Results of Pulmonary Resection
Sarcoma and Germ Cell Tumors

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KEYWORDS

• Pulmonary metastasis • Lung resection • Sarcoma • Germ cell tumor • Outcomes

KEY POINTS

- Patients with controlled primary disease, absent extrathoracic disease, sufficient pulmonary function, and overall functional capacity with pulmonary metastases that can be completely resected are candidates for pulmonary metastatectomy.
- Patients undergoing pulmonary metastatectomy of osteosarcoma may have a 5-year survival of 35% to 50%; for patients undergoing resection of soft tissue sarcoma metastases it is 35% to 52%.
- Large case series of pulmonary metastatectomy of nonseminomatous germ cell tumor (NSGCT) have reported 5-year survival rates of greater than 80%.
- There are no randomized trials on pulmonary metastatectomy in patients with metastatic sarcoma or NSGCT; Survival rates are from case series.

INTRODUCTION: NATURE OF THE PROBLEM

Pulmonary metastatectomy dates back to the 1880s.[1] Sublobar resections, lobectomy, and pneumonectomy described were subsequently in the setting of metastatic sarcoma, renal cell cancer, and colon cancer.[2,3] Selection criteria for pulmonary metastatectomy were proposed formally in a case series of pulmonary metastatectomies by Alexander and Haight.[4] Since then, with increasing supportive data, pulmonary metastatectomy has become a widely accepted treatment modality for patients with metastatic disease.

As many as 88% of patients with sarcoma were found to have single-site pulmonary metastatic disease in a retrospective study by Huth and Eilber.[5] In a case series from Memorial Sloan-Kettering Cancer Center, Billingsley and colleagues[6] reported that 73% of 230 patients with recurrent soft tissue sarcoma had recurrences that initially appeared in the lungs. Eight percent of patients with clinical stage I nonseminomatous germ cell tumor (NSGCT) develop pulmonary metastases. Additionally, an estimated 10% to 20% of patients with stage III disease who were treated with cisplatin-based chemotherapy have residual intrathoracic disease requiring mediastinal dissection or pulmonary metastatectomy.[7] Pulmonary metastatectomy may be the only therapeutic option to render these patients disease free.

THERAPEUTIC OPTIONS AND SURGICAL TECHNIQUE

After systemic therapy and confirmation of limited disease, therapeutic options for controlled pulmonary metastases include continued systemic chemotherapy, isolated lung perfusion or suffusion, radiofrequency ablation, stereotactic body radiation therapy, and surgical resection. Isolated lung perfusion or suffusion, radiofrequency ablation, and stereotactic body radiation therapy are covered more thoroughly elsewhere in this issue.

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Patients being considered for pulmonary metastatectomy should meet the following criteria: (1) controlled primary site of disease, (2) absence of extrathoracic metastases (or, in cases of oligometastases, extrathoracic sites of metastases are controlled or controllable), (3) sufficient pulmonary reserve to tolerate the proposed pulmonary resection, (4) completely resectable pulmonary metastatic disease with predictably sufficient pulmonary reserve. Preoperative planning should include pulmonary function testing and an evaluation of the patient's ability to tolerate an operation. Special consideration should be taken for patients receiving certain chemotherapeutic agents (bleomycin, mitomycin C, busulfan, cyclophosphamide, carmustine, gefitinib, paclitaxel, and methotrexate). These patients are at risk for drug-induced lung disease, including interstitial pneumonitis and fibrosis, hypersensitivity pneumonitis, and acute pneumonia. Fractional inspired oxygen should be minimized to minimize the risk of oxygen toxicity. Finally, patients should be required to engage in smoking cessation for at least 3 weeks before surgery to decrease the risk of postoperative pneumonia and other complications.

Pulmonary metastatectomy can be achieved via thoracoscopy or thoracotomy for unilateral disease. Patients with bilateral pulmonary metastases can undergo bilateral thoracoscopy/thoracotomy, median sternotomy, or bilateral transternal (clamshell) thoracotomy. Proponents of open resection argue that more pulmonary nodules can be identified with manual palpation.[8–11] The identification of more nodules, however, does not translate to improved survival,[12] and proponents of thoracoscopy argue that patients undergoing thoracotomy experience significantly more complications[11] but no greater ipsilateral resections. The European Society of Thoracic Surgeons working group addressed several key issues to take into consideration in this decision-making process.[12] The European Society of Thoracic Surgeons considers open and thoracoscopic approaches equivalent, advising that surgeons should use their most trusted technique. Additionally, there are no data demonstrating a difference in outcome between an initial policy of bilateral versus unilateral exploration or simultaneous versus a staged approach in patients with known bilateral disease. Results from the European Society of Thoracic Surgeons working group survey suggested that an initial approach via median sternotomy is acceptable. In cases not suitable for median sternotomy—such as posterior lesions or patients with previous pulmonary resection—staged thoracotomy with a 3- to 6-week interval was recommended. Zheng and Fernando[13] recommended a similar approach to pulmonary metastatectomy, except that these authors were more supportive of a thoracoscopic approach.

Ultimately, the main principle of surgical resection of pulmonary metastases is complete resection. When possible, preservation of pulmonary function should be maximized by limiting resection. Peripheral nodules can be treated with a wedge resection. More central nodules may require a segmentectomy or lobectomy. Very rarely, a pneumonectomy may be necessary and appropriate to achieve complete resection.

CLINICAL OUTCOMES

Sarcoma

In a study by the Cooperative Osteosarcoma Study group, 81% of patients with sarcoma presenting with metastatic disease had pulmonary metastases.[14] Sixty-two percent of these patients have metastatic disease in the lungs only. Because sarcoma often does not respond to systemic or radiation therapy, complete resection with a pulmonary metastatectomy may be the only means by which to render a patient with single-site sarcoma metastasis free of disease.

There are few prospective studies and no randomized trials evaluating the role of pulmonary metastatectomy in the management of patients with osteogenic sarcoma. The first significant case series was described by Martini and associates,[15] who describe 22 patients who collectively underwent 59 procedures for the resection of 152 nodules. The authors reported a 3-year survival rate of 45%. Similarly, in subsequent case series, Snyder and colleagues[16] and Putnam and colleagues[17] in their series of 21 and 39 patients, respectively, both reported 5-year survival rates of nearly 40% in patients with osteogenic sarcoma who underwent pulmonary metastatectomy. The presence of 3 or fewer nodules on preoperative imaging was found to be the single most useful preoperative risk factor.

In more recent case series, Kim and colleagues[18] published their results in 97 patients who underwent pulmonary metastatectomy between June 2002 and December 2008. They reported an overall 5-year survival of 50.1% and noted that patients with a disease-free interval less than 12 months ($P = .001$), 2 or more pulmonary metastases ($P = .0007$), a lesion greater than 3 cm in diameter ($P = .017$), and a positive resection margin ($P = .004$) had significantly worse survival. Conversely, histology, tumor grade, and use of chemotherapy were found to have no effect on survival. Another series analyzed the outcomes of 47 patients with osteosarcoma. This study found