I read with interest the article titled ‘Sentinel node sampling limits lymphadenectomy in stage I non-small cell lung cancer’ [1]. I want to thank the authors for their great efforts in introducing such good work but I have some comments.

Positron emission tomography (PET) has recently become an important noninvasive tool in mediastinal staging for NSCLC, with reported sensitivity of 61—88% and specificity of 77—96% [2]. I want to ask the authors why they did not use preoperative PET or mediastinoscopy for help in identifying the possible locations for malignant lymph nodes.

In the first study [1] there are cases with N2 showed negative NSN especially in the right upper lobe and left lower lobe that should have been better taken into consideration in the second study.

A variable number of patients who undergo resection of lung tumors with mediastinal lymph nodes have no metastatic involvement of either the hilar or lobar nodes. Such metastatic mediastinal disease is referred to as skip metastases.

Watanabe et al. [3] reported a higher frequency of metastatic involvement of lower, inferior, mediastinal lymph nodes in patients with right upper lobe lesions. They found that subcarinal lymph nodes were the only affected lymph nodes in 11% of those patients with right upper lobe primary lesions.

The lung cancer study group by Thomas et al. reported that the subcarinal lymph nodes should be evaluated in all patients regardless of the primary site of the tumor [4].

The size, site, and pathology of the primary tumor and their relation to mediastinal nodal affection was not mentioned in this study despite its high importance for anticipating nodal affection. Asamura et al. [5] found that the prevalence of mediastinal metastases increases with tumor size. Also, they have found that among patients with resected peripheral NSCLC, the prevalence of lymph node metastases increased from 19.5% in tumors 2.0 cm or smaller to 32.5% in tumors 2—3.0 cm in diameter [5].

References


Reply to the Letter to the Editor

Reply to Ismail

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Keywords: Lung cancer; Diagnosis and staging; Lung cancer surgery; Lymph nodes; Mediastinal lymph nodes

I thank Dr Ismail sincerely for his interest and the comments regarding our paper [1]. I respect his extensive knowledge about the lymph node metastasis of primary lung cancer.

Is his opinion, as current reports suggest, the positron emission tomography (PET) scan is more accurate than CT in detecting mediastinal LN metastases? However, some authors reported that PET and helical CT perform similarly in the mediastinal staging of non-small cell lung cancer (NSCLC) [2], and the staging by PET still has some limitations which include inflammatory condition, the size of mediastinal lymph nodes, mislocalization of the hot nodes, and others [3,4]. We performed the presurgical staging by CT findings only in the first study [5], because our hypotheses were led from our preliminary study which determined the clinical staging by CT. PET scan has not yet become popular in Japan and unfortunately, our institution did not have the PET system in this study period.

We need to pay serious attention to the existence of skip metastases if we undergo selective lymphadenectomy for the patients with lung cancer. In the six patients with skip metastases in our first study, however, macroscopic pleural invasion was correlated with mediastinal LN metastasis rather than the tumor size. We think that the skip metastasis might be caused by the lymph flow from tumors with pleural invasion through the thoracic cavity to the mediastinum and induces LN involvement through the direct lymphatic pathway. We believe that the skip metastasis cases in the mediastinum can be identified by excluding the patients with tumors invading the pleura or with positive lavage cytology.

References


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Inflammation and thoracic surgery: a complex interaction

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Keywords: Inflammation; COPD; Apoptosis; C-reactive protein; Lung cancer

We appreciated the reading of the work of Amar et al. [1]. The authors reported data suggesting that markers of inflammation such as C-reactive protein (CRP) and IL-6 can help to classify patients who are at high risk for major postoperative complications (PC) following thoracic surgery. Systemic inflammation is thus considered to be important in the pathogenesis of important PC. Defining the precise inflammatory response represents a sensitive issue, frequently debated within scientific community. Plasma levels of cytokines or CRP are probably not sufficient to determine whether a patient or experimental animal is hyper-inflammatory or hypo-inflammatory. If only the pro-inflammatory mediators are measured, then the patient will appear hyper-inflammatory. Conversely, if only cytokine antagonists or anti-inflammatory mediators are measured, the subject appears to be hypo-inflammatory. Indeed, both pro- and anti-inflammatory mediators may be circulating at the same time in the plasma [2]. Better methods for determining the precise immunological status may be achieved via either a multiplex format for cytokine measurements or an evaluation of cellular function. Many cellular aspects become dysfunctional in inflammation, for example in chronic obstructive pulmonary disease (COPD), and may be characterized as either excessive activation or depressed function. Excessive activation refers to cells that are primed so that they respond in a very vigorous manner to a second stimulus (for example, neutrophils generating excess toxic products that cause damage to nearby cells [3]). Conversely, an example of depressed function would be neutrophils’ failure to phagocytize any clearly invading pathogens. One of the current areas of active investigation concerning cellular function is the induction of cellular apoptosis or necrosis. The signalling mechanisms and molecules that induce apoptosis are currently being described in great detail by several investigators. The pathobiology of COPD (a disease that can be considered a model of pulmonary inflammation) encompasses multiple injurious processes including inflammation (excessive or inappropriate innate and adaptive immunity), cellular apoptosis, altered cellular and molecular alveolar maintenance program, abnormal cell repair, extracellular matrix destruction (protease and anti-protease imbalance), and oxidative stress (oxidant and antioxidant imbalance) [4]. Apoptosis may contribute to the pathogenesis of sepsis by the delayed removal of those cells that should be removed, i.e., neutrophils, and early removal of those cells that should not be removed, i.e., lymphocytes. Activated protein C has emerged as a novel therapeutic agent for use in selected patients with severe sepsis, even though the mechanism of its benefit is not well established. It has anticoagulant, anti-inflammatory, antiprotic, and pro-fibrinolytic properties, but it is not clear through which of these mechanisms APC exerts its benefit in severe sepsis. Focus has recently turned to the role of APC in maintaining endothelial barrier function, and in vitro and in vivo studies have examined this relationship [5].

In conclusion, CRP and IL-6 alterations are extremely non-specific, and an accurate diagnostic test for sepsis would be a welcome addition in the management of specific patients undergoing thoracic surgery, whereas the condition supporting the surgical indication could easily be correlated with a previous pulmonary inflammation, i.e., lung cancer arising in COPD patients.

References


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Reply to the Letter to the Editor

Reply to Paleari et al.

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