

# Lymph Node Dissection and Pulmonary Metastasectomy



Smita Sihag, MD, Ashok Muniappan, MD\*

## KEYWORDS

• Lymph node • Lung • Metastasectomy

## KEY POINTS

- Intrathoracic lymph node involvement is associated with decreased survival after pulmonary metastasectomy. The data are most convincing for colorectal and renal cell cancers.
- The number of lymph nodes involved may have greater prognostic value than lymph node station involved. There is no clear survival difference between patients with N1 versus N2 nodal disease.
- Risk factors for intrathoracic lymph node metastases include enlarged or hypermetabolic nodes, large solitary metastases requiring anatomic resection, and multiple metastatic lesions. Mediastinal lymph node assessment should be considered in these patients, especially if findings may lead to further adjuvant therapy.
- There is limited evidence as to whether mediastinal lymphadenectomy leads to improved survival in patients undergoing pulmonary metastasectomy.
- The level of evidence to support any recommendations is low because the literature available for review is exclusively retrospective.

## INTRODUCTION

According to the landmark report of the International Registry of Lung Metastases (IRLM), which included 5206 patients, the overall survival after pulmonary metastasectomy is 36% at 5 years, 26% at 10 years, and 22% at 15 years.<sup>1</sup> Given these encouraging findings and generally limited potential for long-term survival with standard systemic therapy for isolated pulmonary metastases, metastasectomy is considered whenever possible. The primary variables affecting survival after metastasectomy are derived from the IRLM and other single-center retrospective studies, and to date, there have been no randomized trials evaluating the effect of pulmonary metastasectomy on survival. The registry revealed that patients with germ cell tumors have the

highest 5-year survival rate at 68%, whereas those with melanoma have the lowest at 21%. Fewer metastases, complete resection, and longer disease-free interval before pulmonary metastasis are all associated with improved survival in patients undergoing metastasectomy. The registry, however, does not offer insight on the impact and relevance of mediastinal or hilar lymph node involvement. Metastasis to mediastinal or hilar lymph nodes was identified in 5% of patients (11% of germ cell tumors, 8% of melanomas, 6% of epithelial tumors, and 2% of sarcomas). Mediastinal lymph node sampling was performed at the discretion of the surgeon and was not routine. Although no survival difference was found with respect to presence or absence of nodal disease in the registry, incomplete resection was

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Department of Thoracic Surgery, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, Blake 1570, Boston, MA 02114, USA

\* Corresponding author.

E-mail address: [amuniappan@partners.org](mailto:amuniappan@partners.org)

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more likely in patients with positive nodes (27% vs 11%). The prognostic relevance of N1 and N2 nodal disease in the setting of pulmonary metastases has remained a topic of investigation in several subsequent studies.

Systematic mediastinal lymphadenectomy or sampling is routinely performed in the setting of primary neoplasms of the lung, including adenocarcinoma, squamous cell carcinoma (SCC), and neuroendocrine tumors. Controversy exists, however, surrounding the need for mediastinal lymph node assessment at pulmonary metastasectomy. Based on a survey of 146 surgeons from the European Society of Thoracic Surgeons, 55% indicated that they regularly sample mediastinal lymph nodes at the time of metastasectomy, whereas 33% avoided nodal dissection.<sup>2</sup> Although approximately 65% of surgeons considered mediastinal nodal metastasis to be an absolute contraindication, only 4% of surgeons regularly performed mediastinoscopy prior to metastasectomy. This article reviews the evidence for prognostic significance of intrathoracic lymph node status by origin of primary tumor. The identification of positive mediastinal lymph nodes may guide further management of metastatic disease to the lung in terms of adjuvant systemic therapy, timing of administration, and extent of pulmonary resection.

### **INTRATHORACIC LYMPH NODE INVOLVEMENT AND ISOLATED PULMONARY METASTASIS BY PRIMARY TUMOR HISTOLOGY**

#### ***Colorectal Carcinoma***

Approximately half of all patients with colorectal cancer develop metastatic disease at some point in the course of their disease. Increasingly, patients undergo pulmonary and hepatic metastasectomy, the primary sites of metastasis.<sup>3</sup> Patients with untreated stage IV disease have a median survival of only 8 months, whereas treatment with 5-fluorouracil-based chemotherapy prolongs median survival to 24 to 28 months.<sup>4</sup> In contrast, patients who undergo complete resection of pulmonary metastases of colorectal cancer have a 5-year survival of up to 60%.<sup>5</sup> Prognostic factors that have been found to affect survival include carcinoembryonic antigen level, disease-free interval before development of metastases, number of metastases, and the completeness of resection of all metastatic disease.

The incidence of intrathoracic lymph node metastases at the time of pulmonary metastasectomy for colorectal cancer is reported to be in the range of 12% to 44%.<sup>3,6</sup> The variability in the reported

incidence of nodal involvement is related to heterogeneity in the burden of metastatic disease as well as inconsistent sampling or dissection of intrathoracic nodes. Intrathoracic lymph node metastasis in colorectal cancer is associated with decreased survival in numerous reports. In a retrospective study from the Mayo Clinic of 518 patients, of whom 319 underwent lymph node assessment, mediastinal lymph node involvement was identified in 40 patients (13%).<sup>6</sup> Of these 40 patients, 9 (23%) had N1 disease, and 31 (77%) had N2 disease. In this study, only lymph node size greater than 1 cm and fludeoxyglucose F 18 (FDG) avidity predicted the presence of lymph node metastases, whereas size, number, and location of pulmonary metastases did not. Furthermore, there was no correlation between location of the metastatic lesion and the lymph node station involved. Five-year survival was 48% in the negative lymph node group and 21% in the positive lymph node group. Although mediastinal lymph node involvement was a significant predictor of inferior survival in this study, long-term survival was possible in a few patients with N2-positive nodes.

Several studies suggest that the 5-year survival rate is approximately halved if intrathoracic lymph node involvement is identified in colorectal metastasis. In a retrospective analysis of 169 patients from Germany who underwent colorectal metastasectomy, 17% were found to have metastases to intrathoracic lymph nodes.<sup>5</sup> Lymph node sampling or regional lymphadenectomy were only performed, however, if lymph nodes appeared abnormal at intraoperative assessment. Five-year survival with positive lymph nodes was 19% as opposed to 42% in patients without nodal metastasis. There were no patients who survived 5 years in the presence of N2 or mediastinal metastasis. Another single-center retrospective report from France similarly observed diminished long-term survival in the setting of positive mediastinal lymph nodes, although they reported that 39% of patients with N1 or N2 metastases survived 5 years.<sup>7</sup> In a larger retrospective study of 320 patients at another French center, where routine lymphadenectomy was performed at the time of metastasectomy, 44% had positive intrathoracic lymph nodes.<sup>3</sup> Of these 140 patients, 91 (65%) had N1 disease, and 49 (35%) had N2 disease. Lymph node involvement was more likely in patients with multiple pulmonary metastases. Median length of survival in patients with positive lymph nodes was half that of patients without nodal metastases (42 months vs 94 months) but was still longer than expected for patients receiving systemic therapy alone for metastatic colorectal

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