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Preoperative Evaluation and Indications for Pulmonary Metastasectomy

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PREOPERATIVE EVALUATION

The purpose of preoperative evaluation of patients referred for pulmonary metastasectomy is twofold.[1–3] The first component focuses on defining the morbidity, risks of surgery, and specific factors in patients that can be addressed to decrease the patient's operative risk. Secondly, the evaluation determines whether the lesions are actually resectable. In assessing the patient's fitness for surgery, it is important to remember that the most common complications after major thoracic surgery include pneumonia, atelectasis, atrial fibrillation, and heart failure.[4] Most patients who undergo pulmonary metastasectomy undergo thoracoscopic wedge resection, but larger resections and the need for thoracotomy are possible. Therefore, it is key to assess the cardiac and pulmonary reserve of a patient being evaluated for pulmonary metastasectomy, especially if a larger or more complex resection is potentially required.

History and Physical Examination

Every preoperative evaluation should begin with a history and physical examination. Although up to 90% of patients with pulmonary metastases will be asymptomatic secondary to the nonobstructing peripheral nature of their disease, the history should start with an assessment of respiratory symptoms. If the patient has respiratory symptoms, then the individual may have endobronchial or pleural involvement, large bulky disease, or a central tumor.[5] Next, the history should determine a patient's functional status. Asking the patient and family about his or her actual daily activities can be enlightening. If it is apparent that the patient's activity level is quite low, then further evaluation of his or her fitness for

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surgery should occur; objective assessments such as a 6-minute walk test or cardiopulmonary exercise testing are often revealing.

During the history, the patient must also be evaluated for symptoms of metastases to other locations (eg, recent fractures, bone pain, new headaches, or other neurologic events or symptoms). A history of pulmonary and cardiac diseases and other comorbidites such as diabetes or renal or liver disease must also be elicted. Medications should be discussed and a perioperative plan made for anticoagulants, immunosuppression, and cardiac medications. Also, social history should be evaluated and screening for substance abuse completed. Current smokers should be required, or at least strongly encouraged, to stop smoking prior to surgery, and they should be provided with smoking cessation resources and education. Alcohol users should also be asked about use, in order to prevent and treat potential withdrawal symptoms. Although it may not be particularly revealing, a physical examination should be performed. A patient with wheezing on examination may have endobronchial disease, or an individual with a pericardial rub have pericardial involvement, for example.

Imaging

Evaluation of the pulmonary lesions typically begins with a chest computed tomography (CT) scan, which has a high detection rate of metastatic pulmonary nodules.[6] McCormack and colleagues[7] have found that despite the use of these high-resolution, thin-section chest CTs that 20% to 25 % of nodules are still not imaged, suggesting that operative manual palpation must be performed. As CT scanning technology evolves, the detection of nodules as small as 1 mm is being achieved, further narrowing the disparity between CT scanning and manual palpation.[6]

Positron emission tomography (PET) scans are frequently performed on patients with epithelial-based primary tumors and melanoma after an abnormality on a CT scan is discovered. The use of these scans in the preoperative evaluation of lung lesions continues to rise. Mayerhoefer and colleagues[8] analyzed the utility of PET in a study of 181 patients with pulmonary metastases. The PET sensitivity was 7.9% for lesions of 4 to 5 mm, 33.3% for lesions 6 to 7 mm, 56.8% for lesions 8 to 9 mm, 63.6% for lesions 10 to 11 mm, and lesions 100% for 12 mm or higher ($P<.0010$); thus the larger the lesion, the more sensitive the PET results.

Bamba and colleagues[9] found that pulmonary metastasis of colorectal cancer can be accurately diagnosed by PET/CT, especially when nodules are larger than 9 mm in greatest dimension. Xi and colleagues[10] performed a meta-analysis and found that fluorodeoxyglucos (FDG) PET/CT was a valuable diagnostic tool for diagnosing lung malignancies in patients with head and neck squamous cell cancer, with a sensitivity of 85% and specificity of 98%. In a series by Fortes and colleagues,[11,12] the sensitivity of PET was evaluated in a series of 83 patients who underwent a pulmonary metastasectomy. In this series, the PET scan was positive in only 67.5% of the malignant nodules (colon, 68.6%; renal cell carcinoma, 71.4%; sarcoma, 44.4%), revealing that PET has its shortcomings. Franzius and colleagues[13] suggest that there is a superiority of spiral CT in the detection of pulmonary metastases from malignant primary bone tumors as compared with FDG-PET. They found spiral CT to have higher sensitivity, specificity, and accuracy than FDG-PET in

detecting pulmonary metastases from malignant primary bone tumors.[14,15] Thus chest, abdomen, and pelvic CT scans are frequently the only imaging used in evaluating patients with a history of sarcoma; however, it is not unreasonable to use PET also.

Mediastinal Staging

Mediastinal and hilar lymph nodes should also be evaluated on the preoperative imaging. Lymph node involvement is an important negative prognostic factor in patients undergoing metastasectomy regardless of histology.[16–18] For that reason, those with mediastinal adenopathy may benefit from surgical staging by mediastinoscopy or endobronchial ultrasound (EBUS) fine needle aspiration (FNA) before pulmonary metastasectomy is performed. Although patients with hilar or mediastinal lymph node involvement have poorer survival than those without, the presence of documented nodal metastasis is not an absolute contraindication for metastasectomy as there are some patients with lymph node involvement who are long-term survivors after metastasectomy.[17]

Pulmonary Function Testing

Pulmonary function testing is an important component to the preoperative evaluation of those who are undergoing an anatomic resection of metastatic lesions. The postoperative diffusion capacity (DLCO) and forced expiratory volume at 1 second (FEV_1) must be determined, as they are important predictors of operative risk, postoperative complications, and even mortality. Although sublobar resection (either wedge resection or segmentectomy) is most often used for patients undergoing metastasectomy, one must consider the potential cumulative parenchymal loss in the setting of multiple lesions. In one study, patients who had at least 3 nonanatomic resections had pulmonary functional losses similar to those undergoing lobectomy.[19] Given this, it is not unreasonable to apply similar standards for baseline pulmonary function for patients in need of metastasectomy as for lung cancer resection. Current guidelines suggest that patients with a predicted postoperative FEV_1 or DLCO between 30% and 60% predicted should have additional risk stratification with an exercise test, such as a shuttle walk test or stair climb, prior to proceeding with surgery. Patients with postoperative predicted FEV_1 or DLCO less than 30% should undergo formal cardiopulmonary exercise testing with measurement of maximal oxygen consumption.[20]

Evaluation of Extrathoracic Metastasis

It is estimated that 75% or more of patients with pulmonary nodules will also have metastases to extrathoracic sites. Only 15% to 25% of patients have lesions confined to the lung and are appropriate candidates for curative resection.[5] For this reason, staging for metastatic disease outside of the lung is performed prior to pulmonary resection, based on the primary tumor. In most patients, CT of the chest and abdomen is performed to exclude liver metastases. For patients with sarcoma, PET scan or bone scan may be performed to assess for the presence of bone metastases.[21] PET scan is also commonly used to assess metastatic disease in patients with epithelial tumors and melanoma. Any patient with pulmonary metastases who presents with neurologic symptoms should undergo brain imaging with either MRI or CT scan with and without contrast to exclude involvement of the central nervous system. Some clinicians routinely obtain brain imaging in patients with

metastatic melanoma, breast cancer, or colon cancer, as each frequently metastasizes to the brain.[22]

Summary

Preoperative evaluation for patients undergoing pulmonary metastasectomy determines whether the patient is fit for surgery. A focused history and physical examination are the cornerstones of this component of the evaluation, and the use of cardiopulmonary testing can be vital for those with low activity or poor pulmonary function. The preoperative evaluation also determines whether the lesions are completely resectable. One should seriously consider the risks and benefits to debulking if the lesions are not completely resectable. CT and PET assess the parenchymal, lymph node, and extrathoracic involvement. Surgical staging may also be required before metastasectomy if there is suspicion of mediastinal adenopathy on imaging. If anatomic resections are planned, then evaluation must include pulmonary function testing also.

INDICATIONS FOR METASTASECTOMY

The purpose of pulmonary metastasectomy is predominantly for curative intent, but a diagnostic wedge may be performed simply for tissue diagnosis or for evaluation of residual disease after other therapy as well.[5] Here the focus is on describing the indications of pulmonary metastasectomy performed for curative intent.

The criteria for pulmonary metastasectomy were orignially described 6 decades ago:

1. Candidates should be of appropriate risk for surgical intervention.
2. The primary malignancy must to be controllable
3. There should not be evidence of metastatic disease in any other part of the body.
4. Imaging should show only metastases to one lung.[23–27]

The criteria adopted today are still similar to those of Ehrenhaft and Thomford; although with anesthetic, surgical, radiologic and critical care advances, some of the criteria have been expanded. Today the criteria include

1. The primary malignancy must be controlled or controllable.
2. There is no extrathoracic metastasis that is not controlled or controllable.
3. All of the tumor must be resectable, with adequate remaining pulmonary reserve.
4. There are no alternative medical treatment options with lower morbidity.

Each of these criteria must be met before offering surgery and will be discussed separately.

Primary Malignancy Must be Controlled or Controllable

When a patient is found to have pulmonary metastases, it is imperative that his or her site of primary malignancy is thoroughly evaluated. Patients will not obtain a survival benefit from

metastesectomy if their primary tumor is not controlled. Whether the metastasis is discovered metachronously or synchronously, the primary site must be investigated to determine whether the tumor or local recurrence is controllable. If the primary site is still present when metastases are discovered, resection of the primary should be achieved prior to metastasectomy. However, in this situation, a trial of systemic therapy followed by reassessment of the disease burden, rather than serial resection of the primary site and metastatic disease, should be strongly considered. Patients with colon cancer will need to undergo colonoscopy and abdominal/pelvic CT once a metastasis is noted. Patients with current or a history of breast cancer should undergo mammography. Head and neck cancer patients benefit from examination under anesthesia with endoscopy and contrasted neck CT, while those with a history of renal cancer frequently undergo a contrasted abdominal CT scan or MRI for better evaluation of the primary tumor. Melanoma patients should have a full skin evaluation by a dermatologist, and sarcoma patients should have CT, MRI, and/or bone scan performed to evaluate their site of primary malignancy. Patients with germ cell tumors should undergo blood work analysis of β-HCG, α-fetoprotein, and lactate dehydrogenase (LDH) as well as evaluation of the testes with ultrasound as necessary. If evaluation determines that a primary tumor is unresectable, then pulmonary metastesectomy should generally not be pursued.

Extrathoracic Metastasis Must be Controlled or Controllable

In almost all cases, extrathoracic metastases are a contraindication for pulmonary metastasectomy performed for curative intent; therefore the presence of metastatic disease outside the lungs excludes the patient from surgery. The exception to this rule is for patients with limited, resectable hepatic metastases from colon cancer in the setting of pulmonary metastases. There has been no reported difference in outcome in patients with and without history of previously resected hepatic metastases at the time of pulmonary resection, and thus many perform pulmonary metastasectomy even in patients who have undergone hepatic resectionfor colorectal metastases at an earlier stage.[18,28] Patients who undergo combination hepatic and pulmonary metastasectomy have a 30% 5-year survival rate.[28] Pfannschmidt and colleagues[18] found similar results with no significant difference in outcome observed between patients with and without history of previously resected hepatic metastases at the time of pulmonary resection, with 5-year survival rates between 30% and 42%.

As a rule, patients with extrathoracic metastases other than limited hepatic tumors should not undergo pulmonary metastasectomy for curative intent. Those who are being considered for such should be evaluated in a multidisciplinary tumor board.

All of the Tumor Must be Completely Resectable with Adequate Remaining Pulmonary Reserve

An appraisal of the ability to achieve complete resection with adequate pulmonary reserve is vital and includes evaluation of the number of nodules, consideration of the location of nodules, and estimation of the postoperative pulmonary function. Data from the International Registry of Lung Metastases indicate better 5-year survival rates for patients with a single metastatic focus (43% 5 year survival) when compared with those with 2 to 3 metastases (34%) or those with 3 or more metastases (27%).[24] For patients with multiple

metastases, there is no consensus as to how many lesions is too many. At this time, if lesions can be completely cleared while allowing for adequate remaining function, then resection can be pursued even if the lesions are numerous, bilateral or if anatomic resection such as segmentectomy or lobectomy is required. In the case of potential pneumonectomy, a thorough discussion of alternative therapies, in a multidisciplinary setting, should be conducted prior to embarking upon surgery.

No Superior Alternative Nonoperative Management

For most tumor histologies, there is no medical option that has a proven survival advantage over pulmonary metastasectomy. The exceptions are patients with nonseminomatous germ cell tumors and potentially those with breast cancer. When patients present with lung metastases from these etiologies, discussion with the medical oncologist should occur, as there are chemotherapeutic and hormonal therapies that can be offered for curative intent, without the risks of surgery.

SUMMARY

Most patients with pulmonary metastases will not be candidates for pulmonary metastasectomy. Preoperative evaluation determines whether a patient is both fit enough for surgery and has disease that is actually resectable and potentially curable. Both components are necessary in patients who undergo resection for curative intent. In general, to be considered for pulmonary metastasectomy, patients must fit several criteria:

- The primary disease is controlled.
- Any extrathoracic disease is controlled.
- Complete resection of pulmonary involvement is achievable with adequate pulmonary reserve.
- There are no effective medical therapies.

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KEY POINTS

- Only 15% to 25% of patients with pulmonary metastases will be appropriate candidates for surgery.
- Preoperative evaluation of pulmonary metastasectomy patients has 2 goals: first, to determine a patient's fitness for surgery; and second, to determine whether the pulmonary metastases are resectable.
- Individuals should undergo pulmonary metastasectomy under the following conditions: 1. the primary tumor site is controlled; 2. there is no evidence of extrathoracic metastases or these metastases are controlled; 3. the pulmonary metastases are completely resectable and resection will leave adequate pulmonary function; 4. there is no medical management with lower morbidity that can be offered in lieu of surgery.