

Videomediastinoscopy: a Ten Year Experience on Lung Cancer Stadiation and Non-Diagnosed Mediastinal Lymphadenopathy

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Rezumat

Videomediastinoscopia: o experiență de 10 ani în stadializarea cancerului pulmonar și a limfadenopatiei mediastinale nediate diagnosticate

Mediastinoscopia cervicală (CM) este o procedură chirurgicală în sine, necesitând o sală de operație și anestezie generală, iar absența tehnicilor minim invazive a dus la nașterea, în trecutul recent, mitului mediastinoscopiei ca standard de aur în stadializarea patologiilor mediastinului. Actualmente, investigarea mediastinului este diferită și necesită o evaluare a rolului de standard de aur al CM. Între ianuarie 1999 și decembrie 2012 un total de 303 CM au fost efectuate; 167 pentru stadializare preoperatorie a cancerului pulmonar și 136 pentru mărire în volum a ganglionilor mediastinali nediate diagnosticate. Stațiile ganglionare investigate au fost acelea accesibile de rutină prin CM. Din 167 de CM efectuate pentru stadializarea cancerului pulmonar, rezultatele a 102 au fost pozitive pentru boală metastatică ganglionară și 65 negative. Din 136 de VAM efectuate din alte motive (alte indicații decât neoplasm pulmonar) 15 au fost diagnostice pentru limfom (NLH/LH 2/4), 8 au revelat boală pulmonară non-metastatică, 55 au fost sugestive pentru sarcoidoză, 10 pentru adenită tuberculoasă și 48 pentru adenită nespecifică. Datele prezentate în această lucrare înglobează activitatea unei singure instituții în perioada 1999-2012, iar rezultatele extrapolate corespund ideii noastre

că, în ciuda dezvoltării de noi metode, nu putem încă renunța la mediastinoscopie.

Cuvinte cheie: mediastinoscopie, cancer pulmonar, stadializare

Abstract

Cervical Mediastinoscopy (CM) is a surgical procedure in its own right requiring an operating room and general anesthesia and, in the recent past, the absence of minimally invasive techniques had created the myth of mediastinoscopy as the "gold standard" for the pathological staging of the mediastinum. Nowadays, investigating the mediastinum is different and this calls for a review of the role of the "gold standard" CM. Between January 1999 and December 2012 a total of 303 CM were performed; 167 for pre-operative lung cancer stadiation and 136 for non-diagnosed enlargement of mediastinal nodes. The nodal stations investigated were those usually obtainable with CM. Out of 167 CM for lung cancer stadiation, 102 were positive for metastatic nodal disease, 65 were negative. Out of 136 VAMs performed for other reason (indications other than lung cancer) 15 were diagnostic for lymphoma (NLH/LH 2/4), 8 revealed non metastatic lung disease, 55 were suggestive for sarcoidosis, 10 for tubercular adenitis and 48 for non-specific adenitis. The data presented in this paper refer to the activity of a single institution in the period between 1999 and 2012 and the results we have extrapolated correspond with our idea that, despite the progress of new methods, we cannot as yet, do without mediastinoscopy.

Key words: mediastinoscopy, lung cancer, stadiation

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Introduction

Cervical mediastinoscopy (CM) was first described by Harken (1) in 1954 and can be considered the first minimally invasive diagnostic surgical technique. Harken described a lateral approach after excision of the scalene fat pad and Carlens in 1959 described the classic midline approach (2) The technique became popular thanks to F.G. Pearson who proved a worse prognosis in a group of lung cancer patients with involved mediastinal lymph nodes. This first work on the prognostic importance of mediastinal lymph node involvement in NSCLC was the basis of the development of the famous lymph node map by Mountain and Dressler. Nowadays CM is mainly used as an invasive staging procedure for assessment of the mediastinum in patients with non-small cell lung cancer (NSCLC) because therapeutic options for non-metastatic NSCLC are largely based on the status of the mediastinal lymph nodes. (3) The use of CM for diagnosing other mediastinal diseases is always valuable but less frequently exercised. Over time the procedure has underwent several improvements up and till the introduction of the video technology (Video Assisted Mediastinoscopy or VAM) that made teaching the procedure much easier. In the recent past, the absence of reliable noninvasive methods for differentiating malignant from benign nodes meant that the CM was the "gold standard" for the study of mediastinal lymph nodes. Today, the development of lesser invasive and non-invasive approaches as PET-CT or ultrasound biopsy (EUS-fna, EBUS-fna) requires a redefinition of the role of videomediastinoscopy in the staging of NSCLC. We herein present data from a single institution from 1999 to 2010.

Materials and Methods

Between January 1999 and December 2012 at General Thoracic Department and Thoracic Endoscopy Department, E.Morelli Hospital in Sondalo (Italy) a total of 303 VAM were performed, CT or PET-CT evidence; 167 for pre-operative lung cancer stadiation and 136 for non-diagnosed enlargement of mediastinal nodes with or without associated lung alterations. The gender ratio M/F was 188/115 with m/f of 2:1 and 3:2 ratio respectively for lung cancer or for other pathology. The median age was 64 yrs respectively (30-80) for lung cancer and 49 yrs (26-78) for non-lung cancer patients. All mediastinoscopies were done under general anaesthesia and the nodal stations investigated were those usually obtainable with CM (stations 2,4,7). For all procedures indicative intra-operative frozen section histological examination was performed.

Results

Median operation duration was 40.3 minutes (min 10, max 105). Our rates of mortality and morbidity were comparable with the literature. The mortality rate was 0.33% (1/303) for irreparable laceration of innominate artery and morbidity rate was 0.99% (3/303) because of minor bleeding (inferior to 300 ml of blood) controlled without modification of operative

procedure and one recurrent nerve impairment. Out of 167 VAM for lung cancer stadiation 102 were positive for metastatic nodal disease, 65 were negative. Out of 136 VAMs performed for other reason (indications other than lung cancer) 15 were diagnostic for lymphoma (NLH/LH 2/4), 8 revealed non-metastatic lung disease, 55 were suggestive for sarcoidosis, 10 for tubercular adenitis and 48 for aspecific adenitis.

Discussion

Today the diagnostic procedures regarding the upper mediastinum are different and we can choose between non-invasive, less invasive and invasive techniques. Each group of procedures have different sensitivities, specificities and Negative Predictive Values (NPV). CT scan is the most common non-invasive procedure based on the known 1 cm criterion but is not particularly sensitive (57%) or specific (82%) in determining the presence or absence of metastases to mediastinal lymph nodes (positive predictive value: 56%; negative predictive value: 83%)(4,5). The 1-cm criterion is only a fair predictor of whether mediastinal tumor involvement is present, in fact, benign diseases can produce a significant nodal enlargement and conversely, neoplastic nodes can be normal in size. Functional PET-CT has enhanced the diagnostic accuracy of mediastinal lymph node involvement in comparison with CT alone; in fact it has a higher sensitivity (from 84 to 90%) but a low specificity (varying from 78% to 90%) with a marked heterogeneity across individual studies. This means that, although it has a high sensitivity, about 10 to 15% of mediastinal nodal metastases from lung cancer will not be detected by PET and the specificity of 80-90% indicates that a moderate number of false-positives will occur (6,7).

The increasing incidence of tuberculosis, and many inflammatory diseases such as sarcoidosis or histoplasmosis may give false-positive results, and then create a variable for the performance of PET in relation to the geographical prevalence of these granulomatous diseases; so, when there are suspect findings with non-invasive imaging modalities, tissue confirmation by invasive techniques is mandatory (6,7). The high NPV of PET-CT (93%) has allowed for CM to be omitted in selected patients with clinical stage I NSCLC peripheral tumors with negative PET-CT images (8). PET-CT does not reduce, however, the need for invasive procedures in detecting station 5 node metastasis (9). The less invasive group includes endoscopic procedures like Endoscopic Esophageal Ultrasound-guided Fine Needle Aspiration (EUS-fna) and Endobronchial Ultrasound-guided Transbronchial Needle Aspiration (EBUS-tbna). EUS-fna permit access to stations 2, 4 (R and L), 5, 7, 8 and is particularly useful for sampling stations 5, 7 and 8. Few studies have compared CT, PET and EUS fna but the few showed more accuracy and higher positive predictive value than for PET and CT scanning. EUS-fna has a pooled sensitivity of 88% and a specificity of 91% but the false negative rate remains high (4). EUS-fna appears to be a safe and minimally diagnostic technique for the re-staging of mediastinal lymph nodes in patients with NSCLC. EBUS-tbna adds another minimally invasive tool for the diagnosis and staging of intra-

thoracic malignancies. The procedure can reach nodes of stations 2, 3, 4, 7, 10 and 11. When combined with EUS the combination can provide nearly total staging of the mediastinum. It has a high sensitivity but a high false negative rate (20%) (10). A combination of CM and EUS-fna significantly improves sensitivity and NPV because EUS-fna reaches stations 5 and 8 that are not accessible to mediastinoscopy. These endoscopic procedures are “operator dependent”, have a lower NPV than VAM (11) and are poorly diagnostic in case of non-primary neoplastic disease of the lung (eg lymphoma) and benign disease (eg sarcoidosis) because they do not provide sufficient diagnostic material for accurate lymphoproliferative diseases (12). These techniques, for these reasons, are not able to rule out nodal disease accurately (13). Finally, in times when a pathologist requires a large number of samples for immunohistochemistry studies we think that invasive techniques remain necessary for determining the diagnosis. The invasive techniques are: classical VAM, Extended Cervical Mediastinoscopy and Transcervical Extended Mediastinal Lymphadenectomy (TEMLA). The Extended Cervical Mediastinoscopy (ECM) explores the anterior mediastinum in conjunction with VAM. The best use of ECM is staging nodes of the anterior mediastinum in case of cancer involving the left upper lobe (stations 5 and 6) (9,13). TEMLA provides a unique possibility to perform very extensive, bilateral mediastinal lymphadenectomy with very high diagnostic yield. The main advantage of TEMLA is, the possibility of removing almost all mediastinal lymph nodes with the surrounding fatty tissue (not station 9) and no other invasive staging technique enables such a complete assessment of the mediastinal nodes (14).

Sensitivity of TEMLA is 96%, specificity 100%, NPV 98,7% (14) and could be considered, according to some authors, the gold standard for primary staging and restaging after induction therapy when a minimally invasive technique has been used to obtain a proof of mediastinal involvement (15). No invasive restaging of the mediastinal nodes except from TBNA is necessary after complete TEMLA and neoadjuvant chemotherapy (15). In addition to staging of NSCLC, TEMLA might have a therapeutic impact but this requires further study. We believe however that CM remains the “gold standard invasive procedure” that offers a good compromise between strong invasive and minimally invasive techniques, allowing for good visualization and extensive lymph node sampling (stations 2, 4 and 7 lymph nodes) with a sensitivity of 81%, specificity of 100% and low incidence of complications in expert hands (4). There is no clear agreement on how many lymph nodes should be taken. According to “The American Thoracic Society (ATS)” all reachable nodal stations should be explored (levels 2R and 2L; 4R and 4L; 7; 10R and 10L) and the “European Society of Thoracic Surgeons (ESTS) working group” recommends to always biopsy the right and left lower paratracheal and the subcarinal nodes while the upper paratracheal nodes should be biopsied if present (4). The ATS also recommend to explore levels 5 and 6 in patients with left lung tumors through parasternal mediastinotomy. Different forms of CM have been described and the most important

development of the technique has been the advent of video technology. Video Assisted Mediastinoscopy or VAM is a well standardized procedure today, not “operator dependent” but remains a surgical procedure requiring an operating room and general anesthesia. The use of videomediastinoscope improves visualisation of the operative field, enables the surgeon to perform bimanual dissection with resection of more lymphatic tissue and lead to a higher accuracy in staging and a better standardization of the technique (16). Some tips, based on our experience are as follows: 1) Right positioning of patient’s head: it is a crucial assumption because it affects the ability to maneuver correctly the instrument. Neck hyperextension is necessary taking care not to create excessive tension. We usually use an elastic band placed on the chin to achieve a good compromise between optimal position and not excessive hyperextension of the neck by pushing the chin cranially and compressing the soft tissues. We can gain those few millimetres that allow instrument maneuverability improving; 2) Incision: we pay attention to perform a not very wide incision, along a fold of the neck when possible, to minimize the aesthetic damage in a visible region particularly important for women. We think that little details like these should be a generic intrinsic part of the elegance of surgical maneuvers, 3) Right anatomic plane: the correct mediastinal exploration presupposes the opening of pretracheal fascia and the introduction of the instrument just along the surface of the tracheal cartilage rings, making the examination faster and easier. 4) Tissue evaluation: experienced surgeons can distinguish, quite easily, nodes from other anatomical structures. For surgeons in training this may not be easy. The classic situation is a structure looking like a pathological lymph node and moving like an artery. The movements are often transmitted pulsed and the only way to resolve the doubt, safely, is to prick the tissue with a needle. Special dedicated needles exist but we usually use a simple spinal anesthesia needle.

Conclusions

Today it is mandatory to obtain diagnosis of mediastinal nodal involvement with less invasive methods (PET/CT, EBUS and/or EUS). However these techniques are not yet sufficiently capable to give adequate diagnostic yield.

Moreover, at a time in which the surgeon is even more pressed for minimally invasive surgical procedures, performing procedures like TEMLA seem exaggerated. In our General Thoracic Surgery Unit, patients are admitted after less invasive study and selection and VAM is the elective technique for complete diagnosis and staging of nodal involvement. Even though we have no prejudice towards novel minimally invasive methods, one must remember that a thoracic surgeon is still required to perform a cervical mediastinoscopy. Finally, the use of “video” technology facilitates teaching for trainee surgeons while maintaining safety for patients, as it is easier to identify lymph nodes and limiting structures.

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