lymph nodes, not only in patients with lung cancer, but also in those with mesothelioma and with potentially resectable lung metastases with radiological or metabolic suspicion of mediastinal nodal disease.

Mediastinal exploration range

During mediastinoscopy, the mediastinoscope follows the whole length of the trachea and bronchi allowing the exploration of the superior and middle mediastinum. For lung cancer staging, the range of exploration includes the cervical lymph nodes of the sternal notch, the lymph nodes along the trachea and both main bronchi, that is, the superior and inferior, left and right, paratracheal lymph nodes (nodal stations 2R, 2L, 4R, 4L, respectively), the subcarinal nodes (4) and the right and left hilar lymph nodes (nodal stations 10R, 10L, respectively) (*Table 1*), according to the International Association for the Study of Lung Cancer (IASLC) lymph node map (9).

Mediastinoscopy in the current staging algorithms for NSCLC

Role of mediastinoscopy for staging locally advanced NSCLC

There is a risk of mediastinal nodal involvement of at least 60% when tumours are classified as clinical (c) N2–3 on PET-CT (10). For this reason, it is recommended to confirm pathologically any mediastinal abnormality detected on the chest CT and or PET. Based on the results of several recent randomized controlled trials (4,11,12), the best strategy for mediastinal nodal staging is to start with an endosonography method (EBUS-FNA, EUS-FNA or their combination). If these explorations are positive for cancer, the information may be adequate to start a multidisciplinary treatment protocol. However, endosonography procedures have a high post-test probability (>0.10) and, therefore, their negative results should be validated with a confirmatory mediastinoscopy (4,12,13) (*Table 2*).

Role of mediastinoscopy for staging early stage NSCLC

According on the current European Society of Thoracic Surgeons (ESTS) guidelines, preoperative invasive mediastinal staging can be omitted if all the following criteria apply: (I) primary tumour located in the outer third of the lung; (II) largest diameter of the tumour is ≤3 cm; (III) absence of intrathoracic lymph node(s) on CT and PET (2). The rationale is that, in this situation, the rate of unsuspected pathologic mediastinal nodal disease is <10% (2,5,23,24). Nevertheless, it is important to have in mind that the current clinical TNM classification is only based on anatomical characteristics of the tumour defined by imaging and metabolic techniques. The heterogeneity of tumours included in the early stage is high because several histological types and different patient's clinical parameters are at play. Some authors have reported that, in early stage NSCLC, the combination of tumour characteristics [histological type, consolidation/tumour ratio, tumour size, maximum standardized uptake value (SUVmax value)] and other clinical parameters [serum carcinoembriogenic antigen (CEA) level, patient's age] have an increased risk of mediastinal involvement (33.8%) (14,15). Therefore, despite the fact that current indications of invasive mediastinal staging are limited, some subgroups of patients with an increased risk may benefit from it (16) (*Table 2*).

Regarding the accuracy of invasive mediastinal staging methods in this type of patients (clinical N0 disease by PET-CT), minimally invasive endoscopic techniques have

Table 1 Accuracy of surgical methods for mediastinal staging in patients with lung cancer

Technique	N	S (median; range)	NPV (median; range)	LN range
CM	9,267 (1)	0.78 (0.38–0.92)	0.91 (0.80–0.97)	2R, 2L, 4R, 4L, 7, 10R, 10L
VAM	995 (1)	0.89 (0.78–0.97)	0.92 (0.91–0.99)	2R, 2L, 4R, 4L, 7, 10R, 10L
PM	238 (1)	0.71 (0,20–0,87)	0.91 (0.89–0.96)	5, 6
ECM	456 (1)	0.71 (0.44–0.81)	0.91 (0.89–0.95)	5, 6
VATS	246 (1)	0.99 (0.58–1.00)	0.96 (0.88–1.00)	Right side: 4R, 7, 8R, 9R, 10R Left side: 5, 6, 7, 8L, 9L, 10L
VAMLA	384 (5-7)	0.95 (0.88–0.96)	0.98 (0.94–0.99)	2R, 2L, 4R, 4L, 7, 10R, 10L
TEMLA	928 (8)	0.96	0.98	1, 2R, 2L, 4R, 4L, 7, 8R, 8L, 3a, 3p, 10L, 10R, 5, 6

CM, conventional mediastinoscopy; VAM, videomediastinoscopy; PM, parasternal mediastinotomy; ECM, extended cervical mediastinoscopy; VATS, video-assisted thoracoscopic surgery; VAMLA, video-assisted mediastinoscopic lymphadenectomy; TEMLA, transcervical extended mediastinal lymphadenectomy; S, sensitivity; NPV, negative predictive value; N, number of patients; LN, lymph node.

Table 2 Summary of current indications of surgical exploration of the mediastinum

Technique	Current ESTS/ACCP guidelines	Additional evidence and comments
CM & VAM	cN2-3—if endosonography methods are negative (1,2) cN0—invasive staging can be omitted (1,2) cN1, central tumours & tumours >3 cm—ACCP: EBUS/EUS over surgical methods as first test (1); ESTS: The election of the invasive method depends on local expertise (2)	Early stage NSCLC (cN0): some subgroups of patients with an increasing risk of N2 (histological type, tumour size, SUVmax, CEA level, patient's age) may benefit of invasive staging (14-16); cN1 tumours: based on the latest evidence, surgical methods should be the staging method of election (5,17,18)
PM & ECM	Left side tumours—ESTS: exploration and biopsy of nodal stations 4R, 4L, 7, 5 and 6 are recommended (2); ACCP: the same recommendation of ESTS but only in left upper lobes (1)	ECM: Use the same incision of the mediastinoscopy; PM & ECM: besides the assessment of aortopulmonary window, both procedures allow the exploration of the pleural space, hilum, lung and pericardium
VATS	Indicated as alternative to PM and ECM for the assessment of nodal stations 5 and 6 (1,2)	For mediastinal staging, VATS only allow the assessment of ipsilateral nodes. In the left side, nodal station 4L remains unexplored; it is also useful for the assessment of the T an M descriptors (synchronous lung cancer, T3, T4 and M1a)
VAMLA & TEMLA	ESTS: their use is limited to clinical studies (2)	Based on latest studies (5,7,8,18,19), these procedures have been demonstrated to be feasible and safe, and represent the best staging methods in terms of accuracy, especially for those tumours classified cN0-1 by PET-CT; both methods are also used as a preresectional lymphadenectomy in VATS lobectomy (5,20-22)

CM, conventional mediastinoscopy; VAM, videomediastinoscopy; PM, parasternal mediastinotomy; ECM, extended cervical mediastinoscopy; VATS, video-assisted thoracoscopic surgery; VAMLA, video-assisted mediastinoscopic lymphadenectomy; TEMLA, transcervical extended mediastinal lymphadenectomy. ESTS, European Society of Thoracic Surgeons; ACCP, American College of Chest Physicians; EBUS, endobronchial ultrasonography; EUS, esophageal ultrasonography; NSCLC, non-small cell lung cancer; SUVmax, maximum standardized uptake value; CEA, carcinoembriogenic antigen; PET-CT, positron emission tomography-computed tomography.

a poor sensitivity (0.17–0.41) (25-28) and the sensitivity and negative predictive value (NPV) of mediastinoscopy is investigator dependent, and accounts for the reported heterogeneity of 0.32 to 0.97 and 0.8 to 0.99, respectively (1,29) (*Table 1*). Transcervical lymphadenectomies [video-assisted mediastinoscopic lymphadenectomy (VAMLA) or transcervical extended mediastinal lymphadenectomy (TEMLA)] are the only pre-surgical staging procedures with the highest sensitivity and NPV reported to date for those patients without suspicion of N2 by PET-CT: 0.88–0.96 and 0.94–0.99, respectively (5-7,30) (*Tables 1,2*). Taking into account the low prevalence of unsuspected mediastinal nodal disease in this scenario and that up to 80% of this patients with unsuspected N2 disease have single station N2 disease (31), some authors suggest that VAMLA or TEMLA should be most valuable at the time of resection instead of being a pre-surgical staging technique (32).

Role of mediastinoscopy for staging tumours with intermediate suspicion of N2–3 disease

Tumours considered with an intermediate suspicion of N2–3 disease and normal mediastinum by CT and PET are the following: central tumour or cN1 tumours (1). The rate of unsuspected pathologic mediastinal nodal disease for this subgroup ranges from 20% to 42% (5,17,18,33-35). Hence, current preoperative staging guidelines recommend invasive staging of the mediastinum over the imaging alone (1,2). However, there is a little disagreement between American and European guidelines about the best staging procedure to start with. The American College of Chest Physicians (ACCP) guidelines suggest endosonography methods over surgical procedures as the best first test (level of evidence 2B) (1), and the ESTS guidelines describe that the choice between mediastinoscopy with biopsies, or with pre-surgical lymphadenectomies (VAMLA or TEMLA) or endoscopic staging by EBUS/EUS with FNA depends on local expertise (level of evidence V) (2) (*Table 2*). Regarding the accuracy of minimal invasive methods for patients with tumours classified as cN1 on PET-CT, Yasufuku *et al.* (35) report a sensibility of 0.43, and Dooms *et al.* (17), based on the results from a recent prospective multicentre study (ASTER II) reported a sensitivity of only 0.38 for endosonography to detect N2 disease. This sensitivity increased to 0.73 by adding a confirmatory mediastinoscopy to validate negative endosonographies (17). Recently, Decaluwé *et al.* (18) have reported the results from the first prospective multicentre study (ASTER III) to evaluate the performance of surgical mediastinal staging (by mediastinoscopy or by VAMLA) in patients with cN1 obtaining a global sensitivity of 0.73 and a NPV of 0.92 with a prevalence of 26%. Regarding those patients staged by VAMLA (31%), it is important to point out its excellent results: no complications and no false negative results. Based on the results from ASTER II and III, the authors concluded that the preferred technique for patients with tumours classified as cN1 should be surgical methods such as mediastinoscopy or VAMLA (*Table 2*).

Finally, there is another subgroup of patients considered as intermediate risk of N2 disease according on the revised ESTS guidelines: those with high SUVmax, cN0 but size greater than 3 cm and especially in adenocarcinomas. Invasive staging would be indicated in this case (2). Again, the decision on the best technique to start with would depend on local expertise to adhere to minimal requirements for staging (2) (*Table 2*). In the literature, the rate of unsuspected N2 disease for tumours classified as cN0 and tumour size >3 cm is: 6–14.8% (23,24). Recently, Call *et al.* (5) reported a rate of 22.2% (19% N2 tumours and 3.2% N3 tumours) based on the results from a prospective study to validate the feasibility and accuracy of VAMLA as a method for pre-surgical mediastinal staging. A comparative well-designed study between endosonography methods and surgical techniques should be necessary to analyse which is the best staging procedure for this subgroup of patients in terms of performance. Meanwhile, it is recommendable to validate negative results of endosonographies with a surgical procedure in the same line of those patients with tumours classified as cN1.

Systematics and requirements for mediastinal surgical staging

Mediastinoscopy for lung cancer staging should be thorough, but the thoroughness of the exploration depends on its indication. If mediastinoscopy is indicated to confirm N3 disease, and confirmation is obtained by intraoperative frozen section, there is no need to continue the exploration unless the patient is in a protocol that requires more information. However, when there are no clear signs of mediastinal disease on CT or PET, mediastinoscopy should be systematic and complete. It is better to start by exploring and obtaining biopsy of the contralateral paratracheal nodes to rule out or confirm N3 disease, and then to proceed with the subcarinal nodes, and finally with the ipsilateral paratracheal nodes (36).

Ideally, five nodal stations (2R, 2L, 4R, 4L and 7)

should be examined routinely (1,2). The ESTS guidelines determine that, at least, the following nodal stations should be explored and biopsied: right and left inferior paratracheal lymph nodes (stations 4R and 4L) and subcarinal lymph nodes (station 7) (2). It is also recommended, when required to determine subsequent treatment strategy, to biopsy station 10R (below the azygos vein) and station 10L (below the upper rim of the left pulmonary artery) (2). For cancers of the left lung, exploration of the subaortic and para-aortic nodes is also required. The biopsy of the lower mediastinal lymph nodes (stations 8 and 9) should be performed if it changes the treatment strategy, especially when extracapsular nodal disease is suspected (2).

Mediastinoscopy does not reach the aortopulmonary window (stations 5 and 6) and stations 8 and 9. When invasive staging of these stations is required, one of the following surgical techniques (described in sections below) can be added: parasternal mediastinotomy, ECM or video-assisted thoracoscopic surgery (VATS).

Other indications

Any mediastinal lesion (tumour, cyst, inflammation, infection or fibrosis) located within the range of the exploration can be diagnosed by mediastinoscopy. Moreover, this procedure can be used as a therapeutic tool such as closure of post-pneumonectomy bronchopleural fistula, removal of mediastinal cysts or parathyroid tumours, among others (37). In addition to its main indication, the lung cancer staging (topic extensively discussed in the previous sections), mediastinoscopy is also useful for the staging of other thoracic malignancies. The ESTS, the European Respiratory Society, and the American Society of Clinical Oncology, in their clinical practice guidelines for the treatment of malignant pleural mesothelioma recommend invasive staging of the mediastinum with EBUS or mediastinoscopy to select patients for radical resection or multimodality treatment (38,39). Likewise, in patients with lung metastases, mediastinal lymph node involvement is also an independent negative prognostic factor for survival after metastasectomy (40-43). Thus, mediastinoscopy may be useful to select potential candidates for pulmonary resection.

Results

The reliability of mediastinoscopy depends on its thoroughness, based on the number of biopsies performed and the number of nodal stations explored (44). This accounts for the important heterogeneity in the reported sensitivity and NPV that ranges from 0.32 to 0.97 (median of 0.78) and 0.8 to 0.99 (median of 0.91), respectively (1) (*Table 1*). In addition to the number of lymph nodes explored and biopsied, the use of a video mediastinoscope could also influence the accuracy of this technique. Videomediastinoscopy (VAM) provides better visualization of the operative field than conventional mediastinoscopy (CM) and facilitates the teaching process. Although some authors found an increase in the number of LN or LN stations biopsied, no difference in sensitivity or NPV was found in favour of VAM (45). However, in the ACCP systematic review, in pooling the data from 995 VAMs, the median sensitivity was higher (0.89) in comparison with the median sensitivity of 9,267 conventional mediastinoscopies (0.78) (1) (*Table 1*).

Other surgical staging procedures

Parasternal mediastinotomy

Anterior mediastinotomy was described by Stemmer *et al.* (46) and McNeill and Chamberlain (47) in 1965 and 1966, respectively. This procedure consists of a left parasternal incision at the level of the second or third intercostal space, to access the subaortic and the para-aortic nodal stations (stations 5 and 6), that cervical mediastinoscopy cannot reach. Thus, this is the main indication of this procedure, mediastinal staging of bronchogenic carcinoma of the left lung in accordance with the recommendations of ESTS guidelines (2) (*Table 2*). Since this technique can be performed on the right side and it also allows the exploration of the pleural space, the hilum, the lung parenchyma and the pericardium if needed, the following indications have been described: (I) completion of lung cancer staging process: diagnosis of pleural or pericardial effusions, additional nodules in the lung and exploration of tumours contacting or invading the mediastinum or vascular structures such as superior vena cava or the aortic arch; (II) diagnosis of anterior mediastinal tumours or inflammations (lymphoma, sarcoidosis, thymic tumours).

For the staging of lung cancer, the median sensitivity and NPV reported are 0.71 and 0.91, respectively (1) (*Table 1*).

ECM

ECM, a technique described by Specht in 1965 (48)

and popularized by Ginsberg (49) years later for staging carcinomas of the left lung, can be a good alternative to the classic parasternal mediastinotomy because it allows the assessment of para-aortic and subaortic nodal stations (stations 5 and 6) through the same incision of the standard cervical mediastinoscopy (*Table 2*). Apart from its main indication, the assessment of the aortopulmonary window in patients with bronchogenic carcinoma of the left lung, this procedure is an excellent tool to obtain a biopsy of undiagnosed anterior mediastinal tumours or lymph nodes that have not been diagnosed by other methods such as transthoracic needle aspiration or Tru-Cut. Similarly, as parasternal mediastinotomy, this approach can be used to enter the pleural space (mediastino-pleuroscopy) to assess the primary tumour, pleural effusion, lung nodules, parietal pleural nodules and diaphragmatic and pericardial lesions (49,50).

Regarding its results in the staging of left lung cancers, a median sensitivity of 0.71 and NPV of 0.91 have been described (1) (*Table 1*). Focusing on the sensitivity of this procedure, when ECM is performed selectively according to the results of CT and PET, the sensitivity increases (51). This could probably be explained by the higher prevalence of N2–3 disease in patients with enlarged lymph nodes or abnormal uptake in PET.

VATS

VATS for the staging of lung cancer, can be useful for the assessment of the T, the N and the M descriptors (*Table 2*). VATS allows the surgeon to biopsy or resect peripheral lung tumours, providing diagnosis and staging information in the following clinical scenarios: (I) synchronous lung cancer; (II) T3 [separate tumour nodule(s) in the same lobe]; (III) T4 [separate tumour nodule(s) in a different ipsilateral lobe]; (IV) M1a [separate tumour nodule(s) in the contralateral lung] (52). In relation to its role in the diagnosis of pleural or pericardial effusion, VATS achieves a definitive diagnosis in the 90–95% of cases (53).

Regarding its indication for mediastinal staging, on the right side, VATS allows the assessment of 10R, 4R, 7, 8R and 9R nodal stations. On the left side, it allows the assessment of 10L, 5, 6, 7, 8L and 9L nodal stations, remaining unexplored the left paratracheal nodes (4L station) due to its difficult access. Although VATS is limited to the assessment of only one side of the mediastinum, it is a procedure to have in mind as an alternative to parasternal mediastinotomy and ECM for exploring the aortopulmonary window. Staging values of VATS show a sensitivity ranging from 0.58–1 (median 0.99) and a false negative rate of 4% (1) (*Table 1*).

Transcervical lymphadenectomies

During the last decade, two new surgical staging procedures were developed allowing a step forward beyond classic mediastinoscopy: VAMLA and TEMLA. The main difference between these procedures is that VAMLA is an endoscopic technique performed through a video mediastinoscope, and TEMLA is an open procedure assisted by a video mediastinoscope or a videothoracoscope, depending on the nodal stations dissected. Their range of exploration also differs: with TEMLA all mediastinal nodal stations from supraclavicular to para-oesophageal can be explored (stations 1, 2R, 2L, 4R, 4L, 7, 8, 3a, 3p, 10L, 10R, 5, and 6), whereas VAMLA explores the right and left paratracheal, subcarinal and hilar nodes (stations 2R, 2L, 4R, 4L, 7, 10R and 10L). The aim of both procedures is the complete clearance of the all mediastinal nodal stations explored (this includes lymph nodes and surrounding adipose tissue), allowing the identification of minimal nodal disease that is not identified on CT or PET. Therefore, the ideal indication for transcervical lymphadenectomies is in tumours without suspicion of N2–3 by CT and PET. In accordance with this premise, the following indications have been described: central tumours, cN1 tumours, left-sided tumours, bilateral synchronous lung cancer and preresectional lymphadenectomy in video-assisted thoracoscopic lobectomy. Regarding the accuracy of these procedures, high sensitivity and accuracy have been reported (5-8,30): 0.88–0.96 and 0.94–0.99, respectively, and, as mentioned in the previous section, these represent the best staging values reported to date for those patients without suspicion of N2 by CT and PET (*Tables 1,2*).

Role of surgical exploration of the mediastinum in restaging

The assessment of an objective response after induction therapy continues to be a diagnostic challenge. For this reason, the use of mediastinal downstaging as a criterion to select patients for surgery requires a reliable restaging method to predict pathologic stage before lung resection. The ESTS guidelines for preoperative lymph node staging for NSCLC recommend histological confirmation of objective response after induction therapy. This

confirmation can be done with endosonography techniques. However, the use of an invasive surgical technique is still recommended when the results of endoscopic procedures are negative (2).

Mediastinoscopy

Mediastinoscopy in restaging can be performed in the following situations: (I) after induction therapy with no pretherapeutic invasive diagnosis; (II) after induction therapy with mediastinal histological confirmation by endoscopic techniques; (III) after induction therapy preceded by staging mediastinoscopy. In this case, mediastinoscopy is a reoperation and is named remediastinoscopy (reMS).

The use of a first mediastinoscopy for restaging is addressed in a small series (54). In this article, NPV of 0.90 with a prevalence of pathologic postinduction (yp) N2 of 46% were reported. Theoretically, this approach could be a good strategy to perform an easier and safer mediastinoscopy due to the absence of adhesions in the mediastinum.

reMS does not differ much from a CM. However, reMS is technically more demanding because of peritracheal adhesions, resulting in a lower accuracy in comparison with the first procedure. The main goal of this procedure is to take new biopsies of those nodes that had been positive at first mediastinoscopy. Moreover, if it is technically feasible, other nodal stations should be reached to rule out subclinical progression of the disease. Although reMS is not a common procedure, several authors have reported its feasibility and the following results for sensitivity and NPV: 0.61–0.71 and 0.73–0.86, respectively (55-58).

Transcervical lymphadenectomies

After a properly performed transcervical lymphadenectomy, the restaging of the mediastinum is unnecessary because there is no material left for a new biopsy. Thus, for primary staging, VAMLA and TEMLA represent a new paradigm. Firstly, transcervical lymphadenectomies could also be considered part of the induction treatment because the mediastinum is staged and downstaged by these operations. Secondly, due to the fact that nodal restaging is unnecessary, new parameters should be used to select patients for lung resection after induction, such as the stability of the primary tumour and the absence of extrathoracic disease based on the results of postinduction CT or PET. Finally, intraoperative pathologic study of the remaining lymph nodes should confirm the absence of nodal involvement before proceeding with lung resection, especially if pneumonectomy is required.

Focusing on the use of these procedures for restaging after induction therapy, only TEMLA has been validated on two retrospective studies conducted in the same institution. In the first series with 63 patients, the diagnosis of N2–3 disease before induction treatment was confirmed with invasive techniques in 27 patients (20 with endosonography and 7 with mediastinoscopy), and with CT in 36. Sensitivity and NPV of restaging TEMLA were 0.95, and 0.97, respectively (59). In the second series with 176 patients treated with chemo or chemoradiotherapy, the restaging values of EBUS and/or EUS (88 patients) were compared with those of TEMLA (78 patients). There was a significant difference between EBUS/EUS and TEMLA for sensitivity (0.64 and 1; $P<0.01$) and NPV (0.82 and 1; $P<0.01$) in favour of TEMLA (60).

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Footnote

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