


E04-04  Advances in Surgical Staging, Mon, Sept 3, 16:00 – 17:30

Re-do-mediastinoscopy

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Introduction

For patients with lung cancer preoperative evaluation of the mediastinal lymph nodes is important to estimate local operability or/and to consider the necessity of neoadjuvant treatment. Cervical mediastinoscopy (CM) is generally accepted as a safe and highly accurate procedure in the staging of lung cancer. Nodes accessible to CM are the levels of superior (level 2R and 2L) and inferior (level 4R and 4L) paratracheal and subcarinal (level 7) nodal stations. Additionally extended CM and left parasternal mediastinotomy allow the exploration of aortopulmonary window (level 5) and anterior mediastinal nodes (level 6). Until the beginning of the nineties, repeat mediastinoscopy (RM) was considered to be contraindicated because of fibrosis, due to prior exploration and the increased surgical risk to injure vital structures. Neoadjuvant clinical trials with induction chemotherapy or chemoradiation made necessary this aggressive re-exploration of the upper mediastinum in order to select patients with a higher probability to undergo complete resection and reduce the number of explorative thoracotomies in patients with locally advanced lung cancer. These series included small number of patients, but demonstrated a technical feasibility and a high diagnostic accuracy. Further indications were reported in patients after insufficient first mediastinoscopy and in the assessment of recurrent or second primary lung neoplasms.

The aim of this presentation is to represent the large experience of one institution with this method, specially the indications, the technical characteristics, the intra- and postoperative complications, at least the efficacy of RM as a staging procedure in view of new methods like the positron emission tomography (FDG-PET and FDG-PET/CT) and the endobronchial (EBUS) or endoscopic (EUS) ultrasound guided fine-needle aspiration (FNA).

Material and methods

From 1968 to 2004 279 patients (66 females and 213 males with a mean age of 58 years, range, 28 to 78 years) with lung cancer underwent a re-do-mediastinoscopy, 12 because of inaccurate first procedure (group A), 67 because of recurrent (group B) and 35 of second primary lung cancer (group C), finally 165 after induction chemo-/radiotherapy for IIIA and IIIB disease (group D). Before induction 116 patients had a N2 and 49 a N3-disease. Neoadjuvant treatment included 3 courses chemotherapy (three cycles of split-dose cisplatin 60mg/m² days 1,7 and etoposide 150mg/m² 3,4,5) followed by concurrent chemoradiotherapy(one cycle cisplatin 50mg/m² days 2,9 and etoposide 100mg/m² days 4,5,6 combined with 45 Gy hyperfractionated accelerated radiotherapy to primary tumor and mediastinal nodes). Restaging was performed by means of CT scan of the chest and upper abdomen, CT of the brain, bone scan and bronchoscopy. Patients with radiological evidence of tumor remission or stable disease and Karnowsky index of more than 70% underwent RM. The interval between first and second procedure were in group A 17 days (range, 12 to 38), in group B 14 months (5 to 29 months) in group C 27 months (19-124 months) and in group D 132 days (113-145). RM was performed with resection of the scar of the first operation and preparation to the pretracheal fascia. Digital maneuver or/and sharp preparation followed with determination and removal of adhesions along the „mediastinoscopy route“. After inserting the mediastinoscope we tried to obtain biopsies from the same nodal stations as by the first mediastinoscopy. Sometimes is technically easier to insert the mediastinoscope through the left side of the trachea, because the careful preservation of the recurrences nerve by the initial mediastinoscopy resulted to less nodal biopsies and less adhesions. All accessible lymph nodes were sampled and mapped according to the revised regional lymph node classification for lung cancer by Mountain. A RM was considered as complete if bilateral inferior paratracheal (level 4R and 4L) and subcarinal (level 7) nodal stations were reached.

Results

Non intra- or postoperative deaths was observed, the loss of blood during the procedure amounted on an average of 26 ml (range 10 to 160 ml) and was not different to the first operation. Three patients developed postoperative a recurrences nerve palsy, two a wound infection and two a cardiac arrhythmia. Because of the presence of diffuse inseparable adhesions. RM was not possible in 5 and incomplete in 14 cases (1.8% and 5.2% respectively). RM proved a N2 or N3 disease in 3/12 cases of group A (25%), in 17/67 of group B (25.4%) and in 6/35 of group C (17.1%). In the group D 116 patients had N2 and 49 N3 disease before induction treatment. The most frequent histological type found was squamous cell carcinoma (59p.) followed by adenocarcinoma (55p.), large cell carcinoma (19p.), small cell carcinoma (28p.) and mixed type of lung cancer in 4 cases. During the 160 RM biopsies was taken by a total of 528 lymph node stations (mean, 3.3).

Comment

46 years after its introduction by Carlens in 1959, CM continues to be an important step in evaluation of the mediastinal lymph node status and in selection of patients with lung cancer before surgery. RM were rare and the number of demonstrated cases very limited, so that any analysis of these data were doubtful and questioned. Furthermore RM considered to be as a difficult and complex operation because of the presence of peritracheal adhesions particularly between the trachea and the innominate artery. Meerschaut et al. reported first about a large series of 140 RM as a routine staging procedure without deaths due to the procedure and without complications necessitating surgical intervention. RM has been performed for different indications: in patients with incomplete first mediastinoscopy, assessment of recurrent tumors, assessment of second primary tumors and in patients after neoadjuvant chemotherapy. Mediastinoscopy has been also compared with other diagnostic examinations, particularly with imaging techniques as computed tomography and magnetic resonance. CT scan and MRI are unable to distinguish hyperplastic, antracotic, granulomatous nodes or fibrotic tissue after induction treatment from malignant nodes. The Copyright © 2007 by the International Association for the Study of Lung Cancer
sensitivity and specificity of 69% and 71% of CT scan and 45% and 65% of MRI respectively does not provide sufficient informations for these patients. Modern techniques as positron emission tomography (FDG-PET or FDG-PET/CT) and endobronchial (EBUS) or endoscopic (EUS) ultrasound guided fine-needle aspiration (FNA) have also been used for mediastinal staging. In a prospective study with 202 patients found Gonzalez-Strawinski and al. that current FDG-PET technology alone does not appear to be sufficient to warrant reliable treatment changes or the avoidance of mediastinoscopy in the evaluation of patients with NSCLC. FDG-PET results have been shown to be difficult to interpret after radiotherapy and the best time to repeat it still remains unproved. An inherent problem of the FDG contrast is that inflamed tissue will absorb it, so that granulomatous or inflammatory mediastinal disease or cases of obstructive malignant processes resulted to difficulty identifying mediastinal malignancy with FDG-PET. In our series we found that patients after induction chemoradiotherapy showed a strongly FDG accumulation due to inflammatory reaction of radiated mediastinal tissue, so that the number of false positive cases ranged by 20%. Hellwig et al reported about the high negative predictive value in mediastinal restaging of FDG-PET so that only low values of lowstandardized uptakes allows for omission of RM. EBUS and EUS guided FNA are promising technique for staging of solid lesions and lymph nodes located adjacent to the trachea, the main bronchi and the esophagus but is not comparable to mediastinoscopy or RM. Selection of the patients for EUS or EBUS-FNA was based on computed tomographic scanning and with that only in patients with pathological radiological findings. Both techniques are used to assess the entire mediastinum or to stage predominantly only one nodal station, but they are not used for the systematical standardized exploration of individual nodes as performed by mediastinoscopy. Moreover, the echogenic characteristics alone of a node might not be as reliable after radiation as they are before. In our experience representative material from scarred and fibrotic lymph nodes after chemoradiotherapy is difficult to be taken, the number of false positive results in the cytologic examination of FNA should be not underestimated. Particularly for local advanced disease and neoadjuvant treatment a histological tissue diagnosis must still be obtained, so that granulomatous or inflammatory mediastinal disease or cases of obstructive malignant processes resulted to difficulty identifying mediastinal malignancy with FDG-PET. In our series we found that patients after induction chemoradiotherapy showed a strongly FDG accumulation due to inflammatory reaction of radiated mediastinal tissue, so that the number of false positive cases ranged by 20%. Hellwig et al reported about the high negative predictive value in mediastinal restaging of FDG-PET so that only low values of lowstandardized uptakes allows for omission of RM.

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Some investigators have focused on an early intensification of preoperative staging by bimodality induction including chemotherapy as well as radiation therapy before surgery. In these patients the clinical classification especially the mediastinal staging after the induction treatment must yield the possible maximal accuracy. Bueno et al and Voltolini et al pointed out in two separate reports that nodal stage after induction therapy for stage IIIA lung cancer determines patient survival. Downstaged patients to NO status survived 59% at 3 years and 35.8% at 5 years respectively. However as have been proved the persistence of lymph node involvement after induction treatment has a discouraging prognosis with 3 years survival of 0% in the first and 5 years survival of 9% in the second study. This data support surgical resection only for downstaged patients and that a direct effort should be made to improve the accuracy of restaging before resection. Because of this, our oncological group considered to performe the RM in order to re-evaluate the mediastinum taken biopsies and verifying the nodal status in all patients entered into two complete phase II and one phase III trial and selecting patients for resection. Technical aspects of RM are well described in previous reports. The presence of peritracheal adhesions makes the exploration more complex than by the initial mediastinoscopy. Analogous to other reports we didn’t have a perioperative or postoperative mortality. A low rate of morbidity was observed (4.2%) concient with reported results from other series. Furthermore additional operations due to intraoperative complications were not necessary. The incidence of recurrent nerve palsy was in accordance with the numbers after first mediastinoscopy.

We conclude that RM is a feasible and safe surgical procedure for restaging of patients with primary locally advanced, recurrent or second primary lung cancer. There are no mortality, the perioperative complications rate are very low. In patients after induction treatment RM proved to be less sensitive than the first procedure because of adhesions and fibrotic tissue. Because of the higher sensitivity, specificity and accuracy in compare to radiological investigations, FDG-PET and ultrasound guided FNA remains RM despite the technical complexity the criterion standard for mediastinal restaging in patients with local advanced lung cancer and induction treatment.

Session EOS: IASLC Staging Project

EOS-01  IASLC Staging Project, Mon, Sept 3, 16:00 – 17:30

The IASLC lung cancer staging project
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The History: Peter Goldstraw.

The Tumoer, Node, Metastases (TNM) system for the classification of malignant tumours was developed by Pierre Denoix in a series of papers between 1943 and 1952 (1,2). In 1953 it was accepted by the International Union Against Cancer (UICC) Committee on Tumour Nomenclature and Statistics. In 1968 it appeared in the 1st edition of their Classification of Malignant Tumours. In 1973 the American Joint Committee on Cancer (AJCC) Task Force on Lung Cancer accepted the recommendations of Drs. Mountain, Carr and Anderson for a clinical staging system of lung cancer (3). The following year the UICC accepted these proposals, unifying the 2 staging systems, in their 2nd edition of the TNM Classification of Malignant Tumours.

The AJCC recommendations were based upon a database which consisted of 1,712 cases of non-small cell lung cancer (NSCLC) diagnosed at least 4 years before the analysis of results. Nearly all of the descriptors used today in staging lung cancer were established in that relatively small database, including the only size cut off for T descriptors (that of 3 cms which distinguishes T1 from T2 tumours), the impact of specific areas of local invasion (visceral pleura, diaphragm, chest wall and the mediastinum and its contents), the proximal bronchoscopic extent of disease, pleural effusion and the extent of atelectasis or pneumonitis. In this version the highest “T” descriptor was 3, that for “N” was 2 and the highest stage was stage III.

Since that pioneering work there have been 4 more revisions. The size of the database on which these changes were made has increased, to 5319 in the 5th revision (4), the review process has become progressively more “International” and a few new descriptors have been added, resulting in the expansion of the “T” category to 4, the “N” category