Could tumor location-specific lymph node dissection be a tailored approach?

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Provenance: This is an invited Editorial commissioned by Section Editor Dr. Gang Shen, MMSC (The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China).

Comment on: Eckardt J, Jakobsen E, Licht PB. Subcarinal Lymph Nodes Should be Dissected in All Lobectomies for Non-Small Cell Lung Cancer-Regardless of Primary Tumor Location. Ann Thorac Surg 2017;103:1121-5.

Submitted Jun 09, 2017. Accepted for publication Jun 12, 2017. doi: 10.21037/jtd.2017.06.76 View this article at: http://dx.doi.org/10.21037/jtd.2017.06.76

With the advent of personalized medicine, the concept of exploiting patient's tumor characteristics to make therapeutic decisions has revolutionized the landscape for lung cancer treatment. In the same way, advances in the early detection of small lung cancers by high resolution computed tomography (CT) and subsequent accumulated findings that patients with small peripheral lung cancer with pure or predominantly ground-glass opacities (GGO) in CT images or lower (or negative) 18F-fluorodeoxyglucose-positron emission tomography uptake have favorable outcomes without any lymph node metastasis, have led to incremental change on treatment planning, follow-up methods, and operations towards "individualized surgery" (1,2). Likewise, the concept of lobe-specific lymph node dissection for lung cancer can be a customized surgical option on a patient-by-patient basis. Several retrospective studies suggest that lobe-specific lymph node dissection could be applied for some cases, especially some upper-lobe cancers in which subcarinal lymph node dissection could be spared because of a low incidence of subcarinal metastases, particularly in T1 tumors (3-7).

This study of the article by Eckardt and colleagues in this issue of Annals of Thoracic Surgery is a Danish national lung cancer registry-based study in which they negated the idea of those lobe-specific lymph node dissections head-on, and claimed that subcarinal lymph nodes should be dissected routinely regardless of preoperative invasive mediastinal staging and tumor location (8).

The points of their views are supported by the result that the unsuspected mediastinal involvement (cN0/1-pN2)

occurred in 11% of their patients after lobectomy for non-small cell lung cancer (NSCLC) even though 73.4% underwent preoperative invasive mediastinal staging. The main rationale behind their assertions is also backed up by the two key studies in which the mediastinal lymph node recurrences were higher in patients in the lobe-specific lymph node dissection group compared to those in the systemic dissection group (9), and N2 disease did not follow a predictable lobe-specific lymphatic drainage pattern (10). Although the complete detection of unexpected N2 disease preoperatively is unavoidable, complete systemic lymph node dissection for every case can allow for reduced risk of understaging, leading to less staging migration and more chance to give optimal treatments. I believe that the great strength of this study lies in its quality based on a large sample size and the relatively high frequency of patients who underwent preoperative invasive mediastinal staging. However, presumably there are several pieces of clinical information in this study that have to be considered in order to clarify this provocative and crucial issue.

First, the authors provide the number of unexpected N2, subcarinal lymph node involvement, and isolated subcarinal lymph node metastasis, histology, and T factor depending on tumor locations while they lack information of hilar lymph node status (and other N1 lymph node status) on lymphatic drainage pathways. Second, there is a total lack of information of survival and recurrence outcomes. Those can probably contribute to better understanding of prognostic significance of lymph node metastasis patterns. Third, left upper division

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and lingual division have to be considered separately because lymphatic drainage route of both divisions is reported to be dissimilar. Finally there is still a low incidence of unexpected subcarinal lymph node involvement that was found in bilateral upper lobe cancers in this study compared to that of patient with middle lobe and bilateral lower lobe tumors, which is more or less the similar number of occurrence as the past reports that were for the lobe-specific approach.

It is undisputed that complete systemic lymph node dissection provides patients with the most accurate staging and the opportunity for more adequate treatment plan, and all the patients who need to undergo lobectomy should be subjected to subcarinal lymph node dissection. However, there should be various behavioural lymphatic drainage patterns depending on tumor location even though there are many exceptions. What if all the patients with less than 2 cm and GGO-predominant adenocarcinoma originated from right upper lobe would have to undergo subcarinal lymph node dissection? Although we still have missed specific prospective studies to demonstrate that lobe-specific lymph node dissection would be feasible and rather preferable, could radical lymph node dissection for those GGO cases be also too much? In addition, the oncological benefit of lymphadenectomy remains unclear. Obviously, lobectomy with systemic nodal dissection has been a benchmark for early stage lung cancer since Cahan introduced the concept of systemic lymph node dissection (11). I therefore agree in part that subcarinal lymph nodes should be dissected routinely for every NSCLC regardless of tumor location while I am convinced that lobe-specific lymph node dissection would be one type of individualized surgical approaches amenable to certain types of patient with NSCLC.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Shimada Y, Ikeda N. Could tumor location-specific lymph node dissection be a tailored approach? J Thorac Dis 2017;9(7):1806-1807. doi: 10.21037/jtd.2017.06.76