Intraoperative Nodal Staging
Role of Sentinel Node Technology

Shinichiro Miyoshi, MD, PhD

KEYWORDS

• Lung cancer • Lymphadenectomy • Sentinel lymph node • Tracer • Radioisotope

KEY POINTS

- Definition of sentinel lymph node (SLN): an SLN is defined as the first lymph node or group of lymph nodes encountered in lymphatic drainage from a primary tumor.
- Intraoperative SLN biopsy (SLNB) navigation: when metastasis is not found in the SLN, it is most likely not present in more distal lymph nodes. Therefore, an additional lymphadenectomy is considered to be unnecessary.
- Indication: SLNB should be performed for patients with clinical node-negative non–small cell lung cancer (NSCLC) to pathologically determine the presence of SLN metastasis.
- Tracer: although many tracers such as dyes, radioisotopes, magnetite, and iopamidol have been investigated, no appropriate agent that produces high identification and accuracy results has been developed for lung cancer.
- Lobe-specific selective lymph node dissection: a lobe-specific selective lymphadenectomy based on biopsy results of predetermined selective lymph node stations might be considered as an alternative to an SLN lymphadenectomy for early-stage NSCLC.

INTRODUCTION

Lymph node status is a major determinant of stage and survival in patients with non–small cell lung cancer (NSCLC). Although computed tomography (CT) or fluoro-2-deoxy-D-glucose (FDG)-positron emission tomography (PET) scanning have been preoperatively used for diagnosing lymph node status, their sensitivity and specificity are not satisfactory (51% and 85%, 74% and 85%, respectively).[1] A combination of node size and metabolic characteristics shown by FDG-PET/CT has improved the accuracy of staging by showing better anatomic localization of FDG hotspots. However, for most cases, FDG-PET/CT does not eliminate the need for invasive testing.[2] Although mediastinoscopy[3] and recently introduced endobronchial ultrasonography transbronchial needle aspiration techniques[4] are reliable for pathologic diagnosis of lymph node status, neither procedure has the ability to detect all lymph node stations. Lymph node dissection (removal of all ipsilateral lymph node-bearing tissues) is the best method to accurately determine pathologic lymph node status. Thus, a lobectomy with a hilar and mediastinal lymphadenectomy is considered to be the gold standard of surgical care for patients with resectable NSCLC.[5,6]

Recently, sublobar resection, including partial resection and a segmentectomy, has been introduced in association with an increase in number of patients with early-stage lung cancer.[7] The possibility to reduce the extent of the lymphadenectomy procedure has been indicated for patients without metastasis to lymph nodes.[8–13] The question remaining is how to reduce the extent of lymph node dissection without leaving metastatic lymph nodes behind.

Department of General Thoracic Surgery and Breast and Endocrinological Surgery (Surgery II), Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-Cho, Kita-ku, Okayama 700-8558, Japan
E-mail address: smiyoshi@md.okayama-u.ac.jp

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For this purpose, a sentinel lymph node (SLN) mapping technique was first introduced for penile carcinoma by Cabanas in 1977,[14] and those concepts have since been more widely applied to melanoma and breast cancer cases.[15,16] The role of sentinel node technology has become established for such superficial malignancies.[17,18]

Little and colleagues[19] first applied an SLN mapping technique for patients undergoing lung resection for NSCLC. Since then, many studies have been performed by lung cancer surgery investigators, which are critically reviewed in this article. As an alternative to SLN biopsy (SLNB), biopsy of lobe-specific selective lymph node stations is also discussed.

HISTORICAL NOTES

Regional node dissection is an accepted part of surgical treatment of many solid tumors. It was first applied to breast cancer in 1894 by Halsted and then later extended to other malignancies, including head and neck cancers, gastrointestinal neoplasms, and melanoma. Lung cancer surgery was started with a successful pneumonectomy by Graham in 1933, and Churchill and colleagues[20] were the first to suggest that a less radical operation such as a lobectomy may be adequate for surgical treatment of lung cancer. Since Cahan's report in 1960,[21] a lobectomy has been used as the standard surgical procedure for lung cancer, in which the extent of mediastinal lymph node dissection (MLND) is determined specific to each lobe with a primary tumor, with the procedure termed a radical lobectomy. However, the magnitude of the operation and the fact that NSCLC recurs in distant sites have reduced the popularity of MLND in Europe and the United States. On the other hand, systematic hilar and mediastinal lymphadenectomy procedures have been widely performed in Japan since Naruke and colleagues[22] created a lymph node map and reported the significance of MLND for lung cancer surgery in 1978.

Cabanas first described the SLNB concept for penile cancer in 1977.[14] However, that method was later found to be unreliable, because the false-negative rate was unacceptably high and the technique difficult to perform.[23] On the other hand, the concept was later adopted for nodal assessment of melanoma and breast cancer,[15,16] and the role of sentinel node technology has now become established for such superficial malignancies.[17,18]

In association with an increase in number of patients with early-stage lung cancer,[7] lung cancer surgical specialists who routinely perform MLND in their patients have generally come to the position that MLND is excessive for patients with N0 disease. On the other hand, surgeons who did not perform MLND for all of their patients have presented it as acceptable for patients with lymph node metastasis, who should benefit from the technique. Thus, the SLN mapping technique was first applied to patients undergoing lung resection for NSCLC by Little and colleagues.[19]

DEFINITION OF SLN AND ITS BENEFITS

The SLN is defined as the first lymph node or group of lymph nodes encountered in lymphatic drainage from a primary tumor.[14] An SLN mapping technique can identify lymphatic drainage path from the site of the primary tumor to the individual lymph nodes within the lymphatic basin and indicate which nodes are most likely to contain metastatic cancer cells. Intraoperative mapping permits selective identification, removal, and intraoperative evaluation by frozen section analysis of SLNs, allowing accurate pathologic staging during the operation. When metastasis is not found in SLNs, it most likely is not present in more distal lymph nodes. Thus, by using a minor procedure, surgeons can identify patients with metastatic nodal disease who would most likely benefit from a standard lymphadenectomy and in those who do not have nodal metastases, thus improving morbidity related to radical lymphadenectomy. An additional benefit of SLN detection is application of more sensitive pathologic detection techniques to specified nodes. In addition, immunohistochemistry (IHC) and reverse transcription-polymerase chain reaction techniques have increased the accuracy of detection of micrometastasis.[24,25]

INDICATIONS

An SLNB should be performed in most patients with clinical node-negative NSCLC, especially clinical T1N0M0 (c-T1N0M0). Thoracic surgeons who have been routinely performing radical lymphadenectomy including hilar and mediastinal lymph nodes for all patients with resectable NSCLC are searching for a reliable method to reduce the extent of lymphadenectomy for such patients with early-stage NSCLC without leaving metastatic lymph nodes behind, in the hope of avoiding lymphadenectomy-related complications in patients who do not need that radical procedure. On the other hand, thoracic surgeons who do not routinely perform lymphadenectomy for all patients would like to select patients with radiologically occult N1 or N2 disease during surgery,