

The role of minimally invasive sublobar resection in pulmonary metastasectomy: a narrative review

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Background and Objective: Pulmonary metastases are one of the main causes of pulmonary nodules, especially if they are multiple. Treatment of lung metastases as part of a multidisciplinary approach can sometimes be surgical when certain medical criteria are met, assuming resectability. Currently, the most commonly performed resection to treat metastasis, when indicated, is atypical segmentectomy. However, with technical improvements, other types of lung resections have begun to be performed, such as anatomical segmentectomies, which offer some advantages when patients are correctly selected. The objective of this narrative review is to understand the role of minimally invasive anatomical segmentectomies in the surgical treatment of lung metastases and discuss further future directions.

Methods: A narrative review was conducted using terms including “VATS” OR “thoracoscopy”, “RATS” OR “robotic thoracic surgery”, “segmentectomy” OR “sublobar lung resection”, “outcomes”, “pulmonary metastasectomy” and “minimally invasive thoracic surgery”. Included studies were published after 1927 to 2022 and were available in English and Spanish.

Key Content and Findings: A growing number of studies indicate us that anatomic sublobar resections are indicated in selected patients taking into account tumor localization and the characteristics of the patients, besides minimally invasive surgery also contributes to this type of surgery an early and intensified recovery with acceptable oncological results and morbidity and mortality comparable to open surgery. We summarize these indications and the role of minimally invasive surgery.

Conclusions: Anatomical segmentectomies play an important role in lung metastasis resection, especially in patients with centrally located nodules and poor respiratory lung function. Minimally invasive surgery combined with early and intensified recovery protocols have shown to reduce hospital stay, pleural drainage time, and postoperative pain. These revisions show that minimally invasive segmentectomies can be carried out with the same security as wedge resections. Although the evidence is weak and the results currently available, mainly obtained in retrospective studies, show that segmentectomies are equally valid and useful procedures than wedge resections. However, randomized studies are needed to generalize these conclusions.

Keywords: Lung resection; metastasis; metastasectomy; anatomic segmentectomy; minimally invasive surgery

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Introduction

One of the most common causes of lung nodules is metastasis, either from other primary tumors or, less frequently, from a primary lung tumor. There are certain types of primary tumors that are more likely to metastasize to the lung, such as colorectal cancer, head and neck tumors, sarcomas, melanoma, or kidney tumors (1).

This entity has, therefore, a special relevance from many points of view and especially from the surgical perspective. Since the first resection of metastatic lung lesions was described in the literature by Divis in 1927 (1), surgical resection has become a widely accepted treatment for lung metastases. This is due to the safety provided by surgery, which is less and less invasive and with rapid and intensified postoperative recovery, allowing for early patients discharge without increased complications rate. Furthermore, improvements in multidisciplinary treatments that allow for better systemic control of the disease, extending life expectancy of patients with stage IV carcinoma (2), has allowed an increase of lung metastasis patients being considered for surgical treatment.

There are currently no randomised clinical trials demonstrating the superiority of surgery for lung metastases over medical treatment. The evidence for treating patients with surgery is due to uncontrolled retrospective studies that show increased disease-free time (DFT) and lung disease free time, but have a selection bias since these studies include patients with advanced stage in a better clinical and oncological situation than patients with advanced stage but with more comorbidities and worse disseminated disease (3). When specific requirements are met, resection of these nodules is required as part of the multidisciplinary treatment of primary tumour (4); although some of the criteria for patient selection remain controversial. Pulmonary metastasectomy can be performed for different purposes; as discussed above, it can be part of multidisciplinary treatment or to restage the disease when relapse is suspected, i.e., to perform a biopsy to provide adjuvant treatment. The widespread use of minimally invasive surgery plays a very important role in the resection of these lesions, which often requires reoperation due to the appearance of new metastases, allowing for an early recovery with an efficiency in terms of oncological results comparable to open surgery (5).

The prognosis of lung metastasis depends on several factors such as lymphatic invasion, systemic treatment at the time of diagnosis, time off from disease, complete resection, surgical technique performed or, for example, the number

of metastases (3,6,7). As expert consensus recommends (8), surgical approach should advocate to spare as much lung parenchyma as possible, thus the most commonly performed operations to treat lung metastasis could be summarized in atypical and typical segmentectomies. Each of them has a specific indication that should be carefully evaluated in every patient.

Anatomical lung resections, although technically more demanding, may present some advantages over wedge resections (8), both for oncological and post-surgical results. No current narrative reviews have been found that shed light on the lack of controlled trials and retrospective studies limited by short follow-up and small cohorts.

The objective of this narrative review is to shed light on and clarify the evidence that currently exists on the surgical treatment of pulmonary metastases, specifically the value of minimally invasive sublobar resections in this setting and discuss further future directions. We present this article in accordance with the Narrative Review reporting checklist (available at <https://vats.amegroups.com/article/view/10.21037/vats-23-31/rc>).

Methods

This narrative review was conducted between January 3, 2023 and January 15, 2023 via query of MEDLINE indexed articles in the PubMed database maintained by the National Library of Medicine. Combinational search terms included “VATS” OR “thoracoscopy”, “RATS” OR “robotic thoracic surgery”, “segmentectomy” OR “sublobar lung resection”, “outcomes”, “pulmonary metastasectomy” and “minimally invasive thoracic surgery”. Inclusion criteria included articles indexed in MEDLINE, published after 1927, with most articles authored after 2005, available in the English and Spanish language and subject relevant of minimally invasive sublobar resection in pulmonary metastasectomy. Exclusion criteria were articles unavailable in English and Spanish and irrelevant to primary search terms.

All the authors reviewed all candidate articles and selected studies for inclusion based on verbal consensus and the above predefined inclusion and exclusion criteria. For a summary of the search strategy, see *Table 1*.

Minimally invasive anatomical metastasectomies

Evidence

Classically, the most commonly performed surgery for lung metastases has been wedge resections. However, the

Table 1 Summary of the search strategy

Items	Specification
Date of search	January 3, 2023 to January 15, 2023
Database searched	PubMed
Search terms used	“VATS” OR “thoracoscopy”, “RATS” OR “robotic thoracic surgery”, “segmentectomy” OR “sublobar lung resection”, “outcomes”, “pulmonary metastasectomy”, “minimally invasive thoracic surgery”
Timeframe	1927 to 2022
Inclusion and exclusion criteria	Inclusion: indexed in MEDLINE, published after 1927 (with most articles authored after 2005), available in the English and Spanish language, subject relevant of minimally invasive sublobar resection in pulmonary metastasectomy Exclusion: unavailable in English and Spanish, irrelevant to primary search terms
Selection process	All the authors reviewed all candidate articles and selected studies for inclusion based on verbal consensus and the above predefined inclusion and exclusion criteria

benefit of anatomical segmentectomies in the treatment of lung metastases is being considered. Currently, the greatest evidence is related to lung metastases of colorectal cancer. Liu *et al.* (9) observed improved DFT and pulmonary disease-free time (PDFT) in patients with colorectal cancer who underwent metastasectomy by anatomical segmental resection compared to wedge resections. Despite these results, they did not observe significant differences in overall survival. As mentioned above, a limitation of this study is its retrospective nature (9). Hernández *et al.* carried out a prospective 3-year follow-up study in patients with lung metastases from colorectal cancer, in which they found the same results regarding DFT and PDFT, although in the group of anatomical resections, most patients were lobectomies instead of segmentectomies (10). Shiono *et al.* (8) compared wedge resection and anatomical segmentectomy in patients with colorectal cancer. They found that segmentectomy was associated with increased DFT and survival at 5 years, as well as a decrease in local recurrence. However, this study failed to show any benefit in overall survival (11). Whether these results may be explained by resection margins and nodal evaluation remains controversial and not clarified up to date. One of the advantages of anatomical segmentectomy is the improvement in intrasegmental lymphadenectomy compared to limited resections (9), which could reduce locoregional recurrence. With reference to this issue, the role of lymph node metastases and lymphadenectomy is not clear; there are studies that show that the presence of mediastinal lymph node metastases is a prognostic factor

that indicates worse results, but there is a lack of evidence regarding the extent of lymph node involvement (11). Consequently, is difficult to establish whether the number of affected nodes is related to the number and location of lung metastases and the quality of the node dissection (10).

In addition, anatomical resections could ensure oncologically acceptable margins and thus reduce the risk of local recurrence in the resection margin (8,12).

Another advantage of anatomical segmentectomies is the possibility to resect central lung metastases or those not peripherally-located. With anatomical segmentectomy, it is possible to resect the metastasis with oncologically acceptable margins and preserve the rest of the healthy lung parenchyma, providing better lung function (10,11) and decreased risk of complications.

Minimally invasive surgery

Although surgery is widely used in the surgical treatment of lung metastases, it is not yet clear whether it is superior to conventional treatment (chemotherapy), since the available studies are not randomized clinical trials (13). It appears that metastases of colorectal cancer have a higher survival rate than those undergoing conventional treatment (9), although currently available studies are controversial (6,7,11). It is not clear that surgical treatment of pulmonary metastases increases survival compared to not operating, when it is decided not to operate it is usually due either because there are multiple metastases, or because they are patients with worse condition, therefore there would be a

selection bias of patients who are treated surgically, who are generally the healthiest, that is, they are more eligible to operate due to better general condition. Until there are no randomized studies, it is not possible to know the real role of surgery. On the other hand, there are non-randomized studies in favor of surgical treatment of metastases (8), but they only include patients with one type of primary tumor (e.g., colorectal cancer), and therefore the results cannot be extrapolated to metastases with another primary tumor types. There are inconsistencies due to several reasons, one of them could be due to the fact that the available studies include patients with tumors of different strains (colon cancer, urological cancer, head and neck cancer, gynecological cancer, etc.) and due to their biology, they could have different behaviors each time one of them.

For all these reasons, randomized studies will be necessary in which the included patients present a single primary tumor and therefore make the groups comparable.

This would help to establish the benefit of lung surgery in each type of metastasis (colorectal, urological, head and neck).

Minimally invasive surgery has had its detractors due to the fact that it is not possible to palpate the entire lung manually, since there are sometimes more pulmonary nodules than those revealed by the computed tomography (CT) scan.

However, the evidence related to this idea is rather weak (13,14). Studies, although not randomized, shows minimally invasive surgery is not worse than open surgery in terms of survival outcomes (15). The Society of Thoracic Surgeons decreed a consensus document to standardize lung metastasectomy. This document recommends minimally invasive surgery with several conditions: (I) that free margins are achieved, (II) lymph node dissection or biopsy, and (III) parenchyma-saving surgery avoiding lobectomy and pneumonectomy, when possible (8). Along with the oncological reasons, minimally invasive surgery also brings the advantages inherent to the approach, such as reduced hospital stay, shorter duration of pleural drainage, as well as reduced postoperative pain. Ultimately, minimally invasive surgery is a safe option with few complications compared to open-ended segmentectomy.

Video-assisted thoracic surgery (VATS) anatomical metastasectomies

As mentioned above, and although the evidence is not strong, VATS anatomical resections can improve time off from disease, so they should be considered whenever it is

possible to perform surgical treatment of them, offering a surgical opportunity, especially in patients with altered pulmonary function and/or central lesions. DFT is not affected by the surgical approach to colorectal cancer (VATS *vs.* thoracotomy) (16). VATS anatomical segmentectomy confers some advantages in the surgical treatment of lung metastases. For example, in patients with several metastases in the same segment, it allows them to be resected all at the same time. Furthermore, in central lesions, this type of resection plays a primary role, preserving the rest of the lung parenchyma and avoiding lobectomy (17,18). In addition, thoracoscopy surgery allows for early and intensified recovery of the patient, avoiding open surgery and its inconveniences in relation to postoperative pain and recovery. VATS surgery is not inferior to open approaches in terms of staging of the intrapulmonary lymph nodes, allowing to perform a minimally invasive lymph resection for proper staging and to avoid locoregional recurrence in the case of lymph node involvement (11).

It is possible to think that anatomical segmentectomies may be related to worse outcomes than wedge resections, however, Bédar *et al.* reported a mortality rate of 0.8% in all surgeries, guaranteeing comparable results to wedge resections (19). In a series of 785 patients, 30-day mortality was 1.1% and overall morbidity was 34.9% in patients undergoing anatomical segmentectomy (18).

Robotic anatomical metastasectomies

Robotic surgery has emerged as a valid alternative to VATS in lung resections (20,21), however there are still some controversies that it needs to face. The first, and probably the most relevant one, is the lack of tactile feedback preventing traditionally advocated 'lung nodule palpation' (22). Some authors have encountered this difficulty even in VATS, where palpation through the thoracoscopic or the utility ports or even indirect palpation using thoracoscopic instruments could become challenging (23,24). With the robotic approach, given the location of the ports and, in some cases, the lack of utility incision, finger palpation is very difficult if not almost impossible. For this reason, a wide range of location strategies have been developed, from navigational bronchoscopy with indocyanine green injection (25) to wire and hybrid approaches (26) for intraoperative (27) or delayed (28) location. In addition, with surgeons' experience, several visual strategies can be developed in the robotic platform to detect irregularities in the lung parenchyma that could help nodule location without other resources. If palpation is not possible and

other strategies for marking and locating the nodules not readily available, resection following anatomic landmarks can be achieved with or without 3D modelling and reconstruction.

As previous disadvantages are overcome, there are multiple advantages related to robotic assisted thoracic surgery. Among them, small structures' dissection, especially in the posterior areas of the thorax. This improved dissection, together with better visualization provided by the platform, has increased, in our experience and in other authors', the number of segmentectomies performed, including atypical segmentectomies (29,30). Furthermore, it also contributed to better margin achievement, shorter length of stay, chest tube duration and rate of conversion to open (29). Robotic surgery also facilitated lymph node dissection with a larger number of intrasegmental stations dissected when compared to VATS segmentectomy (30).

Although randomized studies comparing robotic to VATS and open approaches in the setting of pulmonary metastasectomy seem difficult to conduct, up to date, expert consensus advocates for minimally invasive surgery, including robot-assisted thoracic surgery (RATS) approaches, for pulmonary metastasectomy whenever it is possible (8).

Oncological outcomes

It should be emphasized that segmentectomies ultimate goal should be to obtain acceptable oncological results.

It is necessary to prioritize patient safety and oncological outcomes, at least to obtain similar results compared to wedge resections, which have been the flagship in the surgical treatment of lung metastases in recent times. Shiono *et al.* conducted a retrospective study comparing segmentectomies with wedge resections in patients with lung metastases; the recurrence rate of the resection margin was higher in patients who underwent wedge resection compared to segmentectomy (7.3% *vs.* 2.0%; $P=0.035$). Multivariate analysis revealed that segmentectomy was a significant favorable factor for recurrence (hazard ratio =0.63; 95% confidence interval: 0.44–0.87; $P=0.005$), but not for overall survival (hazard ratio =0.65; 95% confidence interval: 0.38–1.05; $P=0.080$). What they observed was that patients undergoing segmentectomy developed prolonged air leak more often (5.1% *vs.* 1.8%) ($P=0.048$). In addition, the DFT at 5 years was 48.8% in patients with segmentectomy and 36.0% in patients with wedge resections (21). Several studies have compared the oncological results between non-

anatomical pulmonary resections and anatomical pulmonary resections with similar conclusions: increase in DFT and PDFT (7,8), thus providing some evidence to consider anatomical segmentectomies as equally valid and useful procedures than wedge resections regarding oncological results and even improving DFT and PDFT.

Survival

Regarding mortality results, above all, it is necessary to know whether anatomical segmentectomies are safe procedures and not inferior in this respect to wedge resections. Schuchert *et al.*, in their series of 785 anatomical segmentectomies, presented a 30-day mortality of 1.1% and a morbidity of 34.9% (13). Atkins *et al.* presented a series of 77 anatomical segmentectomies, with a mortality rate of 2.6% and a morbidity rate of 32.5% (5). Shiono *et al.*, in their study, showed significantly increased postoperative complications in patients submitted to segmentectomy ($P<0.001$) compared to wedge resections. However, they did not present any death 30 days after surgery and only 2 (0.4%) occurred 90 days after surgery (8). It can be stated that segmentectomies can be performed safely and with acceptable mortality and morbidity without increasing the patients' risk of postoperative morbidity and mortality.

Discussion

Surgical treatment of lung metastases has become a very common procedure and requires a multidisciplinary team consensus when it comes to selecting the patients that could benefit most from such surgery. Consideration should be given to the type of surgery to be performed. As previously mentioned, anatomical segmentectomies play an important role in the treatment of such lesions in very specific cases, favoring pulmonary parenchyma sparing, margin achievement and lymph node resection. As previously mentioned, regarding local recurrence, it is true that segmentectomy could play a very important role when compared to wedge resections. Shiono *et al.*, in their retrospective case series comparing segmental resections *vs.* wedge resections, showed that local recurrences were lower in patients undergoing segmentectomy compared to wedge resections (2% *vs.* 7%) (21).

However, it is necessary to take into account that wedge resections play a very important role in surgical treatment, since, if they are performed with a minimally invasive approach together with intensified recovery protocols,

Table 2 Key findings

Anatomic sublobar resections are indicated in selected patients taking into account tumor localization and the characteristics of the patients. Results are not worse than in wedge resections

Minimally invasive surgery also contributes positively to this type of surgery and early and intensified recovery with acceptable oncological results

Randomized trials are needed to generalise these key findings

there are surgeries with very few comorbidities that can also benefit oncological outcomes. For these reasons, careful selection criteria should be established to classify which patients should be operated on and whether a wedge resection or anatomical segmentectomy should be performed.

Strengths and limitations

The limitations of this review are mainly due to the lack of randomized clinical trials that exist. As strengths of this review, it has been attempted to summarize the existing evidence regarding the role of minimally invasive sublobar resection in pulmonary metastasectomy.

Conclusions

Anatomical segmentectomies play an important role in lung metastasis resection, especially in patients with centrally located nodules, poor respiratory lung function and those who otherwise would need a lobectomy. They also may provide better lymph node assessment. In addition, minimally invasive surgery combined with early and intensified recovery protocols have shown to reduce hospital stay, pleural drainage time, and postoperative pain, along with the individual benefits of VATS and RATS.

Each case should be individually considered in a multidisciplinary team discussion and careful attention to the risks and benefits of the procedure should be evaluated taking into account the clinical situation of each patient and their preferences.

Although the evidence is weak and there are no randomized studies, the results currently available, mainly obtained in retrospective studies, show that segmentectomies are equally valid and useful procedures than wedge resections, even improving DFT and PDFT.

If possible larger and randomized studies are needed to shed light on the type of patient that should be treated surgically, as well as the type of resection that should

be performed in each case in order to provide the best oncological results.

For a summary of the key findings, see *Table 2*.

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appropriately investigated and resolved.

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