Review

Current status of pulmonary metastasectomy

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Summary

Malignant disease’s ability to metastasize remains one of the major obstacles when treating patients with cancer. The change from loco-regional to systemic disease usually renders the patient beyond surgical treatment, as local treatment with surgery in a systemic disease is usually considered without benefit. However, numerous retrospective studies have demonstrated that resection of metastases limited to the lungs may be associated with prolonged survival. No prospective, randomized studies have been published, and most series compare highly selected patients with historical data for unresected patients. In this article, we discuss the current status on pulmonary metastasectomy. Preoperative assessment and selection of surgical candidates is covered. The different surgical strategies including surgical approach, unilateral versus bilateral exploration, lymph node dissection, and repeat surgery are discussed. Finally, we review some of the common tumors that metastasize to the lungs, the role of metastasectomy in their treatment and the prognostic factors with impact on survival.

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1. Introduction

Malignant disease’s ability to metastasize remains one of the major obstacles when treating patients with cancer. The lungs are one of the most common organs to which cancer metastasizes, and approximately 30% of all cancer patients will develop lung metastases at some point [1].

The change from loco-regional to systemic disease usually renders the patient beyond surgical treatment, as local treatment with surgery in a systemic disease is usually considered without benefit. When systemic disease is present, chemotherapy is the mainstay of treatment and radiation and/or surgery is reserved for palliative measures only. However, that is not always the case.

Pulmonary metastasectomy has been performed for decades; Alexander and Haight [2] published the first series of pulmonary metastasectomies in 1947, and proposed the first set of selection criteria for surgery. Thomford [3] revised these in 1965 and, with minor changes, they remain relevant today. They are: (1) primary tumor is controlled, (2) no extrathoracic lesions are present (with the exception of hepatic lesions in which it is possible to completely remove both hepatic and pulmonary metastases), (3) the metastases seem technically resectable, and (4) the general and functional risks are tolerable. Since then, numerous studies have demonstrated 5-year survival rates of 30—50% for a large variety of primary tumors in highly selected patients. These survival rates are far superior to any other treatment. The landmark study of the International Registry of Lung Metastases accrued 5206 patients with different primary tumor histologies treated with pulmonary metastasectomy from 18 thoracic surgical departments in Europe, the USA and Canada. Survival after complete metastasectomy at 5, 10, and 15 years was 36%, 26%, and 22%, respectively, whereas survival after incomplete metastasectomy was 13% and 7% at 5 and 10 years, respectively. The discriminatory power of this study confirmed that pulmonary metastasectomy is potentially curative. Furthermore, multivariate analysis showed that disease-free interval (DFI) < 36 months and more than one metastasis were independent risk factors. Numerous subsequent studies have supported these findings. No prospective, randomized studies have been published and most series compare highly selected patients with historical data for unresected patients.

In this article, we discuss the current status on pulmonary metastasectomy. Preoperative assessment of these patients and different surgical strategies are covered. Finally, we review some of the common tumors that metastasize to the lungs, the role of metastasectomy in their treatment and the prognostic factors with impact on survival and the role of metastasectomy in their treatment.

2. Method and search strategy

Studies and articles were identified using online searches of The U.S. National Library of Medicine via
www.Pubmed.com, regarding the topic of pulmonary metastasectomy. Several searches were conducted to retrieve all potentially relevant articles; the searches were performed between October 2009 and January 2010. Terms and keywords associated with pulmonary metastasectomy were used and included, for example, ‘pulmonary metastases’, ‘pulmonary resection’, ‘thoracoscopy’, and ‘cervical and pulmonary metastasectomy’. None of the retrieved studies were specifically excluded from this review. However, due to the advancement in surgical and anesthesiological techniques, we disregarded studies published before 1980 unless they were of historic value.

All studies identified were retrospective case series and, thus, no randomized trial has been published.

3. Diagnosis and preoperative imaging

A pulmonary lesion in a patient with a history of cancer could represent metastatic disease. It should always be further investigated, as it also could represent a new lung primary and, thus, a different treatment strategy.

In the preoperative assessment of a patient with a pulmonary lesion suspected to be a lung metastasis, computed tomography (CT) has become the standard. With the invention of fast high-resolution CT (HRCT), the size of pulmonary nodules detected may be as small as 3 mm, although the sensitivity at this size diminishes. Margaritora and colleagues [4] evaluated accuracy with conventional CT or HRCT, and found a sensitivity of 100% for nodules measuring 10 mm for both types of scans. However, the sensitivity for nodules measuring less than 6 mm dropped to 62% with conventional CT and to 48% with HRCT. The overall sensitivity for pulmonary metastases was 82.1%.

Diedrich and colleagues [5] reported a sensitivity of 69% for nodules smaller than 6 mm with helical CT and 5-mm slice thickness. For nodules larger than 6 mm, the sensitivity was 95%. Pfannschmidt and colleagues [6] evaluated the slice thickness of helical CT. They found that reducing the slice thickness from 5 to 3 mm resulted in statistically more lesions found during preoperative imaging compared with surgically resected lesions with an overall sensitivity of 88.8% for 3-mm slices and 83.7% for 5-mm slices. The sensitivity in the detection of nodules measuring 1–4 mm was 74.7% for 3-mm slices and 64.0% for 5-mm slices.

With the improvement in scanning techniques, the need for perioperative bimanual palpation of the lung has been questioned. However, with the diminishing sensitivity with nodule size, bimanual palpation of the lung during surgery may still detect small lesions missed by preoperative imaging.

The positron emission tomography (PET) scan is now widely used in the evaluation of cancer patients because of its ability to detect malignant disease. The uptake of the 18F-labeled glucose analog is increased in cells with high metabolic turnover and is, thus, concentrated in malignant cells compared with normal tissue. A study by Fortes and colleagues [7] found an overall sensitivity of 67.5% for the PET scan in the detection of pulmonary metastases. If the lesion was greater than 10 mm, the sensitivity increased to 87.8%. For lesions smaller than 10 mm, the sensitivity was only 29.6%. The sensitivity also varied with primary tumor histology, as only 44% of sarcoma metastases were positive in contrast to 93% for squamous cell carcinomas. The authors conclude that PET scan cannot stand alone in the detection of pulmonary metastases, but it can be useful as an adjunct to the CT scan and also to exclude extrathoracic disease in the selection of patients for surgery.

4. Lymph node status

The question of lymph node sampling and/or involvement remains controversial. The performance of lymph node dissection during pulmonary metastasectomy is infrequent and varies between institutions. Of all the patients in The International Registry of Lung Metastases, only 4.6% underwent lymph node dissection. In a recent survey by Internullo and colleagues [8] amongst the members of the European Society of Thoracic Surgeons, 55% perform mediastinal lymph node sampling whereas 33% perform no nodal sampling at all. The rate of lymph node involvement varies between primary tumors. Pfannschmidt and colleagues [9] performed systemic lymph node dissection in concurrence with pulmonary metastasectomy in 245 patients with metastases from colorectal carcinoma, renal cell carcinoma and sarcoma. Nodal involvement was more frequent in renal cell carcinoma (42.4%) and colorectal carcinoma (31.3%) than sarcomas (20.3%). Several studies have found the presence of positive intrathoracic lymph nodes an ominous prognostic factor. Ercan and colleagues [10] found a 3-year survival of 69% for patients without lymph node involvement versus 38% in patients with positive lymph nodes. Saito and colleagues [11] reported a 5-year survival of 53.6% for patients without hilar or mediastinal node involvement versus 6.2% at 4 years for patients with positive nodes.

In remains unclear whether the removal of these lymph nodes is associated with a survival benefit or merely allows for a more accurate postoperative staging and guidance for additional oncological treatment. The above-mentioned authors proposed the latter.

4.1. Surgical approach

The original surgical approach to pulmonary metastasectomy was simultaneous bilateral thoracotomy or staged surgery. Posterolateral thoracotomy provides excellent exposure of the entire lung, and allows total bimanual palpation of the lung for undetected pulmonary lesions missed by preoperative imaging. The disadvantage is postoperative muscle pain and respiratory problems. The midline sternotomy used in cardiac surgery can provide access to both lungs while sparing the patient from some of the postoperative morbidity associated with thoracotomy. However, access to the posterior parts of the lung is limited, especially the left lower lobe, and, thus, lesions in these areas can be technically difficult to resect. The clamshell incision, which involves bilateral simultaneous thoracotomies and a sternal split, has also been used in pulmonary metastasectomy. While providing excellent exposure to both hemithoraces, it combines the worst of thoracotomy and sternotomy with regard to postoperative morbidity.
The need for bilateral exploration of the lungs is based upon the assumption that pulmonary metastases represent a systemic disease with a great probability of bilateral spread, even though metastases are not detectable by preoperative imaging. Thus, unilateral exploration would result in incomplete resection due to undetected contralateral lesions. This was successfully challenged by Roth and colleagues [12] when they found that bilateral exploration by sternotomy provided no survival benefit when compared with unilateral exploration by thoracotomy. In a more recent study, Younes and colleagues [13] investigated the need for bilateral exploration in patients with unilateral disease from various primary tumors. They performed 179 unilateral thoracotomies in patients with unilateral disease and 88 bilateral thoracotomies for bilateral disease, and followed the patients for contralateral disease-free survival and overall survival. They found no significant difference in survival in patients with unilateral disease with recurrence in the contralateral lung when compared with the patients, who had undergone bilateral thoracotomy. The authors concluded that delaying contralateral thoracotomy until disease becomes radiologically evident does not affect survival and that bilateral exploration for unilateral disease is not indicated.

The newest surgical approach to pulmonary metastasectomy is by video-assisted thoracoscopic surgery (VATS). This minimally invasive approach provides excellent exposure of the lung surface, reduces surgical trauma, minimizes postoperative pain, provides earlier patient mobilization and decreases hospital length of stay. Pulmonary metastases are often small nodules located in the periphery of the lung, well suited for wedge resection by stapler and the VATS approach. The disadvantage is the loss of tactile sensation and the ability to bimanually palpate the entire lung and, hence, miss lesions undetected by imaging. Thus, the quality of the preoperative imaging becomes critical to success with VATS surgery.

McCormack and colleagues [14] have addressed this issue. They retrospectively reviewed 72 patients, who underwent pulmonary metastasectomy by thoracotomy. When the number of metastases removed during surgery was compared with preoperative imaging, they found a 42% error rate and that CT scan underreported the number of lesions in 25% of patients. In another study, they prospectively compared CT scan results, VATS and confirmatory open thoracotomy with bimanual palpation and found a 56% failure rate of CT and VATS to detect all lesions [15]. The study was ended preemptively due to the failure rate, and they concluded that VATS should be reserved for solely diagnostic purposes. However, these studies are confounded by the use of older CT scanners.

More recent studies have demonstrated equal survival outcomes with VATS surgery as compared with open thoracotomy. Landreneau and colleagues [16] performed 80 VATS procedures and reported a 5-year survival of 30.8% for patients with colorectal pulmonary metastases resected. Mutsaerts and colleagues [17] found no significant difference in survival in patients who underwent VATS compared with patients who underwent VATS followed by confirmatory thoracotomy. Only patients with a single, peripherally located lesion, and <3 cm, preoperatively detected by a CT scan were included in this study. Another study by Mutsaerts and colleagues [18] with VATS followed by confirmatory thoracotomy found that in patients with only one lesion detected on preoperative CT, no further lesions were found by confirmatory thoracotomy. Gossot and colleagues [19] investigated the VATS approach in patients with two or less pulmonary metastases from sarcoma and found a 5-year survival rate of 52.5%.

There is no doubt that open surgical exploration can detect lesions missed by preoperative imaging. However, evidence of prolonged survival with the removal of microneedles with a size of 1–2 mm, missed by CT scan and detected by bimanual palpation, does not exit. The assumption of this would be that removal of a 1–2-mm lesion results in survival benefit whereas overlooking a 0.5-mm lesion has no influence of survival. A lesion of that size would also be missed preoperatively, even with modern CT.

Another advantage of VATS is the preservation of the ability to perform repeat operations. VATS results in fewer pleural adhesions than thoracotomy, and does not complicate a potential repeat operation by thoracotomy [20].

To date, no randomized studies regarding VATS versus open surgery have been published. At present, it seems that VATS can be considered for diagnosis and for pulmonary metastasectomy in the presence of few, peripherally located lesions. In case of discrepancy between preoperative imaging and perioperative findings or inability to achieve radical surgical margins, conversion to open surgery should be mandatory.

4.2. Recurrence of disease and repeat surgery

The recurrence of disease after pulmonary metastasectomy is not uncommon. In the International Registry of Lung Metastases [21], the rate of recurrence of disease was 53% for all patients, who underwent complete resection. The rate of recurrence varied amongst the different primary tumors, with sarcomas and melanoma being more frequent (64%) than epithelial tumors (46%). The site of recurrence also differed with sarcoma (66%) being the most frequent as regards intrathoracic relapse in contrast to melanoma where 73% relapsed extrathoracically. The 5-year survival for all patients with repeat surgery was 44%.

Several later studies have analyzed the impact on survival after recurrence of disease and repeated pulmonary metastasectomy, and have confirmed these findings. In patients with recurrence of colorectal metastases, studies by Pfannschmidt [22], Welter [23], and Ogata [24] have reported a 5-year survival of 54.6%, 46%, and 33%, respectively. For sarcomas, studies by Briccoli [25], Harting [26], and Rehders [27] have reported 5-year survival rates of 32%, 22.6%, and 36%, respectively.

Jaklitsch and colleagues [28] investigated the value of sequential pulmonary metastasectomy from various primary tumors. As many as 54 patients underwent at least two metastasectomies and up till six. They found that 5-year survival was stable (>33%) until the 5th or subsequent procedure. With the loss of local control due to unresectable tumor in the thorax, further survival dropped to a 2-year survival of 19%. The authors concluded that repeated
metastasectomy was well justified as long as local control within the thorax was feasible.

None of the above-mentioned studies have found repeat surgery to be an ominous prognostic factor. Thus, if a patient fulfils the initial criteria for pulmonary metastasectomy, repeat surgery does not have an adverse effect on survival. A possible explanation for this could be that these patients represent an even further-selected subgroup of less malignant tumors. Further, the patients must be in good condition to undergo a second operation and, thus, only good candidates for surgery are selected.

It remains unclear whether resection of all metastases at one time is critically important in terms of survival. Naturally, during each surgery, all malignant disease should be removed. Lesions undetected by preoperative imaging or during surgery, but detected during follow-up, may not alter survival as long as they are resected before they become unresectable.

The current status and recent results of pulmonary metastasectomy from various primary tumors are discussed in the following sections.

4.3. Colorectal cancer

Approximately 10—20% of patients with colorectal cancer will develop pulmonary metastatic disease [29]. Isolated pulmonary metastases without extrathoracic disease are, however, rare and account for as little as 2% of patients with metastatic colorectal carcinoma [30]. In a recent article, Pfannschmidt and colleagues [31] evaluated the current status of surgical resection of pulmonary metastases from colorectal carcinoma and prognostic factors significant in patient selection. Inclusion criteria included studies published between 1995 and 2006, more than 40 patients and patients included in the studies should be no later than 1980. Twenty studies were included.

The overall 5-year survival after pulmonary metastasectomy ranged between 38.3% and 63.7% with a median of 52.5%. They suggested that achieving R0 resection is most critical for postoperative survival. In their article, two studies confirmed this and three studies could not. More than 50% of the patients included presented with a single metastasis and seven studies demonstrated a significantly better survival with a single lesion versus multiple lesions. Thus, patients with a single lesion seem to benefit more from pulmonary metastasectomy than patients with multiple metastases. An elevated level of prethoracotomy carcinoembryonic antigen (CEA) had an adverse effect on survival in the majority of studies. However, patients with an elevated level of CEA still fared better than unresected patients, and they concluded that even though an elevated level of CEA is an ominous prognostic factor, these patients should not be excluded from pulmonary metastasectomy. The DFI, one of four different prognostic factors in the International Registry of Lung Metastases, was only significant in two studies and, in the majority of studies, DFI did not influence survival.

Approximately 15% of patients resected for colorectal carcinomas can be expected to have hepatic metastases at the time of exploration [32]. As many as 50% will eventually develop liver metastases, and liver resection for metastatic disease is an established treatment [33]. If control of liver metastases can be achieved, combined resection for liver and lung metastases does not have an adverse effect on survival [34,35].

Shiono and colleagues [36] investigated the prognostic effect of histopathological variables such as the presence of aerogenous spread with floating cancer-cell clusters within the alveoli (ASFCs) and bronchial, vascular, lymphatic or pleural invasion. They investigated 136 metastatic lesions from 89 patients. Patients without any of these features had a remarkable 5-year survival of 93.3% while in patients positive for both AFSC and vascular invasion it was 24.7%. The influence of tumor biology on survival seems emphasized by this study.

4.4. Renal cell carcinoma

Approximately 25—30% of patients with renal cell carcinoma will have metastatic disease at diagnosis and a further 30% of patients will eventually develop metastases, with the lungs being the most common organ [37]. Previous studies have demonstrated 5-year survival rates between 31% and 53% from renal cell carcinoma, after pulmonary metastasectomy [38—40].

Of the studied prognostic factors, completeness of resection was found to be a significant prognosticator of survival in all studies. The number and size of metastases also influenced survival, with few and small metastases having a positive effect on postoperative survival. Further, with a longer DFI, a better survival was reported compared with short DFI. However, the latter prognostic factors could only be verified in some of the above-mentioned studies.

5. Malignant melanoma

Surgical treatment of lung metastases from melanoma is controversial, as the expected outcome is much poorer than for other primary tumors. The ability of malignant melanoma to disseminate widely causes the number of patients eligible for pulmonary metastasectomy to be very small, as patients with isolated pulmonary metastases are rare. Once malignant melanoma has spread to a distant site, the median survival is 8 months, and the 5-year survival is less than 5% [41]. Previous studies with pulmonary metastasectomy from malignant melanoma have demonstrated 5-year survival rates between 22% and 33% [42—44]. This is, however, far superior to medical treatment alone. Of the prognostic factors investigated, completeness of resection seems to be the strongest, as patients without R0 resection have a survival similar to non-resected patients. Further, presence of only a single metastasis and long DFI seem associated with a positive effect on survival. Given the grim prognosis for patients with metastatic melanoma, pulmonary resection is a reasonable option in carefully selected patients.

5.1. Head and neck cancer

Head and neck cancer is comprised of a heterogeneous group of carcinomas such as squamous cell carcinoma of the
larynx, pharynx and oral cavity, and glandular and adenoid cystic carcinomas. They usually metastasize to regional lymph nodes and then to more distant organs, with the lungs being the most frequent [45]. Ferlito and colleagues reported an incidence of metastases of 4.2–23.8% in squamous cell carcinomas and 37.7–58.8% in adenoid cystic carcinomas. The number of reports evaluating the benefit of pulmonary metastasectomy in head and neck cancers is limited. Studies by Mazer [46], Wedman [47], Liu [48], Chen [49], and Winter [50] have reported 5-year survival ranging from 20.9% to 59%. Survival varies with primary tumor histology with best survival reported for adenoid cystic carcinoma followed by glandular and squamous carcinoma (84%, 64%, and 34%, respectively in the study by Liu). Reported prognostic factors with significant influence on survival were completeness of resection and long DFI. Due to the small number of studies, the benefit of pulmonary metastasectomy in head and neck carcinomas is still unclear. Most authors, however, advocate resection if the patient fulfills the standard criteria for pulmonary metastasectomy.

5.2. Breast cancer

The role of pulmonary metastasectomy in metastatic breast cancer is unclear. Several studies have shown decent 5-year survival ranging from 30% to 54% [51–53]. However, it is doubtful whether these survival rates are better than those achieved by modern, systemic oncological treatment with chemotherapy and/hormone therapy. In a study by Rahman and colleagues [54] with 1581 patients treated with chemotherapy, a response rate of 65%, including 16.6% complete responders, could be demonstrated. The overall median survival was 21.3 months and 41.8 months for complete responders. The median survival for resected patients is not superior to patients treated with modern chemotherapy.

Planchard and colleagues [55] and Welter and colleagues [56] found no difference in survival between complete and incomplete resection, which certainly questions the impact of surgery on survival. McDonald and colleagues [57] even found a better 5-year survival for patients with incomplete resection (41.1%) versus complete resection (35.6%). However, the difference was not significant.

Of prognostic factors associated with longer survival in patients with resectable pulmonary disease, a long DFI and single metastasis have been demonstrated as positive prognosticators.

The recent study by Welter [56] also investigated hormone receptor status of the resected nodules and found the presence of positive estrogen receptor or Her2-neu receptor status to have a positive impact on survival.

At present, it seems that the value of pulmonary metastasectomy in patients with breast cancer is of diagnostic purpose. However, the value of histological examination of pulmonary lesions cannot be underestimated to find and resect a possible new lung primary, or, in case of confirmed breast cancer metastases, direct further treatment with regard to grading, estrogen receptor, and Her2-neu receptor status.

5.3. Testicular cancer

Non-seminomatous germ cell tumors are characterized by a wide dissemination, with the lungs being the most frequent organ and a high sensitivity to cisplatin-based chemotherapy. The cure rate has greatly improved to a range of 59–82% over the past decades [55,58,59]. Metastectomy is performed after completion of cisplatin-based chemotherapy. Surgery is directed at removing residual lung disease to determine further treatment. Therefore, aggressive resection of all suspicious lesions is required for prognostic assessment. In case of necrosis/fibrosis or teratoma, no further treatment is required in contrast to detection of viable cancer cells, which require additional chemotherapy. The presence of multiple metastases, elevated tumor marker levels of human chorionic gonadotropin (hCG) or alpha fetoprotein (AFP) or the presence of viable tumor cells in the resected nodules have been demonstrated to be associated with an adverse effect on survival [60–62].

5.4. Osteosarcoma

Osteosarcoma patients are particularly prone to develop pulmonary metastases. A total of 10–20% of patients will have detectable pulmonary lesions at initial diagnosis and up till 70% of patients will develop pulmonary metastases [63–65]. Failure to control thoracic disease is the cause of death of nearly all patients with metastatic osteosarcoma [66]. As discussed previously, sarcoma predominantly relapses in the lungs. Therefore, several studies have shown a possible survival benefit in patients with metastatic osteosarcoma when pulmonary resection is performed aggressively and repetitively. Studies by Tsuchiya [67], Kager [68], and Suzuki [69] have shown 5-year survival rates between 29% and 43%. In almost all reports, the radicality of resection is a strong prognostic factor, as patients without R0 resection have a very poor prognosis. Conflicting data have been reported with regard to DFI, number of metastases, size of metastases and laterality, and the prognostic importance of these factors remains unclear.

Surgery remains the mainstay of treatment in the case of disseminated osteosarcoma to the lungs, and in non-metastatic disease, chemotherapy also plays an important role in prolonging survival [65]. The addition of neo-adjuvant chemotherapy before pulmonary resection has also been demonstrated to be associated with a positive effect on survival, in particular when histologic response to chemotherapy can be demonstrated. However, patients treated only with chemotherapy have a very poor prognosis [70], and surgical resection of metastatic disease to the lungs remains the most efficient therapy.

5.5. Soft tissue sarcoma

Soft tissue sarcoma (STS) is a heterogeneous group of malignant tumors with more than 50 histological subtypes [71]. In metastatic STS, the lungs are the most frequent organ affected and is seen in 20% of patients [72], less than with osteosarcoma. Several studies on pulmonary metastasectomy for STS have been published and the 5-year survival ranges from 25% to 43% [73–76]. All these studies showed
that complete surgical resection of pulmonary metastases is a significant prognostic factor of STS. There is less concordance in terms of other prognostic factors such as number, size, and laterality of metastases. However, in most studies, a short DFI was associated with a worse prognosis. Usually, the many different histologies of STS are grouped together and reported as a whole. However, studies by Billingsley [74], and Casson [77] have demonstrated histology of the primary STS to be a significant prognostic factor of postoperative survival. Malignant fibrous histiocytoma, rhabdomyosarcoma, and synovial sarcoma are regarded as more favorable while liposarcoma or peripheral nerve sarcomas have a worse prognosis. In general, metastatic STS is less sensitive to chemotherapy than osteogenic sarcoma, and the response and survival data with chemotherapy remain disappointing. Therefore, surgical treatment of metastatic pulmonary STS is the best hope for cure in selected patients.

6. Conclusion

Patients with untreated metastatic disease have a 5-year survival rate of less than 5—10% and, for a patient with isolated metastatic disease to the lungs, pulmonary metastasectomy is often the best hope for cure. It is a safe and effective treatment that leads to possible cure in selected patients. Regardless of primary tumor, completeness of resection is the key to improved survival. Low morbidity and mortality rates, in contrast with the lack of any other effective systemic oncological treatment, justify the aggressive approach of surgery. Thoracoscopic resection is a valid option in selected patients with few, peripherally located metastases. In case of recurrence of pulmonary disease, and if the patient fulfills the initial criteria for pulmonary metastasectomy, repeat surgery should be performed. Aggressive postoperative follow-up is warranted. The patient should be treated in close collaboration between the medical oncologist, diagnostic radiologist and thoracic surgeon.

However, despite numerous studies and decades of metastasectomies, the lack of randomized studies continues to make the effect of pulmonary metastasectomy questionable. Most studies have been retrospective and the biases are many: possibly, only patients with slow-growing tumors are referred; possibly only patients in good physical condition are referred. Most reports recommend pulmonary metastasectomy for a properly selected group of patients. However, the case-mix from which patients are selected for surgery is rarely described.

Whether the survival of these patients is based on selection rather than surgery is still not clear. As argued by Treasure and colleagues [78,79], amongst others, it remains ‘a common practice based on weak evidence.’

Further, prognostic factors that determine which patients will benefit from surgery are still not clearly established. To determine how to select surgical candidates for pulmonary metastasectomy more precisely, further analysis of prognostic factors is evident and the need for a prospective, randomized, multicenter study is clear. The recently opened Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) trial [80], a multicenter and randomized trial, may provide some answers.

Furthermore, the Lung Metastasectomy Working Group, a working group under the European Society of Thoracic Surgeons established in 2006, is working towards evaluating the evidence and to generate guidance for the future in pulmonary metastasectomy [81].

References


