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Review Article

Pulmonary metastasectomy: indications, surgical principles, prognosis and outcomes

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ABSTRACT

Surgical resection of pulmonary metastases is now widely considered for patients who meet the following criteria: controlled primary disease, absence of extensive extrapulmonary disease, fully resectable lung metastases, sufficient cardiopulmonary reserves, and lack of superior systemic treatment alternatives. Since the development of these selection criteria, additional prognostic factors have been proposed to better predict survival and optimize the selection of surgical candidates. Factors such as the disease-free interval (DFI), completeness of resection, surgical approach, number and laterality of lung metastases, and lymph node involvement play a dynamic role in determining patient outcomes.

Pulmonary metastasectomy is a common practice among thoracic surgeons, accounting for approximately 15% of all lung resections. While it is widely believed that pulmonary metastasectomy from a primary tumor elsewhere improves survival in selected patients, evidence for the additional benefit provided by surgery remains weak.

For patients with untreated metastatic disease, the five-year survival rate is less than 5–10%. Pulmonary metastasectomy often represents the best hope for treatment in cases of isolated metastatic disease to the lungs. It is a safe and effective treatment that offers potential recovery for selected patients. Regardless of the primary tumor, achieving complete resection is the key to improving survival. Low morbidity and mortality rates justify the aggressive surgical approach in the absence of effective systemic oncologic treatments. Thoracoscopic resection is a valid option for selected patients with a small number of peripherally located metastases. In cases of recurrent pulmonary disease, surgery should be repeated if the patient continues to meet the initial criteria for pulmonary metastasectomy. Postoperative aggressive follow-up is mandatory. Patients should be treated in close collaboration between medical oncologists, diagnostic radiologists, and thoracic surgeons.

Keywords: pulmonary metastasectomy, surgical resection, disease-free interval, thoracoscopic surgery, survival outcomes, thoracic oncology

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Introduction

This review examines the evaluation of pulmonary metastases, criteria for suitability for resection, outcomes for different tumor histologies, the feasibility of surgical resection, alternative approaches, and prognostic factors.

Approximately one-third of patients with malignant diseases develop pulmonary metastases [1-4]. Pulmonary metastasectomy (PM) is an established treatment that can improve long-term survival in patients with metastatic lung cancer originating from various primary solid tumors. Surgery is generally recommended for cases in the oligometastatic stage and for all patients who can tolerate the procedure.

The most common primary solid tumors causing pulmonary metastases include colorectal, renal, breast, prostate, and oropharyngeal carcinomas. Other tumors that primarily metastasize to the lungs include choriocarcinoma, osteosarcoma, soft tissue sarcomas, testicular tumors, Ewing sarcoma, and thyroid carcinoma [4].

Historically, systemic therapy has been considered the standard of care for stage IV cancer due to the systemic nature of the disease. However, local treatment options for metastatic pulmonary nodules are expanding, providing significant evidence for optimal local control to prolong life, delay recurrence, and relieve patients from ongoing chemotherapy [5].

While there is no absolute upper limit to the number of resectable nodules, having more than three during the first metastasectomy increases recurrence risk (especially in CRC). Nevertheless, larger numbers of lesions have been resected safely with good outcomes. The total number of metastases is less significant than the ability to achieve an R0 resection with a lung volume that the individual patient can tolerate [5].

The patient's comorbidities are particularly important in determining the recommended form of local treatment for pulmonary metastases. In some cases, systemic therapy before surgery can reduce tumor volume, increase the effectiveness of subsequent radiation or ablative treatments, and decrease the amount of parenchyma required for resection [5].

The role of pulmonary metastasectomy has been extensively studied since the 1970s and was highlighted in a landmark publication in 1997 reporting the results of the International Registry of Lung Metastases. This study provided critical data supporting the role of surgery in selected patients and identified key prognostic factors influencing survival [6].

The lungs are the most common site for metastatic malignancies [7]. Once primary tumors metastasize, treatment becomes more challenging, leading to significantly higher morbidity and mortality. However, pulmonary metastasectomy can be performed with curative intent in selected patients. Complete surgical excision is technically feasible, usually with low perioperative morbidity and mortality. Pulmonary resection is only suitable for patients whose primary disease is controlled, who have no widespread or uncontrolled extrapulmonary metastases, whose lung metastases can be fully resected, and who have adequate cardiopulmonary reserves to tolerate surgery [7].

The first pulmonary metastasectomy was reported in 1882. As chest imaging became available, planned resections of lung metastases were introduced. Criteria for pulmonary metastasectomy have since been defined and updated. These include control or apparent controllability of the primary disease, feasibility of complete resection of metastatic lung disease, patient tolerance for planned procedures, and the absence of better alternative treatments [8].

The Expert Consensus Document on Pulmonary Metastasectomy emphasizes the importance of multidisciplinary approaches and standardized criteria for optimizing surgical outcomes [9]. Minimally invasive techniques, such as VATS, have increasingly demonstrated improved perioperative outcomes in selected patient populations [10,11].

For patients with untreated metastatic disease, the five-year survival rate is less than 5-10%. In cases of isolated metastatic disease to the lungs, pulmonary metastasectomy often represents the best hope for treatment [12,13].

Preoperative evaluation

Preoperative evaluation consists of obtaining a detailed history, performing a physical examination, conducting physiological tests, and utilizing radiological imaging. Radiological investigations are essential for determining the differential diagnosis of pulmonary nodules, assessing the exact number, location, and characteristics of the nodules, and identifying any extrathoracic metastases. Advanced techniques like PET-CT have been

instrumental in enhancing the detection and staging of metastatic disease, aiding in precise treatment planning [14,15]. Mediastinal lymph node evaluation through systematic dissection or sampling remains critical for prognostic and diagnostic accuracy [16,17]. Indications for pulmonary metastasectomy should be evaluated from both physiological and oncological perspectives [2,13]. Nichols et al highlighted the critical role of imaging in determining surgical candidacy for pulmonary metastasectomy, ensuring all nodules are resectable and systemic disease is controlled [18].

Patient selection

When pulmonary metastatic disease is encountered, and surgical options are being considered, several key criteria must be evaluated to determine the most appropriate treatment plan for the patient. First, all pulmonary nodules should be resectable, or if not, they should be amenable to management using a hybrid approach that includes additional local therapies. Second, the primary tumor must either be fully controlled or controllable with appropriate treatment. Third, any extrathoracic disease present must also be under control or manageable to ensure that surgery can provide meaningful benefits. Fourth, it is essential that complete resection (R0) is feasible, as achieving clear surgical margins is critical for improving survival outcomes. Finally, the patient must have an acceptable preoperative risk profile, ensuring that they can safely tolerate the procedure and its associated recovery process. These considerations are vital for optimizing surgical outcomes and ensuring that the benefits of the procedure outweigh the risks for each individual case.

Studies have documented that surgical resection provides significant survival benefits in properly selected patients, particularly when criteria for complete resection are met [19]. Furthermore, redo metastasectomy has shown comparable outcomes to initial surgeries, particularly in sarcoma patients [20,21]. Laser-assisted surgical techniques have also been highlighted as promising approaches for achieving precise resections while preserving lung parenchyma [22,23]. If these criteria are met, the decision regarding surgery should then consider whether the patient has an acceptable operative risk. For patients with prohibitive surgical risks, nonoperative techniques such as radiofrequency ablation or stereotactic body radiation therapy may be considered. If the outlined criteria cannot be achieved, a nonoperative or hybrid approach may still be considered if the patient's condition allows [5,6].

Guidelines for patient selection for pulmonary metastasectomy were established after the publication of a landmark retrospective study in 1997, which analyzed data from 5,206 cases in the International Registry of Lung Metastases. This study identified four key prognostic factors that significantly influence survival outcomes. These factors include the number of metastases present in the lungs, the disease-free interval between the treatment of the primary tumor and the emergence of pulmonary metastases, the feasibility of completely resecting all visible lesions, and the histology of the primary tumor [24]. Pulmonary metastases are generally asymptomatic, and specific symptoms may indicate advanced disease. However, 15-20% of patients may present with symptoms such as cough, hemoptysis, chest pain, or post-obstructive pneumonia [1].

Detailed information on the treatment history of the primary tumor, including tumor stage, histological type, the interval between treatment of the primary tumor and detection of pulmonary metastases, presence of other metastatic sites, and chemotherapy regimen, is required. These factors serve as significant prognostic indicators [2].

For patients undergoing cytotoxic chemotherapy, pulmonary resection should be scheduled after the white blood cell count normalizes (typically around four weeks). In cases treated with bevacizumab, pulmonary resection should be delayed until at least six weeks after the last dose to minimize the risk of postoperative pulmonary fistulas. While most candidates for pulmonary metastasectomy are asymptomatic, it is essential to investigate respiratory symptoms that may indicate endobronchial involvement or centrally located bulky lesions [2].

When pulmonary nodules are detected in patients with a history of malignancy, a differential diagnosis is crucial. Multiple nodules are likely to be metastatic disease from the primary tumor, but distinguishing pulmonary metastases from primary lung cancer can be challenging when there is only a single nodule. For solitary pulmonary nodules (SPN), the decision on whether to proceed with an invasive diagnostic procedure depends on the treatment strategy for the SPN, which should consider factors such as the type of primary tumor, the type of resection performed (if applicable), and the patient's overall condition [2].

When preoperative imaging reveals mediastinal and hilar lymph nodes, their assessment is critical. Lymph node involvement, regardless of histology, is a significant negative prognostic factor for patients undergoing

pulmonary metastasectomy. Therefore, patients with mediastinal adenopathy should undergo invasive mediastinal staging (e.g., mediastinoscopy or endobronchial ultrasound-guided fine-needle aspiration) before undergoing pulmonary metastasectomy. Although the presence of hilar or mediastinal lymph node involvement correlates with poorer survival compared to patients without nodal involvement, documented nodal metastases are not an absolute contraindication for metastasectomy, as some patients with lymph node involvement have achieved long-term survival following surgery [8].

Radiologic studies

Radiologic evaluation is a critical component of the preoperative assessment for pulmonary metastasectomy, serving several essential purposes. It helps differentiate pulmonary nodules, assesses their number, location, and characteristics, and identifies the presence of extrathoracic metastases [2]. High-resolution computed tomography (CT) scans with 1-2 mm slices are considered the gold standard for evaluating pulmonary nodules. In addition, positron emission tomography (PET) scans complement CT by staging metastatic disease and ruling out distant metastases, with the sensitivity of PET varying based on the histology of the metastases [1].

Additional imaging modalities may also be utilized in specific scenarios. Bone scans are often used to detect osseous metastases, particularly in patients with sarcomas. Brain imaging, such as magnetic resonance imaging (MRI) or CT, is employed to exclude central nervous system involvement in symptomatic patients or those with high-risk tumor histologies [25]. These imaging techniques collectively provide a comprehensive evaluation, enabling effective surgical planning and optimized patient outcomes.

Mediastinal and hilar lymph node evaluation

Mediastinal and hilar lymph node metastases are associated with worse prognosis. Enlarged or hypermetabolic nodes identified on imaging warrant invasive staging through mediastinoscopy or endobronchial ultrasound (EBUS)-guided fine-needle aspiration [1,25].

While CT scans detect more nodules than chest radiographs, they may still underestimate the total number of metastatic lesions compared to manual palpation during surgery. Studies suggest that up to 20-25% of nodules remain undetected by imaging but can be found intraoperatively [25]. Advances in CT technology, including the ability to detect nodules as small as 1 mm, have reduced this discrepancy, although manual palpation remains valuable for certain histologies like osteosarcoma [25].

Indications and contraindications for pulmonary metastasectomy

Pulmonary metastasectomy is a well-established treatment option for patients with metastatic lung disease, provided that certain conditions are met. Patients considered for surgery must be in good overall health and have no significant operative risks. Most importantly, the primary tumor should either be controlled or manageable through additional treatment. While the absence of extrathoracic disease is ideal, metastases in other organs may still allow for surgery if they are resectable or have already been effectively treated [1,6].

Complete surgical resection (R0 resection) is critical for improving survival outcomes. Incomplete resections (R1 or R2) are strongly associated with poor prognosis, making the ability to fully remove all visible metastases a key criterion. Furthermore, the decision to perform metastasectomy must consider the availability of systemic or alternative therapies. Recent advancements in targeted treatments and immunotherapy have introduced new options that must be weighed against surgical intervention [1,26].

Despite these criteria, not all patients are suitable candidates for metastasectomy. Uncontrolled primary tumors, unresectable pulmonary disease, or severe comorbidities often disqualify patients. Mediastinal lymph node involvement (N2 disease) and widespread extrathoracic metastases, although not absolute contraindications, require careful evaluation. Multidisciplinary discussions are essential to determine whether surgery is the best option in these complex cases [19,26].

Pulmonary metastasectomy principles

Pulmonary metastasectomy is primarily performed with curative intent, aiming to improve survival in carefully selected patients. The key objective of the procedure is to completely resect all visible metastases while preserving as much pulmonary parenchyma as possible. Achieving this balance requires tailoring the surgical approach to the location and characteristics of the metastases [1,3,4]. Hornbech et al discussed the evolving practices in metastasectomy, with a focus on achieving complete resection while minimizing morbidity [12].

For peripheral lesions, wedge resections are commonly used, often with the aid of surgical tools such as staplers or laser devices. These techniques ensure minimal tissue loss while achieving clear surgical margins. For central or larger lesions, more extensive procedures such as segmentectomy, lobectomy, or even pneumonectomy may be necessary to achieve complete resection [1,4].

The International Registry of Lung Metastases, which analyzed over 5,000 cases, reported that wedge resection was the most frequently performed procedure, accounting for 67% of cases. Lobectomy, segmentectomy, and pneumonectomy followed at 21%, 9%, and 3%, respectively. These findings underscore the importance of individualized surgical planning based on the size, location, and number of metastases [3,4].

Minimally invasive techniques, such as video-assisted thoracoscopic surgery (VATS), are increasingly used for patients with small, peripherally located nodules. These approaches offer advantages such as reduced pain, shorter hospital stays, and quicker recovery. However, VATS may not always allow complete assessment of the lung, and manual palpation through open thoracotomy remains the gold standard for detecting smaller or occult nodules [4,13].

In cases of recurrent pulmonary disease, repeat metastasectomy can be performed if the patient continues to meet the criteria for surgery. Repeat procedures have been shown to provide survival benefits comparable to initial resections, particularly when complete resection is achievable [12,13].

Thoracotomy or a minimally invasive approach?

Open thoracotomy has historically been the standard surgical approach for pulmonary metastasectomy due to its ability to allow thorough manual palpation of the lung parenchyma. This method is particularly valuable for detecting nodules that are not visible on imaging. Even with advances in high-resolution computed tomography (CT), 20-25% of nodules may remain undetected preoperatively but can be identified through manual palpation during surgery [11,27]. This is especially critical in cases involving tumors like osteosarcoma, where small, occult metastases are more common [26].

However, video-assisted thoracoscopic surgery (VATS) has emerged as a minimally invasive alternative, offering significant advantages in perioperative outcomes. VATS is associated with reduced pain, shorter hospital stays, quicker recovery, and better tolerance for adjuvant therapies. Retrospective studies comparing VATS and thoracotomy have shown comparable overall survival rates, particularly in patients with small, peripherally located metastases [10,11,27]. Despite these benefits, VATS is not without limitations, particularly its inability to allow comprehensive manual palpation. This limitation can lead to undetected metastases and potentially compromise surgical outcomes in certain patients [22,28].

Recent studies and meta-analyses have examined the long-term outcomes of VATS versus thoracotomy. One meta-analysis found that VATS is associated with superior overall survival (OS) compared to thoracotomy, while recurrence-free survival (RFS) rates were similar between the two groups. Additionally, VATS has been shown to provide equivalent outcomes for patients with colorectal cancer metastases [10,22]. The advantages of VATS, such as improved postoperative mobility and reduced morbidity, make it an attractive option for selected patients [11,23]. Nichols highlighted the trade-offs between open thoracotomy and VATS, particularly in terms of manual palpation and patient recovery [13].

For patients with centrally located lesions, multiple metastases, or histologically aggressive tumors, open thoracotomy remains the preferred approach. It ensures complete exploration and resection of all lesions, thereby maximizing the likelihood of achieving R0 resection [22,26]. In practice, the choice between VATS and thoracotomy should be individualized, taking into account the patient's clinical condition, the characteristics of the metastases, and the surgeon's expertise [27,28].

Complete vs incomplete resection

Achieving a complete resection (R0) is critical for improving survival in patients undergoing pulmonary metastasectomy. Studies have consistently shown that patients who undergo incomplete resections (R1 or R2) have significantly worse survival outcomes compared to those with R0 resections [19,12]. The importance of complete resection is underscored by data from the International Registry of Lung Metastases, which demonstrated that survival rates are substantially higher in patients with R0 resection, regardless of tumor histology [27].

In cases where complete resection is not feasible due to the extent of disease or the location of metastases, surgical intervention should be avoided. Incomplete resections

not only fail to improve survival but also expose patients to unnecessary surgical risks [19,26]. The only exception may involve specific palliative scenarios, such as controlling life-threatening complications like hemoptysis or pneumothorax caused by metastatic lesions [12,26].

Timing of pulmonary metastasectomy

The timing of pulmonary metastasectomy is a critical consideration in treatment planning and is influenced by the status of the primary tumor, the presence of extrathoracic disease, and the overall clinical context. Surgery is generally performed after the primary tumor has been controlled and any extrathoracic metastases have been adequately treated or stabilized. However, certain clinical circumstances may warrant deviations from this sequence [5].

In cases where patients present with synchronous metastases or a short disease-free interval (DFI), it may be prudent to delay surgery and monitor disease progression with serial imaging, such as CT scans performed every 6-8 weeks. This approach can help identify patients with rapid extrathoracic disease progression, sparing them from unnecessary surgical interventions. Conversely, patients with isolated pulmonary lesions and no active extrathoracic disease may benefit from earlier resection, particularly when systemic therapy options are limited [19,12,26].

The surgical approach can also influence timing decisions. For instance, minimally invasive techniques like VATS may allow for earlier interventions due to shorter recovery times, while patients requiring open thoracotomy for more complex resections might benefit from a longer observation period to fully assess disease progression [19,29].

Ultimately, the timing of metastasectomy should be determined through a multidisciplinary approach that considers the patient's overall condition, tumor biology, and the available systemic therapy options. Tailoring the timing to the individual clinical scenario ensures that patients derive the maximum benefit from surgery [29].

Margins

The surgical margin plays a crucial role in determining the success of pulmonary metastasectomy. Achieving tumor-free margins (R0 resection) significantly reduces the risk of local recurrence and is strongly associated with improved survival outcomes. While there is no universal agreement on the ideal margin size, most studies recommend a margin of at least 10 mm for wedge resections to minimize the risk of recurrence. However, for larger tumors, wider margins may be necessary [3,19].

Recent studies have emphasized the importance of the tumor-to-margin ratio. A ratio greater than 1.7 has been linked to better outcomes, as it reflects sufficient clearance of the tumor from surrounding healthy tissue. This finding is particularly relevant for patients with small peripheral nodules undergoing wedge resection [3,26].

Advances in surgical techniques have introduced tools such as curved staplers, which facilitate achieving uniform and adequate margins while preserving lung parenchyma. These devices are especially useful in cases involving deep or central lesions where maintaining consistent margins can be technically challenging [22,26].

Failure to achieve adequate surgical margins is associated with a higher risk of local recurrence and poorer survival. This is particularly evident in aggressive histologies, such as sarcomas and colorectal cancer metastases, where even small residual disease can significantly impact outcomes [19,23]. Therefore, ensuring appropriate margins is a critical aspect of surgical planning and execution.

Number of lung metastases

The number of pulmonary metastases is a well-established prognostic factor in patients undergoing metastasectomy. Although patients with fewer metastases generally exhibit better survival outcomes, the absolute number of nodules is not necessarily a strict determinant for surgery. The feasibility of achieving a complete resection (R0) is a more critical consideration [3,26].

Studies have consistently shown that patients with solitary metastases achieve the best survival outcomes, reflecting limited disease burden. However, patients with multiple metastases can still benefit from surgery, provided that all visible lesions can be completely resected. For instance, data from the International Registry of Lung Metastases suggest that even patients with three or more nodules can achieve long-term survival if R0 resection is feasible [26,27].

It is essential to emphasize that the ability to resect all visible disease outweighs the absolute number of nodules. For patients with extensive metastatic disease, modern imaging techniques, such as high-resolution CT and PET scans, are crucial for preoperative planning. Additionally, intraoperative palpation can help identify smaller nodules that might be missed during imaging, particularly in cases involving histologies like osteosarcoma or soft tissue sarcomas [19,22].

Ultimately, surgical decision-making should be individualized, taking into account not only the number of metastases but also the patient's overall health, tumor biology, and the likelihood of achieving a complete resection. When these factors align, even patients with multiple metastases can derive significant survival benefits from metastasectomy [3,26].

Pulmonary metastasectomy for specific histologies

Each histological type behaves differently, making it logical to assume that the effectiveness and role of surgery depend on the primary tumor's histology. Independent of histology, factors such as incomplete resection, the number and size of resected tumors, lymph node (LN) metastases, and short disease-free intervals (DFI) are recognized as predictors of poor prognosis. In contrast, certain prognostic indicators are specific to individual histological types [3].

Colorectal cancer (CRC)

Colorectal cancer is the most frequent primary malignancy among patients undergoing pulmonary metastasectomy (PM). Key prognostic factors include the number of pulmonary metastases, carcinoembryonic antigen (CEA) levels, and the disease-free interval (DFI). Patients with a longer DFI, fewer nodules, and normal preoperative CEA levels exhibit significantly better survival outcomes [2,3,12].

Additionally, the location and timing of metastases play a crucial role. Synchronous liver and lung metastases are not a contraindication for surgery if both sites are resectable. Data indicate that combined hepatic and pulmonary metastasectomy can yield five-year survival rates of approximately 30% in carefully selected cases. However, the presence of mediastinal lymph node involvement or elevated preoperative CEA levels are associated with worse outcomes [26,30].

Renal cell carcinoma

Renal cell carcinoma (RCC) is the second most common primary tumor in patients undergoing PM. Achieving R0 resection is vital, as incomplete resections (R1 or R2) do not provide survival benefits. Prognostic factors include tumor burden, lymph node involvement, and the disease-free interval. Shorter DFIs and nodal metastases are associated with poorer outcomes, while patients with solitary nodules and long DFIs fare better. Five-year survival rates for RCC patients after PM range from 20% to 74%, depending on these variables [2,12,26].

Osteosarcoma

Osteosarcoma frequently metastasizes to the lungs, with up to 30–40% of patients developing pulmonary nodules during the course of their disease. Pulmonary metastasectomy offers significant survival benefits, particularly in young patients with solitary or limited nodules and longer DFIs. Achieving complete resection is critical, as residual disease negatively impacts survival. Studies report five-year survival rates ranging from 20% to 40% for osteosarcoma patients undergoing PM [6,26].

Histological factors also influence outcomes. Subtypes like chondroblastic osteosarcoma tend to exhibit worse prognoses. Moreover, patients who develop metastases during chemotherapy generally experience poorer survival compared to those whose metastases develop after completing treatment [6,31].

Soft tissue sarcoma

Soft tissue sarcomas predominantly metastasize to the lungs, making PM the primary curative option for many patients. Prognostic factors include tumor grade, disease-free interval, and the number of pulmonary nodules. Lower-grade tumors, longer DFIs, and fewer metastases are associated with improved survival. Studies suggest that achieving R0 resection is crucial, as incomplete resections fail to provide survival benefits [6,26,31].

For patients with multiple metastases or recurrent disease, repeat metastasectomy has shown to improve survival, highlighting the importance of tailored surgical strategies [26].

Germ cell cumors

Nonseminomatous germ cell tumors (NSGCTs) are highly responsive to chemotherapy. However, for patients with residual or recurrent disease after systemic treatment, pulmonary metastasectomy can significantly enhance survival. Five-year survival rates after R0 resection range from 73% to 94%, depending on the extent of disease and the success of systemic therapy [6,32].

In cases where nodal or extrathoracic disease is present, careful patient selection is necessary. Achieving complete resection remains the most important factor influencing survival. Patients with incomplete resection or unresectable disease have significantly worse outcomes compared to those who undergo R0 resection [6,33].

Head and neck cancers

Pulmonary metastases are a common occurrence in pa-

tients with head and neck cancers, as the lungs are the most frequent site of distant metastases for these malignancies. Despite the poor prognosis associated with metastatic head and neck cancers, pulmonary metastasectomy (PM) has been shown to improve survival in selected patients [6]. Evidence also supports the role of pulmonary metastasectomy in improving outcomes for head and neck cancers, as shown in systematic analyses [34,35].

Several factors influence the outcomes of PM in head and neck cancers. A disease-free interval (DFI) longer than 12 months is associated with significantly better survival rates. Similarly, patients with a limited number of metastases and no evidence of mediastinal lymph node involvement fare better. In contrast, patients with squamous cell carcinoma histology, shorter DFIs, and metastases originating from oral cavity cancers often have worse prognoses [2,3,6].

Five-year survival rates following PM for head and neck cancers vary widely, ranging from 20% to 60% depending on the tumor's histology, the extent of metastases, and the completeness of resection. Patients with adenoid cystic carcinoma, for example, tend to have much better survival outcomes compared to those with squamous cell carcinoma. Documented mediastinal lymph node involvement and plevral infiltration are associated with worse outcomes [6,31].

Complete resection (R0) remains the most critical determinant of improved survival. For patients presenting with a higher metastatic burden or additional risk factors, multidisciplinary discussions are essential to evaluate the potential benefits of surgery. While PM is often recommended for isolated metastases, patients with extensive disease may benefit more from systemic therapies [6].

Gynecologic cancers

Pulmonary metastases from gynecologic cancers, though less common, present unique challenges in patient management. The lungs are the most frequent site of distant metastases for cervical, endometrial, and ovarian carcinomas, as well as choriocarcinoma and uterine sarcomas. While systemic therapies are often the first line of treatment, pulmonary metastasectomy (PM) can provide survival benefits in selected cases [6,26].

The prognosis of patients undergoing PM for gynecologic cancers depends on several factors, including the histology of the primary tumor, disease-free interval (DFI), and the number of metastases. Patients with squamous cell carcinoma of the cervix generally exhibit poorer outcomes compared to those with endometrial carcinoma. A longer DFI, limited number of pulmonary nodules, and absence of mediastinal lymph node involvement are associated with improved survival [6,31].

Encouraging results have been reported for patients undergoing PM for gynecologic cancers. Five-year survival rates vary significantly by histology, ranging from 40% for cervical carcinoma to 76% for endometrial carcinoma. In one study involving patients with uterine malignancies, a five-year survival rate of 69% was reported for those with isolated pulmonary metastases who underwent complete resection [12].

For patients with choriocarcinoma, systemic chemotherapy is often curative [31], but PM may be considered for those with persistent pulmonary nodules after treatment. Similarly, for patients with uterine sarcomas, PM is reserved for isolated metastases and cases where systemic options have been exhausted.

Complete resection remains the cornerstone of successful surgical outcomes. Patients with incomplete resections or widespread disease have significantly worse survival rates. Therefore, patient selection and multidisciplinary decision-making are critical when considering PM for gynecologic cancers [6,31,36].

Breast cancers

Pulmonary metastases are a frequent manifestation in advanced or recurrent breast cancer, with an estimated incidence of 7–24%. Although systemic therapies, including chemotherapy, hormonal treatment, and targeted therapies such as trastuzumab for HER2-positive tumors, are the cornerstone of management, pulmonary metastasectomy (PM) has demonstrated potential survival benefits in appropriately selected patients [1,3].

The prognosis of breast cancer patients undergoing PM is influenced by several factors. A longer disease-free interval (DFI), particularly exceeding three years, has consistently been associated with improved survival outcomes. Hormone receptor status also plays a critical role, with hormone receptor-positive tumors responding better to therapy and correlating with a more favorable prognosis. Additionally, patients with a limited number of pulmonary metastases tend to achieve better long-term outcomes compared to those with extensive disease [1,3,31].

Meta-analyses indicate that the five-year survival rate for breast cancer patients undergoing PM is approximately

45–46%. However, factors such as incomplete resection (R1 or R2), short DFI, and negative hormone receptor status significantly worsen survival. Achieving complete resection (R0) remains paramount to improving outcomes, particularly in cases of oligometastatic disease [12,26].

One of the challenges in managing pulmonary metastases in breast cancer lies in the difficulty of distinguishing metastatic lesions from primary lung cancers based on imaging alone. Solitary pulmonary nodules, in particular, require pathological confirmation to differentiate between metastatic breast cancer and primary lung malignancies. Accurate diagnosis is essential for guiding treatment strategies and ensuring optimal outcomes [31,37].

Patients with HER2-positive breast cancer or those who respond well to systemic therapy may benefit from a combined approach integrating surgery with ongoing systemic treatments. Multidisciplinary evaluation is crucial in determining the timing and appropriateness of PM, especially in patients with isolated metastases and stable systemic disease. In such cases, PM can offer meaningful survival benefits, highlighting its role as a vital component of the treatment plan for selected breast cancer patients [31].

Hepatocellular cancer

Pulmonary metastases are the most common form of extrahepatic recurrence in hepatocellular carcinoma (HCC), with an incidence ranging from 6% to 56%. Despite advances in systemic therapies, effective treatment options for metastatic HCC remain limited, making pulmonary metastasectomy (PM) a valuable intervention for selected patients [31,38].

The prognosis of patients undergoing PM for HCC is influenced by several factors. A longer disease-free interval (DFI), typically exceeding 12 months, is associated with significantly improved survival outcomes. Additionally, patients with fewer and smaller metastases, normal preoperative alpha-fetoprotein (AFP) levels, and no evidence of uncontrolled intrahepatic disease tend to achieve better long-term survival. By contrast, patients with extensive pulmonary disease, higher AFP levels, or concurrent active liver disease often experience worse outcomes [31,48].

Reported five-year survival rates for patients undergoing PM for HCC vary widely, ranging from 12% to 67%, depending on the extent of disease and the completeness of resection. Complete resection (R0) is critical, as incomplete resections do not provide survival benefits. For patients with extensive disease, surgery is typically contraindicated unless performed with palliative intent to address complications like hemoptysis or airway obstruction [48].

Careful patient selection is essential when considering PM for HCC. Multidisciplinary evaluation involving hepatologists, oncologists, and thoracic surgeons ensures that patients most likely to benefit from surgery are identified. While PM may not be suitable for all HCC patients with pulmonary metastases, it remains a valuable tool in the management of select cases where systemic therapies alone are insufficient [31,48].

Gastric cancers

Pulmonary metastases from gastric cancer are relatively rare, with an incidence of 0.3% to 6%. Most cases involve lymphangitic spread or pleural dissemination, while isolated nodular metastases to the lungs are uncommon. For selected patients with limited metastatic disease, pulmonary metastasectomy (PM) can provide survival benefits, but the role of surgery remains controversial [6,39].

The prognosis of patients with pulmonary metastases from gastric cancer is generally poor. However, certain factors are associated with better outcomes. Patients with longer disease-free intervals (DFI), smaller and fewer pulmonary nodules, and no evidence of systemic progression tend to achieve better survival rates. Studies have reported five-year survival rates ranging from 9% to 45% for patients undergoing PM, with the best outcomes observed in those who achieve complete resection (R0) [31,39].

Despite these findings, systemic chemotherapy remains the mainstay of treatment for metastatic gastric cancer, and surgery is rarely performed. PM is typically reserved for highly selected cases, such as patients with long DFIs, isolated pulmonary nodules, and no active extrathoracic disease. In such cases, the potential for prolonged survival justifies the risks associated with surgery [31,39].

Given the aggressive nature of gastric cancer and its propensity for widespread dissemination, careful patient selection is critical. Multidisciplinary discussions involving oncologists, thoracic surgeons, and gastroenterologists are essential to determine the feasibility and timing of PM. For most patients, systemic therapy remains the primary treatment modality, with surgery reserved for rare cases where it can provide meaningful survival benefits [39].

Malignant melanoma

Pulmonary metastases are a common manifestation of malignant melanoma, as the lungs are the most frequent site of visceral spread. Metastatic melanoma has historically been associated with poor survival outcomes; however, pulmonary metastasectomy (PM) has emerged as a potential option for improving survival in selected patients [1,6].

The prognosis of patients with pulmonary metastases from melanoma is influenced by several factors. A disease-free interval (DFI) of more than 12 months, a limited number of pulmonary nodules (typically fewer than three), and the absence of extrathoracic or lymph node metastases are associated with better outcomes. Achieving complete resection (R0) is critical, as incomplete resections are linked to significantly worse survival rates. In addition, patients who respond well to systemic immunotherapy or chemotherapy before surgery tend to achieve more favorable results [6,31].

Despite the aggressive biology of melanoma, several studies have reported promising results for patients undergoing PM. Five-year survival rates range from 4% to 40%, depending on the extent of disease, DFI, and the completeness of resection. Patients with solitary pulmonary nodules and no evidence of systemic progression are the best candidates for surgery [31].

One of the primary challenges in managing pulmonary metastases from melanoma is the high likelihood of recurrence. Even after complete resection, many patients experience disease recurrence, underscoring the need for close postoperative surveillance. For recurrent disease, repeat metastasectomy or systemic therapies, including immunotherapy with immune checkpoint inhibitors, can be considered [1,6].

Multidisciplinary evaluation is essential in determining the role of PM in metastatic melanoma. While surgery alone is unlikely to cure the disease, it can provide meaningful survival benefits for selected patients, particularly when integrated with modern systemic therapies. For patients with limited disease and good systemic control, PM remains an important component of the treatment strategy [31].

Lung cancer

Pulmonary metastasectomy (PM) is occasionally considered in patients with non-small cell lung cancer (NSCLC) who develop secondary lung lesions. Differentiating whether these lesions represent metastases from the primary lung cancer or new primary tumors is critical, as it significantly impacts treatment strategies. For selected patients, PM can serve both diagnostic and therapeutic purposes [31].

In patients with oligometastatic NSCLC, local therapies such as PM have been shown to delay disease progression and, in some cases, improve survival. However, the role of PM in NSCLC is limited to carefully selected patients with controlled primary disease and isolated secondary lesions. Surgical resection is most beneficial when complete resection (R0) is achievable and the patient has no extrathoracic disease [26,31].

For small cell lung cancer (SCLC), systemic therapy remains the primary treatment modality. Metastatic or recurrent SCLC rarely benefits from surgical interventions due to its aggressive nature and widespread dissemination. In exceptional cases, where disease progression is slow and localized, PM may be considered, but such instances are exceedingly rare [31].

A significant challenge in managing pulmonary metastases in lung cancer lies in distinguishing metastatic lesions from second primary lung cancers. This is especially relevant for patients with solitary nodules or lesions in the contralateral lung. In such cases, PM can provide a definitive pathological diagnosis and guide subsequent treatment decisions. Achieving R0 resection remains crucial for maximizing potential survival benefits [31].

Although PM is not a standard treatment for metastatic lung cancer, studies have reported five-year survival rates ranging from 15% to 30% in carefully selected NSCLC patients. These outcomes underscore the importance of patient selection and the need for multidisciplinary discussions to assess the feasibility of surgery. For SCLC, however, survival outcomes with PM remain poor, reinforcing the importance of systemic therapies [26,31].

Pediatric cancers

Pulmonary metastases are a common occurrence in pediatric cancers, particularly in solid tumors such as osteosarcoma, Ewing sarcoma, hepatoblastoma, and Wilms tumor. These metastases are often associated with poor prognosis, but pulmonary metastasectomy (PM) has proven to be a valuable component of multimodal therapy for selected pediatric patients [6,40].

Osteosarcoma and Ewing sarcoma are among the most frequent pediatric cancers to metastasize to the lungs. In osteosarcoma, approximately 30–40% of patients develop pulmonary metastases, often during or after initial treatment. PM offers significant survival benefits for patients with limited disease and a longer disease-free interval (DFI). Studies on surgical morbidity and survival outcomes in osteosarcoma patients emphasize the critical role of pulmonary metastasectomy in improving long-term survival [41-43]. Five-year survival rates for these patients range from 20% to 40%, provided that R0 resection is achieved. Similarly, in Ewing sarcoma, PM combined with systemic therapy and, in some cases, radiotherapy has been shown to improve long-term outcomes [6,40].

Hepatoblastoma frequently metastasizes to the lungs, particularly in advanced cases. For patients with persistent pulmonary nodules following chemotherapy, PM can provide a pathway to long-term survival. Studies report five-year survival rates of 50-65% for patients undergoing PM after initial systemic therapy. Complete resection is critical, as incomplete resections do not offer survival benefits [40].

Approximately 10% of children with Wilms tumor present with pulmonary metastases. Advances in chemotherapy and radiotherapy have significantly improved outcomes for these patients, but PM remains an important option for those with residual disease following systemic therapy. In selected cases, PM has been associated with five-year survival rates as high as 88% [40].

The decision to perform PM in pediatric patients requires a multidisciplinary approach involving pediatric oncologists, thoracic surgeons, and radiation oncologists. Factors such as the number of metastases, the response to systemic therapy, and the feasibility of achieving complete resection are critical in determining the suitability of surgery. Repeat metastasectomy may also be considered for recurrent disease, provided that the patient's overall condition allows for additional surgical intervention [6,40,44].

Lymph node status

Lymph node involvement plays a pivotal role in determining the prognosis and treatment outcomes of patients undergoing pulmonary metastasectomy (PM). Studies consistently demonstrate that intrathoracic lymph node metastases are associated with worse survival outcomes, regardless of tumor histology. As such, evaluating lymph node status is a crucial step in the preoperative assessment and surgical decision-making process [2-5,12]. Systematic lymphadenectomy has been shown to provide prognostic value, though its therapeutic benefit remains under discussion [16]. Meta-analyses have demonstrated the prognostic significance of lymph node assessment during metastasectomy, underscoring its importance in surgical planning [17].

Patients without lymph node involvement (N0) experience significantly better survival outcomes compared to those with lymph node metastases (N1 or N2). While hilar lymph node involvement (N1) negatively affects survival, mediastinal lymph node metastases (N2) are particularly associated with poor outcomes. Data suggest that the five-year survival rate for node-negative patients ranges from 40% to 50%, whereas it drops below 20% for patients with node-positive disease [17,26,29].

Preoperative imaging, including computed tomography (CT) and positron emission tomography (PET), is essential for identifying suspicious lymph nodes. Hypermetabolic or enlarged lymph nodes on imaging warrant further investigation through invasive staging techniques, such as mediastinoscopy or endobronchial ultrasound (EBUS)-guided fine-needle aspiration. Accurate staging not only refines patient selection but also informs postoperative management and adjuvant therapy decisions [14,26].

The role of systematic lymph node dissection during PM remains controversial. While lymph node sampling or dissection provides valuable prognostic information, its therapeutic benefit is less clear. Recent studies suggest that systematic dissection does not significantly improve overall survival but helps guide postoperative strategies. For patients with documented lymph node involvement, complete resection of both pulmonary and nodal disease is essential to achieve potential survival benefits [16,26,29].

The impact of lymph node involvement varies depending on tumor histology. For instance, renal cell carcinoma patients with lymph node metastases may still benefit from PM, provided that complete resection is achievable. In contrast, node-positive patients with aggressive histologies, such as colorectal cancer or sarcoma, often have worse outcomes. These cases require careful evaluation, as incomplete resection does not provide meaningful survival benefits [16,26,29].

Given the substantial prognostic implications of lymph node involvement, multidisciplinary discussions are crucial in determining the appropriateness of PM. Comprehensive staging and thorough surgical planning can optimize outcomes for patients with node-positive disease [14,26].

Repeated metastasectomy

Pulmonary metastasectomy (PM) is frequently performed in patients who experience disease recurrence following an initial surgery. Recurrence rates can reach as high as 50-70%, depending on the primary tumor type. Despite these high recurrence rates, repeated metastasectomy has consistently been shown to provide meaningful survival benefits in selected patients. Recent systematic reviews highlight that repeat metastasectomy in sarcoma and colorectal cancer patients is associated with substantial survival benefits [28,34-36]. Studies report five-year survival rates of 30% to 50% for patients undergoing repeat resections, particularly when complete resection (R0) is achieved. The International Registry of Lung Metastases highlights the importance of achieving R0 resection during repeat surgeries, as it remains a key determinant of survival outcomes [12,26,27]. In colorectal cancer, combined hepatic and pulmonary resections have been associated with improved survival in carefully selected cases [47].

The suitability of repeat metastasectomy depends on multiple clinical factors. Patients with a longer disease-free interval (DFI), limited recurrent lesions, and good overall health are more likely to benefit from the procedure. Conversely, patients with aggressive tumor biology, rapid recurrence, or short DFIs may have less favorable outcomes. Thorough preoperative evaluation is essential to assess the feasibility of surgery and to determine whether complete resection is achievable [16,19,26].

Planning for repeat metastasectomy requires a multidisciplinary approach involving thoracic surgeons, oncologists, and radiologists. Advanced imaging techniques, such as high-resolution computed tomography (CT) and positron emission tomography (PET), are indispensable for evaluating the extent of recurrent disease and assessing resectability. Accurate imaging and staging are critical to optimizing surgical outcomes and avoiding unnecessary procedures [16,26].

While repeat metastasectomy offers significant survival benefits, it is not without challenges. Adhesions and scarring from previous surgeries can complicate the procedure, requiring meticulous surgical planning and technique. Despite these technical difficulties, repeat resections provide an opportunity for prolonged survival and improved quality of life for patients who meet the criteria for surgery [16,20].

Bilateral pulmonary metastasectomy

Bilateral pulmonary metastasectomy poses unique challenges, as it requires addressing metastatic disease in both lungs while preserving adequate pulmonary function and minimizing perioperative risks. Despite the technical complexities, the procedure offers comparable survival benefits to unilateral resections when complete resection is achieved.

Comprehensive preoperative evaluation is essential for determining the feasibility of surgery. High-resolution imaging techniques, such as computed tomography (CT) and positron emission tomography (PET), play a crucial role in identifying the number, size, and location of metastatic lesions in both lungs. Intraoperative assessment, including manual palpation or thoracoscopic evaluation, ensures that smaller or undetected nodules are not missed during the procedure.

The timing and approach for bilateral resections are highly individualized. Simultaneous bilateral resections, performed via median sternotomy or clamshell thoracotomy, enable the removal of all detectable lesions in a single operation. However, this strategy may carry higher perioperative risks and requires careful planning to ensure sufficient postoperative pulmonary function. Alternatively, staged resections addressing one lung at a time are often preferred for patients with higher surgical risks or more extensive disease.

Long-term outcomes for patients undergoing bilateral pulmonary metastasectomy depend on factors such as the extent of disease, the feasibility of achieving complete resection, and the biology of the primary tumor. While technically demanding, the procedure remains a viable and effective option for patients with resectable disease in both lungs. Postoperative care, including close surveillance for recurrence and pulmonary rehabilitation, is critical to optimizing outcomes and ensuring long-term survival.

Prognostic factors for overall survival

Treasure and Macbeth emphasized the importance of patient selection in ensuring the credibility and benefits of pulmonary metastasectomy [45]. Several prognostic factors significantly influence overall survival outcomes for patients undergoing pulmonary metastasectomy (PM). These include the histology of the primary tumor, completeness of resection, disease-free interval (DFI), number and distribution of metastases, and lymph node

status. Understanding these factors is essential for optimizing patient selection and tailoring surgical interventions. Emerging evidence highlights the role of molecular and radiological markers in improving patient selection and refining prognostic predictions [48].

The histology of the primary tumor remains one of the strongest determinants of survival. Favorable outcomes have been observed in patients with germ cell tumors and colorectal cancer metastases, where five-year survival rates often exceed 40%. Conversely, more aggressive tumor types, such as sarcomas and melanomas, are associated with poorer outcomes, emphasizing the need for careful patient selection [7,25].

Achieving a complete resection (R0) is paramount to improving survival. Incomplete resections (R1 or R2) are strongly associated with poor outcomes and are generally considered a contraindication unless performed for palliative reasons. Studies consistently show that patients undergoing R0 resection have significantly better survival outcomes compared to those with residual disease [7,12].

The disease-free interval (DFI) also plays a critical role. Longer DFIs, particularly those exceeding 12 or 36 months, correlate with improved survival. Patients with synchronous metastases or shorter DFIs may still benefit from surgery, but their prognosis tends to be less favorable. For example, patients with DFIs shorter than 12 months generally have lower five-year survival rates compared to those with longer intervals [7].

The number and distribution of pulmonary metastases also impact outcomes. While patients with solitary metastases tend to have the best results, survival benefits can still be achieved in patients with multiple nodules if complete resection is feasible. Modern imaging techniques and intraoperative palpation are indispensable for detecting all metastases, particularly in patients with smaller or deeper lesions.

Lymph node involvement remains a major prognostic factor. Patients without lymph node metastases (N0) have superior outcomes compared to those with hilar (N1) or mediastinal (N2) involvement. While N1 disease carries a moderate impact on survival, N2 involvement is associated with significantly worse outcomes. Accurate preoperative staging using advanced imaging and, when necessary, invasive techniques is crucial for determining surgical eligibility.

Overall, the literature reports five-year survival rates following pulmonary metastasectomy ranging from 20% to 48%, and 10-year survival rates from 15.8% to 37.7%, across all primary tumor types [7,25]. These survival outcomes highlight the potential benefits of PM in carefully selected patients, even in cases with a high metastatic burden.

The laterality of metastases also influences survival outcomes. Patients with unilateral disease generally achieve better results than those requiring bilateral resections. However, bilateral resections can still provide survival benefits when complete resection is achievable and sufficient pulmonary reserve is preserved.

In summary, a comprehensive understanding of these prognostic factors enables clinicians to better identify patients who are most likely to benefit from pulmonary metastasectomy. Multidisciplinary collaboration remains critical in optimizing patient selection and maximizing the therapeutic potential of surgery.

Alternative local therapies to metastasectomy

For most tumor histologies, pulmonary metastasectomy (PM) remains the primary local treatment option, as no proven medical alternatives offer equivalent survival benefits. Exceptions to this include patients with nonseminomatous germ cell tumors or, potentially, metastatic breast cancer, where systemic therapies may achieve curative outcomes without surgical risks. In such cases, consultation with a medical oncologist is essential before proceeding with surgery [25].

For patients who do not meet the criteria for metastasectomy or are unable to tolerate surgery, ablative therapies provide an alternative. These nonoperative options include stereotactic body radiation therapy (SBRT), radiofrequency ablation (RFA), and microwave ablation (MWA), which have been increasingly employed in the management of pulmonary metastases [1,22].

Stereotactic ablative body radiation

Traditionally, radiation therapy has been used for palliation in patients with pulmonary metastases. However, retrospective studies have shown promising local control rates with SABR in select patients. Three-year control rates range from 75% to 90%, with particularly high success observed in small, well-defined lesions. Institutions typically use criteria such as poor surgical candidacy, centrally located lesions, or short disease-free intervals to identify appropriate candidates for SABR [1,9].

SABR is an excellent noninvasive alternative to surgery, delivering high-dose, highly conformal radiation while minimizing exposure to surrounding healthy tissues. Meta-analyses of colorectal cancer (CRC) patients undergoing SABR report local control rates of 81% at one year, 66% at two years, and 60% at three years. These outcomes highlight the expanding role of SABR as both a primary treatment and a consolidative therapy following surgery [49].

Transthoracic ablation

Radiofrequency ablation (RFA) and microwave ablation (MWA) are widely used transthoracic techniques that cause thermal necrosis of tumor tissue. RFA, which uses alternating current to induce coagulative necrosis, is particularly effective for lesions smaller than 3 cm and located away from critical structures. MWA uses higher frequencies and greater thermal energy, allowing it to treat larger tumors or those near vascular structures [1,9].

These techniques are most often employed in patients who are ineligible for surgery but meet specific criteria, such as controlled extrapulmonary disease, three or fewer nodules per hemithorax, and nodules ideally smaller than 2 cm. Studies on colorectal pulmonary metastases have shown that tumor size greater than 2 cm is associated with poorer survival and local control, while low carcinoembryonic antigen (CEA) levels (<10 ng/mL) predict better outcomes [49].

While PM remains the gold standard for patients eligible for surgery, SABR, RFA, and MWA are valuable alternatives for non-surgical candidates. The choice of treatment depends on tumor size, location, patient condition, and prior therapies. Emerging evidence suggests that MWA may offer improved local control compared to RFA, but further data from large cohorts are needed to validate these findings.

Future

Recent advancements in surgical techniques and perioperative management have expanded the possibilities for pulmonary metastasectomy (PM). Innovations such as radial staplers, near-infrared (NIR) imaging, and laser-assisted surgery are at the forefront of these developments, offering potential improvements in precision, safety, and outcomes.

Radial staplers, although not yet widely adopted, represent a promising innovation in thoracic surgery. Compared to conventional linear staplers, radial staplers allow for more precise wedge resections while preserving lung parenchyma and maintaining adequate surgical margins. Their role in PM is expected to grow as evidence supporting their benefits becomes more robust [3].

Laser-assisted surgery (LAS) is another emerging technique that offers distinct advantages in cases with multiple pulmonary metastases. LAS enables surgeons to perform precise and tissue-sparing resections, allowing for the removal of a higher number of metastases compared to stapler resections. Furthermore, its ability to preserve parenchyma makes it particularly valuable in patients with limited pulmonary reserve or recurrent disease requiring multiple resections. However, comparative studies evaluating LAS versus conventional methods remain limited, and further data are needed to validate its long-term safety and efficacy [3].

Near-infrared (NIR) spectroscopy, used alongside minimally invasive techniques like video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracoscopic surgery (RATS), is transforming the landscape of pulmonary metastasectomy. NIR imaging, often guided by the intravenous administration of indocyanine green (ICG), allows for real-time identification of intersegmental planes during segmentectomy. This technology enhances the precision of anatomical resections, reducing the risk of incomplete resection and improving outcomes [3].

As systemic therapies continue to evolve, their integration with surgical interventions is becoming increasingly relevant. Immunotherapy and targeted treatments, such as checkpoint inhibitors and tyrosine kinase inhibitors, have shown promise in reducing metastatic burden before surgery or preventing recurrence after metastasectomy. Future studies are needed to optimize the sequencing and combination of systemic therapies with PM to maximize survival [3,49].

While PM remains the gold standard for many patients, non-surgical options such as stereotactic ablative radiotherapy (SABR) and percutaneous ablation techniques are gaining traction. These approaches, which offer minimally invasive alternatives for non-surgical candidates, are continuously being refined with the advent of new technologies and improved imaging. Ongoing clinical trials are evaluating their role in extending survival and reducing complications in patients with pulmonary metastases [49].

The future of PM lies in the personalization of care. Advances in genomic and molecular profiling will enable clinicians to better predict which patients are most likely to benefit from surgery. Additionally, the identification of biomarkers for treatment response and recurrence risk will further refine patient selection, ensuring that interventions are tailored to individual tumor biology and patient characteristics [49].

Pulmonary metastasectomy is an ever-evolving field, driven by technological innovation, improved systemic therapies, and a deeper understanding of tumor biology. As these advancements continue, they hold the potential to further improve outcomes and expand treatment options for patients with metastatic lung disease.

In conclusion, pulmonary metastasectomy (PM) remains a cornerstone of treatment for selected patients with metastatic lung disease, offering a potential survival benefit in carefully chosen cases. The procedure's success is largely dependent on a multidisciplinary approach that incorporates the expertise of thoracic surgeons, oncologists, radiologists, and other specialists. This collaboration ensures that patients are appropriately selected based on key prognostic factors, such as histology, disease-free interval (DFI), number of metastases, and lymph node status.

The primary goals of PM are to achieve complete resection (R0), prolong survival, and, in some cases, improve quality of life by alleviating symptoms caused by metastatic lesions. Achieving clear surgical margins is critical, as incomplete resections (R1 or R2) fail to provide survival benefits and may expose patients to unnecessary risks.

Despite the significant advances in systemic therapies, including immunotherapy and targeted treatments, PM continues to play a vital role in the management of metastatic lung disease. For patients with isolated pulmonary metastases and controlled primary disease, surgery offers a unique opportunity for long-term survival that may not be achievable through systemic treatments alone.

Future research should focus on integrating metastasectomy with evolving systemic therapies to further enhance outcomes. The development of novel imaging techniques, more precise surgical tools, and predictive biomarkers will also help refine patient selection and optimize surgical planning. Ultimately, a personalized approach that considers tumor biology, patient condition, and treatment goals will be essential to maximizing the benefits of PM.

Pulmonary metastasectomy remains a valuable intervention in the multidisciplinary management of metastatic lung disease. By leveraging the latest advancements in surgery and systemic therapy, clinicians can continue to improve outcomes and provide meaningful survival benefits to selected patients.

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