Video-assisted mediastinoscopic lymphadenectomy (VAMLA) for staging & treatment of non-small cell lung cancer (NSCLC)

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Abstract: Precise preoperative staging and restaging of mediastinal lymph nodes in patients with potentially resectable non-small cell lung cancer (NSCLC) is of supreme importance. Over the last years, algorithms on preoperative mediastinal staging incorporating imaging, endoscopic and surgical techniques have been widely published, offering more evidence concerning different mediastinal staging techniques. Current guidelines well define when and how to receive tissue confirmation in case of computed tomography (CT)-enlarged or positron emission tomography (PET)-positive mediastinal lymph nodes. Endosonography [(endoscopic bronchial ultrasonography/oesophageal ultrasonography (EBUS/EUS)] with fine needle aspiration still is the first choice (when accessible) since it is minimally invasive and has a high sensitivity to confirm mediastinal nodal disease. If negative, surgical staging with nodal dissection or biopsy is indicated. Video-assisted mediastinoscopic lymphadenectomy (VAMLA) and transcervical extended mediastinal lymphadenectomy (TEMLA) are preferred over conventional mediastinoscopy if a mediastinal R0-resection can be achieved. The mutual use of endoscopic and surgical staging effects highest accuracy. Straight surgical resection of tumors ≤3 cm (located within the external third of the lung) with systematic nodal dissection is justified as soon as there are no enlarged lymph nodes on CT-scan and once there is no nodal uptake on PET-CT. In case of central tumors and enlarged or FDG avid nodes regardless of cytological result, preoperative invasive mediastinal staging is indicated to rule out mediastinal nodal spread. However, accuracy needed in preoperative nodal staging has been under continuous debate ever since and with the advent of immunotherapy is right now intensely revived. During the last two decades VAMLA has been growing up from being a merely staging tool to an expert-recognized therapeutic tool in the context of minimal invasive lung cancer resection.

Keywords: Video-assisted mediastinoscopic lymphadenectomy (VAMLA); nodal staging; mediastinoscopy; video-assisted thoracic surgery (VATS); lung cancer

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Introduction

Correct invasive mediastinal staging of resectable lung cancer is clinically imperative concerning two aspects: (I) in the forecast of postoperative prognosis and (II) in the implementation of multimodal therapy. In the midst of the three components of the TNM staging system, the nodal denominator is the most challenging to conclude appropriately owed to the limited specificity of imaging modalities (1). Therefore, numerous invasive staging techniques have been established to increase the accuracy of mediastinal nodal staging. Conventional mediastinoscopy, presented by Carlens in 1959, has been broadly used to biopsy the mediastinal lymph nodes, and subsidized to more precise nodal staging (2). However, inter alia its restricted visualization of the mediastinal structures has forbidden the thorough resection of the mediastinal lymph nodes.

During the 1990s, video cameras became popular in various sectors comprising surgical endoscopy. Video-mediastinoscopy has been proposed by Lerut in 1993 (3), and commercially available tubular video-mediastinoscopes emerged few years later. The technical revolution of the imaging system led to enhanced visibility, facilitating the performance and teaching of the procedure as well as the stowing of visual information. It was the concept and realization of a two-bladed spreadable video-mediastinoscope by Linder and Dahan that provided a widespread operation field, thus enabling bimanual maneuvers (4).

In expanding the application of the Linder-Dahan mediastinoscope, video-assisted mediastinoscopic lymphadenectomy (VAMLA) increases the exposure and the imaging of the mediastinal structures and thus allows the complete dissection of lymph node stations instead of nodal sampling (4,5). The initiation of VAMLA marks an iconic basis for systematic lymph node dissection in thoracic oncologic surgery: the thorough removal of all potentially involved lymph nodes and lymphatic tissue in order to provide complete oncologic resection, precise nodal staging, and an accurate indication for multimodality treatment, resulting in improved local tumor control and extended survival (6). Furthermore, the minimally invasive approach is equal to open lymphadenectomy in terms of diagnostic accurateness and surgical radicality, and has expanded its clinical applications from preoperative examination and sampling to a therapeutic instrument for intraoperative complete mediastinal dissection (7). Additionally, with a rising amount of minimally invasive pulmonary resections, where oncologically ideal mediastinal lymph node dissection is not always achievable (particularly in left-sided lung cancer), VAMLA is evolving as a supplement to video-assisted thoracic surgery (VATS) lobectomy (8,9). We hereby sum up both indications and technique for VAMLA and discuss its results in relation to the other available mediastinal staging procedures like TEMLA, EUS-FNA (endoscopic ultrasonography with fine-needle aspiration), and EBUS-FNA (endoscopic bronchial ultrasonography with FNA).

VAMLA indications

It is a popular fallacy to equate conventional mediastinoscopy with VAMLA. The first is in general defined as "a surgical procedure to examine mediastinal lymph nodes with the possibility of taking surgical biopsy specimens". Typing the acronym "VAMLA" says it all: it means a complete mediastinal lymphadenectomy rather than merely taking biopsies; it means staging & treating rolled into one rather than staging alone. In this sense we declare an upgrade of the VAMLA procedure from a solely diagnostic and dissection tool to a combined staging and advanced therapeutic intervention.

The contemporary performance of VAMLA for both mediastinal staging and dissection is a distinct decision in every aspect. Developing an institutional choice, the well-known arguments in favor of VAMLA to mediastinal staging and dissection should be measured (10-12): the high staging accuracy, the prevention of re-mediastinoscopies afterwards neoadjuvant treatment, the enhancement of mediastinal dissection in combination with left-sided and VATS lung resections, the unison of staging and dissection within one method, the conceivable mixture with extended mediastinoscopy to sample stations 5 and 6, mediastinoscopic ultrasound, right-sided video-thoracoscopy contained by the same procedure and in general the option of bilateral mediastinal lymphadenectomy regardless of the tumor location or surgical approach for tumor resection. The latter, otherwise could only be achieved via sternotomy or bilateral VATS thus exposing the patient to an unacceptable extent of surgery. To come to a suitable individual indication, the likelihood of mediastinal involvement, the extent and resectability of mediastinal nodes, the laterality of the primary, and the capability of the patient to resist invasive mediastinal staging and probably multimodality treatment should be taken into account (10).

Novel indications are eased by the clinical adaptability of VAMLA. It seems evident to combine VAMLA and nonsurgical modalities as radiation therapy and radiofrequency ablation (13). VAMLA rules out nodal disease in such restricted local treatment techniques. In certain patients, there might be a role for VAMLA in palliative treatment concepts. The rationale is always the enhancement of local mediastinal control in patients inappropriate for lung resection to avoid local difficulties like bleeding, infection, respiratory insufficiency, and asphyxia, thus conserving quality of life and a constant clinical state enabling palliative treatment.

In terms of clinical research, VAMLA offers several potentials, mainly in its surgical assessment of other procedures of mediastinal staging (e.g., EUS-FNA, EBUS-FNA, and PET-CT) (12,14). This aspect is all the more important as the majority of studies assessing new treatments or new prognostic aspects still offer very low diagnostic certainty with respect to mediastinal staging. The recognized survival differences amid cN and pN stages are well inside the array of the variances perceived in many oncological trials, suggesting the application of VAMLA to offer precise staging, and, if surgery is part of the procedure, suitable dissection (15,16).

Principal VAMLA technique

The two doctrines of VAMLA are (I) minimally invasive access analogous to conventional mediastinoscopy and (II) the compartmental *en bloc* resection of the complete mediastinal adipose tissue conducted by anatomical landmarks comparable to open systematic nodal dissection (17). To overcome this obvious contradiction, VAMLA necessitates a bimanual dissection technique, reliant on a spreadable video-mediastinoscope (18).

Elementary dissection technique comprises two steps. First, applying tension on a dissection plane and second, dividing. The dissection plane is most often exposed by maneuvering the specimen. Stirring the specimen inwards or sideward and thus away from the optic is beneficial to preserve a proper view. The specimen is straightforwardly maneuvered by a large grasper with blunt fenestrated claws. Strong closure of the instrument is almost never required and should be circumvented, as it will cause tissue fragmentation. Division of connective tissue planes requires blunt and sharp dissection. The suction-coagulation device provides both modalities and does no damage, as long as the coagulation current is kept within a range that avoids carbonization (soft-coagulation mode). Herein lays the particular advantage of modern energy devices: following coagulation the soft tissue can usually be dissected without the use of a cutting current. Whenever cutting current is used, utmost care must be taken to avoid any proximity or even contact with vessels, the tracheobronchial tree or nerves. Even in no-contact situations sparks from cutting current can produce holes in those anatomical structures. The newer energy devices using bipolar current or ultrasound for coagulation may help avoiding such complications. However, their tips can remain hot after or while dividing tissue and contact with surrounding tissue can have detrimental consequences.

Prerequisite for any dissection is a clear vision. For this purpose, both the suction-coagulation device as well as the suction-irrigation channel incorporated into the mediastinoscope should be kept in continuous action through the procedure. Irrigation is very cooperative to clear not only the dissection site but also the tip of the optic. The latter necessitates forceful flushing of 5–10 mL isotonic solution, and sometimes supplementary cleansing by a small sponge stick.

To accomplish VAMLA, the mediastinum is separated in three compartments according to anatomy and useful surgical reason, which are dissected sequentially. Remarkably, this very kind of compartmentation was reproduced by the concept of mediastinal zones and the IASLC lymph node map (15).

Regular dissection was well-defined to comprise all lymph node stations within the range of conventional mediastinoscopy. It contains (I) the subcarinal compartment including the subcarinal lymph nodes, (II) the right compartment enclosing the pretracheal, right paratracheal, and tracheobronchial nodes and (III) the left compartment covering the left paratracheal and tracheobronchial nodes, thus providing bilateral clearance of the nodal stations 2, 4, and 7. As the range is not limited by this definition but by the dimensions of the video-mediastinoscope in relation to the patient, it is conceivable to embrace supraclavicular, prevascular, paraesophageal, hilar, and interlobar pulmonary nodes (stations 1, 3a, 8, 10, and 11R) and, via extended mediastinoscopy, the para- and subaortic nodes (stations 5 and 6). The resection quality of the latter comprises sampling as well as systematic dissection and its performance depends on the individuals' anatomy along with the necessity within an individual clinical context.

Parallel to conventional mediastinoscopy, VAMLA begins with a small jugular access to the cervical trachea and digital mobilization of the airway and the innominate artery. An extremely helpful addition to this is to flex the finger that is introduced underneath the innominate artery around it ventrally and to mobilize the lymphatic tissue away from the artery and dorsally in direction to the trachea. The closed mediastinoscope is then inserted identifying the main carina and both main bronchi as important landmarks for orientation in the central mediastinum just like in conventional mediastinoscopy. The sequence of dissecting the mediastinal compartments is choice of the performing surgeon. However, starting with the left side has several advantages. The recurrent nerve is visualized, and the fascia is divided between the nerve and the left tracheobronchial angle to expose the station 4L nodes. Often, the left bronchial artery is crossing these nodes and lying above the left main bronchus. Dividing the artery between clips opens the left compartment wider and reduces bleeding during later dissection of the subcarinal compartment. Protecting the nerve and thus its function, cautious dissection and removal of all evident lymph nodes are desirable to *en bloc* resection of the left paratracheal and tracheobronchial adipose tissue. For the same reason, electric current is not appropriate on the left side, and hemostasis is trusting on clips, momentary compression, or resorbable hemostats. This should also be considered in the supravascular zone, where both recurrent nerves are possibly at risk. To expose the subcarinal nodes, tracheal bifurcation and pulmonary artery are carefully separated with spreading of the blunt forceps. The scope is positioned in-between, stacking the artery on its upper blade, and then secured and spread to show the subcarinal compartment and to remove the subcarinal tissue *en bloc*, ensuing the medial borders of both the main bronchi and the anterior wall of the esophagus. Then, the scope is withdrawn to the innominate artery and focused to the right side. As described above, the pretracheal and right paratracheal fat pad has already been mobilized downwards and now is further pushed with the upper blade of the scope exposing the parietal pleura and superior vena cava. The fat pad is removed *en bloc* down to the azygos vein and the right main bronchus reaching as far as 10R between the azygos vein and the first branch of the right pulmonary artery. Dissection of station 11 nodes and other extensive techniques are not to be described here.

Minor hemorrhage is best disallowed by clipping the habitually appearing bronchial artery branches crossing the subcarinal space and the small veins draining into the vena cava. Major hemorrhage is very unlikely, if the pulmonary artery is adequately mobilized afore the scope is spread open. Protective measures to minimize the intrinsic risk of tumor spillage are vital and embrace the cautious treatment of the specimen, avoiding the crushing or cutting through diseased nodes.

Imaging techniques

Chest computed tomography (CT) remains important in lung cancer imaging. Despite its low sensitivity (55%) and specificity (81%) in terms of solely relying on CT scan, it is moreover a guide in choosing the suitable technique for tissue sampling due to the anatomical images it offers (19). When the CT scan is added by the information given by positron emission tomography (PET)—thereby binding into PET-CT—the results are more accurate concerning lymph node staging than CT scan alone with an elevated overall sensitivity (80–90%) and specificity (85–95%) (20-23). It has a high negative predictive value for detecting mediastinal nodal disease in peripherally located non-small cell lung cancer (NSCLC) except (I) suspicious N1 nodes; (II) tumor >3 cm; and (III) centrally located tumor without suspicious nodes on CT or PET scan.

Improvements in magnetic resonance imaging (MRI) technology have allowed attainment of diffusion-weighted MRI (DWI), which offers exceptional tissue disparity because of the variance in the diffusion of water molecules amongst tissues. The technique profits qualitative and quantitative information that echoes changes at a cellular level and provides unique insights about tumor cellularity and the integrity of cell membranes. Up to now there exist only few studies comparing the value of DWI and PET-CT. Even it is too early in this context to determine the true value of DWI in nodal staging of patients with NSCLC, the sensitivity for DWI seems to be significantly better than for PET-CT (95% *vs.* 89%) (24).

Endoscopic techniques

Endoscopic ultrasonography (EBUS and EUS) are performed in an outpatient setting under local anesthesia with moderate sedation. EBUS-TBNA (EBUS with trans-bronchial needle aspiration) is able to visualize superior and inferior mediastinal lymph nodes at stations 2R/2L, 4R/4L and 7, as well as hilar lymph nodes at stations 10, 11, and even 12 (15). EUS-FNA particularly visualizes superior mediastinal lymph nodes in station 4L, and inferior mediastinal nodes in stations 7, 8 and 9 (15). Thus, EUS-FNA complements other techniques, as several of these lymph nodes (stations 8 and 9) are not accessible by EBUS-TBNA or conventional mediastinoscopy. If EUS-FNA is to be considered in lymph node stations 5 and 6 remains to be an object of ongoing debate (25). In our experience lymph node station 5 is reachable in case of a wide aortic pulmonary window and additional lymph node augmentation, whereas lymph node station 6 is hardly accessible.

It is conceivable to envision and sample lymph nodes with a short axis of >5 mm with the ideal number of aspirations being made per lymph node is three (26). For mediastinal staging, systematic nodal aspiration of at least 3 stations including 4R, 4L and 7 is required (26-31). Additionally, the biggest node gauging >5 mm on ultrasonography inside each of these stations as well as PET-CT positive nodes within each of these nodal stations should be included. On indication nodal station 10R and 10L can be biopsied. To evade contamination while using one single needle for an EBUS or EUS procedure, the order of nodal sampling should start at the level of N3 nodes tailed by N2 nodes before finishing with N1 nodes.

Numerous meta-analyses on endobronchial and esophageal endosonography with FNA stated a mutual sensitivity of 83% to 94% for mediastinal nodal staging of lung cancer (32-38). Equating the two staging strategies proposed in the ESTS guidelines (either conventional mediastinoscopy, or alternatively endosonography followed by conventional mediastinoscopy) there was no variance in sensitivity or negative predictive value when conventional mediastinoscopy was compared with endoscopic staging (17,27). However, the staging strategy starting with endosonography and if negative joining it with surgical staging has confirmed to detect significantly more mediastinal nodal N2/3 disease compared to conventional mediastinoscopy alone (27). Another consequence is that the application of endosonography for baseline mediastinal nodal staging evidently reduces the necessity for mediastinoscopy (39). As from today's perspective, these studies have several potential sources of error. The two most important points of discussion are: (I) the expertise in the respective study centers is much higher for endosonography than for conventional mediastinoscopy; (II) there are not enough powerful investigations on the comparative examination of endosonography and VAMLA. Despite guessing the misalignment, the results of these biased studies conduct the slightly imprudent clinical pathways, thus leaving VAMLA and its benefits-to-prove in disgraceful light.

Contrariwise, the negative likelihood ratio stated by three of the meta-analyses indicates that the possibility of having mediastinal nodal contribution for any distinct patient with a negative endosonography result is at least 13–15% (34-38). This possibility founded on endosonography alone is definitely not low enough to directly proceed to a surgical resection in any oncological concept that tries to avoid unforeseen N2 or N3 at tumor resection. Consequently, in routine practice a preoperative surgical staging procedure (i.e., VAMLA) as a consequence of a negative endosonography shall be provided. When it comes to prospective studies in experienced endosonography centers, it is of importance that the lack of improved sensitivity of conventional mediastinoscopy after well-performed negative endosonography has not to be equated with the possible sensitivity of VAMLA (as there is still a lack of appropriate studies) (28,40,41).

Surgical techniques (VAMLA *vs.* TEMLA)

VAMLA and transcervical extended mediastinal lymphadenectomy (TEMLA) aim for a complete mediastinal dissection (4,42). VAMLA is utterly accomplished with the use of the video-mediastinoscope whereas TEMLA uses a 5–8 cm collar incision in the neck and uplifts the sternum with a Cooper retractor. The dissection is achieved in an open manner and with additional use of the video-mediastinoscope. In comparison to VAMLA, where usually the same lymph nodes are removed which are generally reachable through conventional mediastinoscopy, by TEMLA there are more lymph node stations routinely accessible such as the prevascular, the paraaortic, the subaortic and the paraesophageal lymph node stations. The negative predictive value is very high and approaches 98.7% for TEMLA. TEMLA has a higher morbidity and mortality. The complications after VAMLA and TEMLA are well documented and are perhaps more studied in detail than after conventional mediastinoscopy—as these procedures are done in very experienced centers (4,5,42-47).

VAMLA complications

Intra- and postoperative complications happen in fewer than 5% (5,45). The range is comparable to conventional mediastinoscopy, counting wound infection, mediastinal hematoma and seroma, mediastinitis, pleural effusion, pneumothorax, chyloma and chylothorax, left-sided recurrent nerve paralysis, minor hemorrhage from thyroid and mediastinal veins as well as bronchial artery branches, and damage of larger vessels, central airways, and esophagus. But major events are undoubtedly extremely exceptional, also in our institutional experience. Several precautionary methods are advisable: prophylactic single-shot antibiotics; low-voltage coagulation without cutting current; avoiding electrocautery within the left compartment; clip occlusion of small veins, bronchial artery branches, and lymphatic vessels; and usage of resorbable local hemostats.

Separate consideration needs to be given the following technically inherent risks. First, to avoid catastrophic laceration of the pulmonary artery throughout subcarinal dissection, the vessel has to be unfettered from the main carina, both the main bronchi, and the subcarinal lymph nodes afore insertion of the scope and its spreading. Second, to avoid wall necrosis of the airway and the esophagus, subcarinal dissection and hemostasis by electrocautery has to be precise and effective.

VAMLA-results

The first portrayal of VAMLA compared the mediastinal harvest of 40 complete VAMLA dissections compared to 80 cases of open mediastinal dissection (which were extracted in the course of an open thoracotomy lobectomy) in terms of a single center prospective comparative study. The mass of the VAMLA specimen was significantly higher and containing significantly more lymph nodes (20.7 *vs.* 14.3 nodes) than those of the open surgery group (4). To complement these findings, an investigation of 20 VAMLA procedures labelled dissection rates of different mediastinal nodal stations within a range of 92–100% (6). Both studies highlighted a new era in thoracic oncology: the simple perception that the profit and the radicality of VAMLA is at least as equivalent as open mediastinal dissection.

The recital of VAMLA under routine clinical and training situations was evaluated in a prospective manner in 144 successive VAMLA procedures counting 9 procedures performed after neoadjuvant treatment (5). VAMLA had a mean duration of 54.1 (range, 40–175) minutes, no mortality or conversion rate to open surgery, and a complication rate of 3.98% tumbling from 5.3% to 2.6% with rising knowledge of the surgeons involved. The most common complication was momentary left-sided recurrent nerve paralysis that happened in 4 out of 144 VAMLA patients (2.8%). An underlying connection is possible, although all of these patients had additional extended mediastinoscopy for assessment of the left-sided para- and subaortic nodes. To determine the staging accurateness, 130 nodal-negative patients experienced mediastinal re-exploration at the time of lung resection. Sensitivity, specificity, and false-negative rate were 0.938, 1, and 0.009. Mediastinal adhesions existed in 19.2%, most often in case of time intervals between VAMLA and lung resection beyond one week. Uninterrupted healing of the bronchial stump was witnessed in all but one patient (99.2%). This institutional series called VAMLA as a innocuous and practical procedure in patients with normal or slightly enlarged mediastinal lymph nodes and its capacity as a minimally invasive nevertheless complete technique of systematic nodal dissection prevailing under conditions of clinical routine, producing accuracy data superior to conventional mediastinoscopy, endoscopic FNA procedures, and PET-CT scan (48-50)—even if those are applied in combination and, characteristically, in oncologic cohorts presenting high prevalence of extensive mediastinal disease (27,29,31,51,52).

Collective VAMLA and selective extended mediastinoscopy for left-sided tumors with distrustful nodes in the para- and subaortic lymph node stations had an influence on mediastinal staging in 78% of 92 studied patients (53). It resulted in mortality and complication rates of zero and 4.5%. Staging sensitivity, specificity, and negative predictive value were 0.94, 1.0, and 0.96 (54).

Joint mediastinal dissection by VAMLA and VATS lobectomy rose in the dissection of suggestively more mediastinal lymph node stations (6.4 *vs.* 3.6), yielding mediastinal specimen of a significantly higher weight (10.7 *vs.* 5.6 g) matched to mediastinal dissection by VATS only (9). This effect was most noticeable at the subcarinal and contralateral mediastinal lymph node stations, and for left-sided procedures. For none of the viability factors being conversion rate, blood loss, operation time, complications, and drainage time, a substantial difference was perceived. The VAMLA part of the combined procedure yielded two thirds of the mediastinal dissection and required about a fourth of the total operation time. This is of economic importance, as the mediastinoscopic part of the procedure requires only one surgeon.

Numerous studies strengthened these outcomes (55,56). One of the few could confirm the clinical results in an individual series of 104 VAMLA procedures, the majority of which was carried out for clinically resectable left-sided NSCLC in combination with VATS lobectomy, reporting a mean duration of 39.8 (range, 14–85) minutes, a median yield of 16.0 (range, 3–37) lymph nodes, dissection rates between 71.3% and 100%, zero mortality, and a complication rate of 3.4% recurrent nerve paralyses having been the only complication perceived (45).

Taking up the idea and carry it further, the first long time survival after stage-oriented tumor therapy focused by VAMLA and lung resection was described in a cohort of 89 patients containing 33.7% pN2 and 6.7% pN3 involvement (57). Five-year overall survival was 90%, compared to 66% observed after standard staging video-mediastinoscopy and lung resection in 344 patients of the same institution. Multivariate analysis recognized an odds ratio of 1.34 for longer survival after VAMLA (95%

confidence interval, 1.1–3.2; P=0.2). Last not least, pooled VAMLA and mediastinoscopic ultrasound (MUS) can increase clinical T staging and resection rates of central tumors over-staged by CT scan (58,59).

Conclusions

In previous eras, the gold standard of mediastinal staging was conventional mediastinoscopy. Modern imaging techniques and erudite studies on lymphatic spread allow us to differentiate cases in whom to approve, in whom to dismiss, and in whom to disregard the option of mediastinal blowout (60,61). The standard diagnostic examination has been stratified consequently, recommending endoscopic FNA techniques, standard video-mediastinoscopy, and intra-operative lymph node dissection, respectively.

A distinctive contour has to be pinched amid meager staging procedures like PET-CT, EUS-FNA, and EBUS-FNA, which justifiably have substituted standard mediastinoscopy as a staging tool in many cases, and the techniques of minimally invasive systematic lymphadenectomy by VAMLA or TEMLA, which still are perceived as staging tools, whereas they allow a nodal dissection at least as adequate as open lymphadenectomy. Replacing a staging procedure by complete systematic nodal dissection has impact beyond enhanced accuracy of mediastinal staging. Known implications are as follows: (I) mediastinal dissection becomes independent of lung resection or any other kind of treatment, e.g., radiation of the primary; (II) mediastinal re-exploration at lung resection is no longer required; (III) neoadjuvant treatments of tumors with minor mediastinal disease otherwise only detected intra-operatively or by pathologic examination is possible; (IV) re-mediastinoscopy to assess mediastinal response to neoadjuvant treatment is omitted; (V) mediastinal dissection is improved and facilitated in situations when complete bilateral mediastinal dissection is complicated by anatomical or technical conditions, as it is known for left-sided lung resections or the thoracoscopic approach; and (VI) studies in clinical oncology can be based on minimally invasive standardized mediastinal dissection.

Plain common sense rules logical sequence of diagnostic procedures. EBUS-TBNA and EUS-FNA are recommended—truly acclaimed by oncologists—as initial most likely minimal-invasive tissue staging procedures. Combining the results of EBUS-TBNA and EUS-FNA seems to be the most optimal methods in generating a precise mediastinal nodal map. Based on this diagnostic pathway, mediastinoscopy is recommended only in case of ruling out false-negative endosonography. However, debate persists about its value due to its (seemingly) limited nodal metastasis detection rate, morbidity, associated treatment delay, and questionable impact on survival. This debate has resulted in wide variation in practice and deviance from guideline recommendations in clinical practice. The trap-door is the misinterpreted equation of *the old* conventional mediastinoscopy and *the new* VAMLA.

Classically, for the assessment of a new surgical technique, initial published evidence was the result of single-institutional prospective observational clinical research. In the meanwhile, these outcomes have been recurrently confirmed by other groups and are broadly recognized in the oncologic society. Long-term survival data after VAMLA are still kind of preliminary, but nevertheless inspiring. For these motives, VAMLA was consequently well-thought-out as a practical and effective method to mediastinal staging and dissection for thoracic malignancy.

Exact mediastinal lymph node staging of NSCLC is decisive in guiding treatment options and determining prognosis (62,63). When both FDG-PET and CT-scan do not illustrate any marks of distant metastases (M1 disease), mediastinal nodal status determines treatment options. The ESTS guideline dating from 2014 endorses invasive mediastinal lymph node staging in patients with clinical N1 to N3 (cN1–3) disease, a centrally located primary tumor, a non–FDG-avid primary tumor, or a peripheral tumor larger than 3 cm. This guideline has the goal to offer neoadjuvant treatment or definitive chemo-radiation therapy to patients with positive mediastinal nodes and primary resection to those without nodal involvement (N0) or exclusive hilar node involvement (N1). However, the incrementing routine use of minimal invasive resection techniques on one hand and the advent of immunotherapy on the other have started to challenge and complicate this simple rule. With lower risk, lower complications and faster recovery after minimal invasive resection, primary resection and adjuvant treatment is advocated for limited stage III disease. With neoadjuvant immunotherapy and systemic treatment options offered not only to patients with nodal spread (regardless to which extent), pre-therapeutic accurate detection of even minor nodal disease gains increasing importance. VAMLA can provide this perfectly.

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