

# Lymphadenectomy During Pulmonary Metastasectomy



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## KEYWORDS

• Lung metastasis • Metastasectomy • Lymphadenectomy

## KEY POINTS

- Pulmonary metastasectomy improves survival in selected patients.
- The role of involvement of hilar and mediastinal lymph nodes remains poorly understood.
- This article summarizes the incidence and prognostic implications of thoracic lymph node metastases in the setting of pulmonary metastasectomy.

## INTRODUCTION

The primary cause of death of patients with cancer is generally metastatic disease. Frequently, the lung is a site of metastatic disease and often portends widespread, systemic disease. The first pulmonary metastasectomy was reported in 1882.<sup>1</sup> Since this report, hundreds of articles have been published regarding the results of pulmonary metastasectomy. Despite a paucity of randomized clinical trial data, it is now generally accepted that overall survival for many tumor types is improved with resection of limited metastases in carefully selected patients.<sup>2</sup>

Despite improvements in disease-free and overall survival with pulmonary metastasectomy, few patients are effectively cured of their disease with this approach. Prognostic factors for patients undergoing pulmonary metastasectomy include cell type, time interval between primary tumor resection and identification of pulmonary metastases, number of pulmonary metastases, metastases to other sites, and the ability to completely resect all metastatic disease.

Only recently has there been significant attention given to the status and evaluation of lymph

node metastases during pulmonary metastasectomy. Most surgical oncologists would agree that patients with bulky nodal metastases to the mediastinum are unlikely to benefit from surgical resection, and hence are not candidates for metastasectomy; this article analyzes only studies evaluating patients with minimal nodal disease burden or radiologically negative mediastinal nodes. This article focuses its discussion on the incidence of lymph node involvement, the impact on survival along with therapeutic implications, and recommendations regarding the management of these patients.

## INCIDENCE

Pastorino and colleagues<sup>2</sup> validated the concept of pulmonary metastasectomy with the International Registry of Lung Metastasectomy published in 1997. Patients undergoing complete resection of all metastases were found to have an overall 5-year survival of 36% at 5 years, 26% at 10 years, and 22% at 15 years. However, the issue of mediastinal lymph node involvement by metastases was not addressed. The registry reported only a 5% incidence of lymph node metastases;

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however, in this large database, only 4.6% of patients had lymph nodes resected or sampled. Therefore, this is not a representative statistical sample and likely largely underestimates the true incidence of lymph node metastases. Earlier reports suggested widely varying incidence of lymph node involvement for patients considered for pulmonary metastasectomy, ranging from 9.8% to 50%.<sup>3,4</sup> This wide variability is not unexpected given the time period, with chest radiograph being the main imaging modality available to identify a pulmonary metastasis.

In a Mayo Clinic pulmonary metastasectomy series, 70 patients had complete mediastinal lymphadenectomy with an incidence of lymph node metastases of 28.6% (20/70).<sup>5</sup> This included N1 level nodes in 9 patients (13%) N2 nodes in 8 patients (11%), and both in 3 patients (4%). A more recent Mayo Clinic report evaluated lymph node dissection in patients undergoing pulmonary metastasectomy for colorectal adenocarcinoma. From over 500 patients undergoing pulmonary metastasectomy, 319 patients underwent lymph node dissection, which revealed the incidence of positive lymph nodes to be 12.5% (40/319).<sup>6</sup>

Seebacher and colleagues<sup>7</sup> recently published their retrospective experience with lymph node evaluation in resections for pulmonary metastases. They found an incidence of 17% in all patients, with similar rates of involvement with radical lymphadenectomy 15.8% and sampling 18.8%. They found an incidence of 35.5% in patients with breast cancer (17 patients), 9.2% for colorectal cancer, and 20.8% in renal cell carcinoma.

**Table 1** collates the list of the major papers to date illustrating the range of reported incidence of lymph node metastases at the time of pulmonary metastasectomy. The European Society of Thoracic Surgeons metastasectomy supplement combined 5 previous studies to come to a weighted average incidence of lymph node metastases of 22%.<sup>8</sup>

The role of thoracic lymph node dissection in pulmonary metastasectomy has been studied in a variety of patients with epithelial cancers, sarcomas, germ cell tumors, renal cancers, and melanoma. Some have argued that given sarcoma's low propensity for lymphatic metastases, the incidence of thoracic lymph node metastases with pulmonary metastasectomy should be low or nonexistent. This, however, has been refuted by multiple studies, and it is now known that sarcoma metastases to the lungs have a higher incidence of associated lymph node metastases than suspected. In Pfannschmidt's series of 70 patients with different types of sarcomas, 20.3% of patients (16 patients) had nodal metastases.<sup>9</sup>

In the same series, this was less than for colorectal (31.3%) and renal carcinomas (42.4%).

From the retrospective data available, it is clear that metastases to thoracic lymph nodes occur at a higher rate than previously recognized: roughly one in five patients. Several questions arise:

Does sampling versus lymphadenectomy make a difference?

What is the impact of these metastases on survival?

Do these patients still benefit from pulmonary metastasectomy?

What other therapeutic options are available?

Attempts to elicit potential risk factors for lymph node metastases have not been consistently reliable; however, this likely is related to study design and small patient numbers. Bolukbas and colleagues,<sup>10</sup> in their series of 165 patients, found that the number of pulmonary metastases has a nonlinear association with the risk of positive lymph node metastasis. The risk of lymph node metastasis increases 16% with each additional metastasis from 1 to 10; above 10 metastases the risk does not appear to increase further. Seebacher and colleagues also found the number of metastases to be prognostic for metastases to lymph nodes as well as metastasis size in their study of 209 patients with all types of cancers. A metastasis with a diameter of 2 cm or less had an incidence of lymph node involvement of 19.3%, but with a diameter of more than 4 cm, the incidence was 37.1% ( $P = .04$ ). However, other authors have not found the number of metastases to be predictive of lymph node metastasis.<sup>5,6</sup>

## LYMPH NODE SAMPLING VERSUS LYMPHADENECTOMY

Given the surprising incidence of lymph node metastases, a logical question is the appropriate surgical assessment of mediastinal lymph nodes at the time of metastasectomy. The following section will discuss what constitutes lymph node sampling versus dissection, and what data exist comparing the 2 methods.

The definition of a standard mediastinal lymph node sampling is considered as follows: right lung-lymph node stations 2R, 4R, 7, 9R, 10R; left lung-lymph node stations 5, 6, 7, 9L, and 10L. Lymphadenectomy for the right side includes removal of all lymph tissue in the 2R and 4R stations, defined by the takeoff of the right upper lobe bronchus, innominate artery, superior vena cava, and the trachea; removal of all tissue in the subcarinal space (station 7) as well as lymph nodes in the inferior pulmonary ligament and

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