



Endoscopic mediastinal staging: present and future issues

Lung cancer is the first cause of cancer-related mortality (1). The definition of mediastinal lymph node status is of utmost importance in the choice of the ideal treatment of early-stage and locally-advanced non-small cell lung cancer. Non-invasive staging, based on CT and PET scan, has relatively limited accuracy in mediastinal assessment, and therefore invasive staging still has a major role (2). In particular, endoscopic techniques as endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound fine-needle aspiration (EUS-FNA) have gained increasing acceptance as an alternative to surgical staging. The potential advantages of an endoscopic approach are a reduced invasiveness and a more thorough assessment of the mediastinum in comparison with surgical procedures. According to the current international guidelines endobronchial ultrasonography (EBUS) and/or esophageal ultrasonography (EUS) have therefore a pivotal role in the invasive staging of the mediastinum (3). Tissue confirmation of mediastinal nodes is indicated in patients with a high risk of mediastinal involvement as those with positive hilar or mediastinal nodes at CT or PET scan, centrally-located or larger than 3 cm tumors (4).

However, several issues concerning mediastinal staging are still a matter for discussion. The first point concerns the cost-effectiveness of the different staging approaches, which should be assessed not only in terms of accuracy and costs for the healthcare system, but more broadly analyzing the impact of the procedures on patients' quality of life, gained life years, reduction of unnecessary surgical procedures and impact on the time delay before an appropriate treatment of the tumor can be initiated. Factors that may influence the cost-effectiveness of the staging process include issues related to tumor characteristics as prevalence of mediastinal nodal disease and specific issues of the staging procedures as operator expertise and adherence to mediastinal staging guidelines (5). Furthermore, in the seek for better diagnostic results and improved cost-effectiveness, different combinations of non-invasive, endoscopic and surgical staging techniques have been proposed and are still being evaluated. EBUS-TBNA is the pivotal technique in invasive mediastinal staging, but allows only a partial assessment of the mediastinum, and therefore EUS, originally developed for the evaluation of gastroenteric tumors, may play a complementary role, improving the exploration of mediastinal nodal stations (6). However, a combined ultrasound (CUS) approach has still not gained widespread acceptance due to higher costs and the need of specific expertise with both techniques, but certainly requires further analysis. Moreover, despite the continuous technological improvement of endoscopic instrumentation, optimal sensitivity and negative predictive values have not been reached yet, and surgical confirmation with videomediastinoscopy may still be indicated to rule out false negative results after endoscopic evaluation in patients at high risk of mediastinal involvement (7).

The development of endoscopic instrumentation is an ongoing process, and the introduction of smaller scopes and new biopsy tools could improve the sensitivity of the procedures, extending nodal assessment from the mediastinum to intrapulmonary nodal stations (8). This issue could be essential in the development of new therapeutic strategies such as induction treatments in early-stage non-small cell lung cancer or parenchyma sparing procedures as segmentectomy (9,10). Other issues that may significantly add to the present results of endoscopic staging concern non-invasive techniques as elastography and doppler pattern analysis, that may further improve the efficacy of endoscopic staging, providing an alternative approach to tissue sampling and improving biopsy accuracy allowing a targeted tissue assessment, with potential advantages on the costs and risks of the procedures (11).

Other factors that may influence the results of endoscopic staging include the type of anesthesia used during the procedure and the setting where staging is performed. General anesthesia could potentially improve patient comfort and allow a better assessment of the mediastinum by reducing airway movements during the procedure. However, it may be associated with higher costs and anesthesiological risks, and therefore moderate and deep sedation are used as an alternative to general anesthesia (12). The impact of different anesthesiological techniques on staging accuracy and cost-benefit ratio is therefore an issue that requires further analysis.

Pathological assessment also has a major impact on the diagnostic yield of mediastinal staging. Factors as the availability of rapid on-site evaluation (ROSE), and different techniques used to collect and analyze cytological and histological samples may significantly influence the results of mediastinal nodal staging (13). This taking into due consideration the role of mediastinal tissue sampling not only in lung cancer staging but also in mutation analysis, a main issue in the era of immunotherapy and

gene-targeted therapy (14). The role of endoscopy is also crucial in lung cancer re-staging following induction treatment or after tumor recurrence, considering the limits and risks of re-do mediastinoscopy, and is certainly an interesting topic to be discussed.

Endoscopic mediastinal staging is mainly performed by specialists in interventional pulmonology or gastroenterology, and less frequently by thoracic surgeons. However, since surgery has a main role in the treatment of early-stage and locally-advanced tumors, the field in which endoscopic mediastinal staging is crucial, a multidisciplinary point-of view of surgeons and interventional pulmonology or gastroenterology specialists concerning the present role and indications of endoscopic staging is certainly useful to reach a consensus on the topic.

The aim of the focused series is to give a thorough and up-to-date view of mediastinal staging in patients with lung cancer, discussing the present and future role of endoscopic techniques. Thanks to the continuous technological development and considering the growth of new therapeutic strategies, minimally-invasive endoscopic techniques will certainly play a growing role in the diagnosis and treatment of lung cancer.

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Angelo Carretta

Angelo Carretta

Department of Thoracic Surgery, San Raffaele Hospital; School of Medicine, Vita-salute San Raffaele University, Via Olgettina, 60-20132 Milan, Italy. (Email: angelo.carretta@bsr.it)

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