Turkish Journal of Thoracic and Cardiovascular Surgery 2018;26(2):254-259
http://dx.doi.org/doi: 10.5606/tgkdc.dergisi.2018.15117

Original Article / Özgün Makale

Is open surgery necessary for metastatic pulmonary tumors evaluated with thorax tomography?

Göğüs tomografisi ile değerlendirilen metastatik akciğer tümörleri için açık cerrahi gerekli midir?

Hüseyin Çakmak[1], Arif Osman Tokat[2], Sezgin Karasu[2]

Institution where the research was done:
Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey
Ankara Training and Research Hospital, Ankara, Turkey

Author Affiliations:
[1]Department of Thoracic Surgery, Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey
[2]Department of Thoracic Surgery, Ankara Training and Research Hospital, Ankara, Turkey

ABSTRACT

Background: This study aims to compare the tomographic evaluations and intraoperative findings of patients treated surgically for primary tumors and who had pulmonary metastasis.

Methods: The study included 160 patients (102 males, 58 females; mean age 34.6±14.3 years; range, 11 to 64 years) who underwent pulmonary metastasectomy. The primary focus was surgically excised and no metastases other than pulmonary were detected on scans. Preoperative tomographic images together with the findings of the open surgical intervention were evaluated and compared.

Results: A total of 296 surgical resection were performed and 345 metastatic lesions were excised in 166 open surgical procedures. In 35 patients (21.9%), 71 (20.6%) metastatic lesions were detected in tomographic evaluations although no lesions had been detected on direct radiographs. In 29 patients (18.1%), 33 (9.6%) metastatic lesions, which had not been detected radiologically, were found intraoperatively.

Conclusion: Tomographic evaluation is used in the follow-up of patients with malignancy but as for pulmonary metastasis it is not efficient and adequate. Therefore, open surgery should be the preferred approach for intraoperative detection of metastases that cannot be detected radiologically. Open surgical resection for pulmonary metastasis can be performed safely with low rates of perioperative morbidity and mortality.

Keywords: Metastasectomy; pulmonary metastases; thoracotomy.

ÖZ

Amaç: Bu çalışmada primer tümörler nedeniyle cerrahi olarak tedavi edilen ve akciğer metastazı olan hastaların tomografik değerlendirmeleri ile ameliyat sırası bulguları karşılaştırıldı.

Çalışma planı: Çalışmaya akciğer metastazektomisi uygulanan 160 hasta (102 erkek, 58 kadın; ort. yaş 34.6±14.3 yıl; dağılım, 11-64 yıl) dahil edildi. Primer odak cerrahi olarak eksize edildi ve taramalarda akciğeri dışında metastaz tespit edilmedi. Açık cerrahi girişimin bulguları ile ameliyat öncesi tomografik görüntüler değerlendirildi ve karşılaştırıldı.

Bulgular: Toplam 296 cerrahi rezeksiyon uygulandı ve 166 açık cerrahi işlemde 345 metastatik lezyon eksize edildi. Direkt radyografilerde lezyon tespit edilmemiş olmasına rağmen 35 hastada (%21.9) tomografik değerlendirmelerde 71 (%20.6) metastatik lezyon tespit edildi. Yirmi dokuz hastada (%18.1) radyolojik olarak tespit edilmemiş olan 33 (%9.6) metastatik lezyon ameliyat sırasında bulundu.

Sonuç: Tomografik inceleme maligniteli hastaların takibinde kullanılmaktadır ancak pulmoner metastazlar için yeterli ve etkin değildir. Bu nedenle, radyolojik olarak tespit edilemeyen metastazların ameliyat sırasında tespiti için tercih edilen yaklaşım açık cerrahi olmalıdır. Açık cerrahi rezeksiyon akciğer metastazları için düşük perioperatif morbidite ve mortalite oranları ile güvenilir bir şekilde uygulanabilir.

Anahtar sözcükler: Metastazektomi; akciğer metastazları; torakotomi.

Received: July 20, 2017 *Accepted:* October 23, 2017

Correspondence: Arif Osman Tokat, MD. Bozok Üniversitesi Tıp Fakültesi, Göğüs Cerrahisi Anabilim Dalı, 66900 Yozgat, Turkey.
Tel: +90 532 - 316 09 94 e-mail: aostokat@hotmail.com

Cite this article as:
Çakmak H, Tokat AO, Karasu S. Is open surgery necessary for metastatic pulmonary tumors evaluated with thorax tomography?. Turk Gogus Kalp Dama 2018;26(2):254-259.

With complete resection of pulmonary metastases, a five-year survival rate of 62% is possible.[1] Surgical resection of pulmonary metastases is considered to be a standard therapeutic procedure in selected patient groups and performed routinely in many thoracic surgery departments.[1,2] In patients with pulmonary metastasis, preoperative thoracic computed tomography (CT) is suggested for preoperative grading of the patient and to detect the exact number of metastases. Computed tomography is fast, painless and has high spatial resolution, providing excellent morphological information.[3] However, many authors have stated that the sensitivity of thoracic CT is not sufficient for the detection of all metastatic nodules.[3,4] In this study, we aimed to compare the tomographic evaluations and intraoperative findings of patients treated surgically for primary tumors and who had pulmonary metastasis.

PATIENTS AND METHODS

The study included 160 patients (102 males, 58 females; mean age 34.6±14.3 years; range 11 to 64 years) who underwent pulmonary metastasectomy due to lung metastasis between June 2003 and June 2013 at Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital and Ankara Training and Research Hospital Department of Thoracic Surgery. All operations were performed by the same surgical team. An evaluation was conducted of patients with pulmonary metastases only, after having undergone surgery for a primary tumor in the previous five years. The study protocol was approved by the Ministry of Health Ethics Board. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient data including demographics and tumor characteristics were recorded. Tumor types of the primary focus were grouped according to the originating germinal tissue as mesenchymal, epitheloid or mixed tumors.

Preoperatively, standard conventional thoracic CT (index: 10 mm, thickness: 10 mm) was applied to all patients. At the beginning of the study, positron emission tomography (PET)-CT was not a routine evaluation method, so only patients with a preoperative CT examination were included in the study. All operations were performed with open surgical approaches. Before starting the surgical procedure, the lungs were evaluated with palpation for possible lesions which had not been detected radiologically. Resected nodules that were evaluated as metastatic intraoperatively, but had not been detected on the preoperative CT were confirmed with postoperative pathological examination. Metastatic nodules detected by palpation during the operation were compared with the preoperative CT examination.

To eliminate the risk of not detecting millimetric nodules intraoperatively, tomographic evaluations were repeated one month later and the enlarged nodules were accepted as metastasis and excised.

Statistical analysis

Statistical analysis of the data obtained was performed with Statistical Package for the Social Sciences (SPSS) for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). Mean and standard deviations were used as descriptive statistics to reach the numerical variables. Categorical variables were stated as number (n) and percentage (%). The Chi-square test was used to evaluate the relationships between categorical variables. A p value of <0.05 was considered statistically significant.

RESULTS

During the 10-years study period, 164 patients underwent metastasectomy due to lung metastasis.

Table 1. Distribution of number of nodules in preoperative evaluation and additional nodules in intraoperative evaluation

Number of nodules in preoperative evaluation per patients	Preoperative tomographic evaluation		Additional metastasis in the Intraoperative evaluation	
	Patients	Total number of nodules	Patients	Total number of nodules
1 nodule	78	78	12	13
2 nodules	41	82	6	6
3 nodules	24	72	6	6
4 nodules↑	17	80	5	8
Total	160	312	29	33

Table 2. Histological distribution of metastases after pathological examination

				Total	
	Histological diagnosis	n	%	n	%
Originating tissue	Osteosarcoma	64	40	110	68.75
	Chondrosarcoma	17	10.63		
	Synovial sarcoma	16	10		
	Leiomyosarcoma	8	5		
	Rhabdomyosarcoma	5	3,12		
Mesenchymal originating tumors	Leiomyosarcoma	8	5		
	Rhabdomyosarcoma	5	3,12		
	Invasive ductal carcinoma	11	6.87		
	Colorectal carcinoma	10	6.25		
Epitheloid tumors	Squamous cell carcinoma	9	5.63	41	25.62
	Seminoma	7	4.37		
	Cervix adenocarcinoma	4	2.5		
Tumors originating from more than one germinal lamina	Teratocarcinoma	9	5.63	9	5.63
Total		160	100	160	100

Four patients were excluded due to intraoperative diffuse pleural metastasis. Of the total 160 patients, 102 (63.8%) were males and 58 (36.3%) were females, with a mean age of 34.6±14.3 years (range 11 to 64 years). Following surgery for the primary tumor, patients were operated on again for pulmonary metastases after mean 22.5±12.8 months (range 4 to 58 months).

Only six patients (3.8%) had symptoms (dyspnea and/or coughing) while the remaining patients (96.3%) were diagnosed with metastasis from radiological examination. In 35 patients (21.9%), 71 metastatic lesions (22.8% of the lesions detected by CT) were detected in CT evaluation although these lesions had not been detected on direct radiographs. A total of 312 metastatic lesions were detected in CT investigations. Only one metastatic lesion was detected in 78 patients (48.8%), two metastases were detected in 41 patients (25.6%) and three metastases were detected in 24 patients (15%). There were four or more metastases in 17 patients (10.6%). In 29 patients (18.1%), 33 metastatic lesions (9.6%), which had not been detected in CT evaluation, were found intraoperatively (Table 1). There was no statistically significant relationship between the number of the metastases in the preoperative CT evaluation and the number of metastases detected in the intraoperative evaluation ($p>0.05$).

Metastases of mesenchymal originating tumors (n=110, 68.8%) were the most frequently observed group, followed by epithelial tumors in 41 patients (25.6%) and teratocarcinomas which had originated from more than one germinal lamina in nine patients (5.6%). The most frequent metastasis was osteosarcoma metastasis (n=64, 40%). The distribution of tumor subtypes found after metastasectomy is shown in Table 2. No statistically significant relationship was determined between the number of metastases in the pre- and intraoperative evaluations and the origin of the tumors ($p>0.05$).

A total of 166 surgical interventions were performed, comprising 148 posterolateral thoracotomies on 142 patients, of which six were bilateral, and median sternotomy on 12 patients, clamshell incision intervention on six patients. Wedge resection was performed on all patients who had median sternotomy and clamshell incision. Posterolateral thoracotomy was performed on all patients for whom an anatomical resection was planned such as segmentectomy, lobectomy and pneumonectomy.

In total, 296 surgical resections were performed, 345 metastatic lesions were excised and 272 wedge resections were applied. In cases where metastases had invaded the hilum, entire lobe or segment by size and number, anatomical resections were preferred. In these patients, two segmentectomies, 18 lobectomies and four pneumonectomies were performed. Pneumonectomies were performed because of large main pulmonary artery invasion in two patients (one osteosarcoma and one synovial sarcoma), large bronchial invasion in one patient (osteosarcoma) and six giant metastases (leiomyosarcoma) in both lobes of the left lung.

Mortality due to cardiopulmonary complications within the early postoperative period was recorded for two patients (1.25%) (one pneumonectomy, one lobectomy). The tube thoracostomy remained in place for more than 10 days in six patients (3.8%) due to prolonged air leakage and lung expansion difficulty.

DISCUSSION

Primary malignant tumors frequently have systemic metastasis despite surgical and medical treatment. However, being confined to the lung as well as being resectable does not mean that the systemic disease has advanced.[4] Compared with cases of metastases in more than one organ, cases with isolated lung metastases respond well to local and systemic treatment.[2,5] The current approach is the acceptance of such lesions as primary bronchial cancers. The results of The International Registry of Lung Metastases revealed that metastasectomy is a form of potentially curative therapy which can be safely performed with low mortality rates.[6]

Routine follow-up examinations of patients are performed with direct chest radiographs. However, in direct chest radiography, there is the possibility of overlooking lesions which are 1 cm or smaller. In 1998, Lien et al.[7] reported that approximately half of the patients with non-seminomatous testis tumor had metastatic lesions on CT with negative direct chest radiographs. Similarly, in the current study, in 35 of 160 patients, 71 metastatic lesions were detected by CT which had not been observed on direct chest radiographs.

For accurate preoperative grading and detection of the number of metastases, preoperative thoracic CT is used. However, many studies have shown that preoperative CT does not demonstrate all the metastases in the lung which are detected during thoracotomy.[2,4] In 2004, Parsons et al.[3] reported that it is possible to detect 78% of all metastases preoperatively when the nodules detected on thoracic CT were compared with those found in intraoperative exploration. Furthermore, Kayton et al.[8] stated that despite advanced technology, only a very rough correlation exists between CT findings and the number of lesions identified at thoracotomy. It was reported that metastases were not detected by radiological evaluations in more than one third of their open surgery interventions, and therefore, thoracotomy was recommended for complete resection in cases of osteosarcoma metastases.[8] Sengul et al.[4] showed that the mean number of metastatic nodules detected on preoperative CT was 2.7±2.4, compared to 7.6±10.5 nodules found during surgery.

Positron emission tomography-CT is a widely used scanning method for lung evaluation. However, at the beginning of this study, PET-CT was not established in our hospital, so it was not possible to use PET-CT evaluation on the early patients in this series. Currently, PET-CT in a follow-up surveillance setting is generally not recommended in clinical practice for lung metastasis.[9,10] In the follow-up evaluations of malignancy patients, PET-CT is not used as a routine scanning method in lung surveillance in our hospital.

Mineo et al.[11] stated that resection type had no effect on survival when complete resection was performed. The basic principle in metastasectomy is to protect as much lung parenchyma as possible. Although very few, there are also cases in the literature in which pneumonectomy has been performed, but the most frequent resection type is wedge resection.[9,12,13] In the current series, the most frequent resection type was wedge resection. Only four patients had pneumonectomy compared to 272 wedge resections.

Commonly used surgical approaches for pulmonary metastasectomy can be basically named open surgical approaches and thoracoscopic approaches. Surgeons differ in the approach to resections, with some favoring procedures that minimize the trauma to the patient, and others performing open procedures with the goal of maximizing the likelihood of resection of all detectable sites of disease.[14]

Video assisted thoracoscopic surgery (VATS) is a technique that has been recommended and used in metastasectomy. Despite the many technological advances in VATS, including high-definition resolution and monitors, flexible-tip thoracoscopes, and the development of dedicated VATS instruments, a substantial number of nodules are missed by VATS alone.[15,16] In patients operated on for nodules suspected to be lung metastases, a substantial number of additional nodules were detected during thoracotomy despite advancements in CT imaging and VATS technology.[15-17] Nakas et al.[16] reported that VATS can be safely used in patients with lung metastases with the aid of a detailed CT evaluation. However, Kuritzky et al.[17] performed a retrospective study of 298 patients undergoing either VATS or muscle-sparing thoracotomy in the application of a lung lobectomy, and found that the operative time with muscle-sparing thoracotomy was shorter and hospital stay was shorter with VATS, but otherwise, no difference was determined in the major parameters, such as postoperative complications, disease-free survival, or overall survival.

Video assisted thoracoscopic surgery has been reported to be of limited value in hilar lesions. Pfannschmid et al.[18] showed that up to 20% of patients with pulmonary metastases have hilar or mediastinal lymph node involvement at the time of metastasectomy and this obviously has a negative impact on five-year survival. It is essential to excise all metastases and perform a complete resection in order to make a realistic prognosis estimation and treatment program, which is possible with meticulous intraoperative exploration. Mutsaerts et al.[19] reported that hilar metastases which could not be found with VATS were detected in five of 17 patients.

Most of these studies, however, were retrospective studies which compared open procedures with VATS procedures in different time periods. Therefore, selection bias could have impacted the results of these studies. It must be kept in mind that if a metastasis is not identified by VATS and remains, it may potentially spread to the parenchyma and regional lymph nodes. It is also important to note that early complete metastasectomy can help to increase the overall five-year survival rate.

Bimanual digital palpation can be considered to be an absolute requisite for the detection of pulmonary metastases in the lung parencyhyma.[20] The detection of a total of 33 metastatic lesions (9.6%) in 29 patients (18.1%) in the current series implies that proper exploration and palpation are essential to detect lesions which have not been found in radiological evaluations. Internullo et al.[21] reported that in a survey of members of the European Society of Thoracic Surgeons, 65% considered bimanual palpation of the lung necessary, whereas 35% "consider it not always necessary" and 40% use VATS techniques with curative intent.

Our study has some limitations. In the current series, all nodules which were detected intraoperatively by digital examination were located peripherally. They could not be detected in the CT evaluation, since all were small. Finally, all these lesions could be resected completely by wedge resection with the assistance of digital examination.

In conclusion, in cases with a surgically controlled primary tumor and no metastasis in any region other than the lung, open surgical resection of lung metastases is safe and associated with low perioperative morbidity and mortality rates. Open thoracotomy should be the preferred approach for intraoperative detection of metastases which cannot be detected radiologically. It is important to bear in mind that despite technological developments, radiological evaluation may not always be sufficient. Therefore, open surgical intervention and careful intraoperative exploration are necessary for a complete resection. Surgeons need to take this into consideration and patients should always be informed that if they choose to have a minimally invasive approach, there is a risk of leaving undetected malignant nodules behind.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Yenigun BM, Yuksel C, Enon S, Ozkan M, Cangir AK, Kutlay H. Prognostic factors in metastasectomy of lung metastases from colorectal cancer. Turk Gogus Kalp Dama 2015;23:75-81.
2. Ozkan M, Tokat AO, Kavukçu S. Metastatic lung tumours. [Article in Turkish] Tuberk Toraks 2003;51:207-15.
3. Parsons AM, Detterbeck FC, Parker LA. Accuracy of helical CT in the detection of pulmonary metastases: is intraoperative palpation still necessary? Ann Thorac Surg. 2004;78:1910-6.
4. Şengül AT, Başoğlu A, Büyükkarabacak YB, Yetim TD, Kutlu T. Assessment of metastasectomy and prognostic factors in the treatment of metastatic lung tumors. Turk Gogus Kalp Dama 2009;17:87-91.
5. Monteiro A, Arce N, Bernardo J, Eugénio L, Antunes MJ. Surgical resection of lung metastases from epithelial tumors. Ann Thorac Surg 2004;77:431-7.
6. Pastorino U, Buyse M, Friedel G, Ginsberg RJ, Girard P, Goldstraw P, et al. Long-term results of lung metastasectomy: prognostic analyses based on 5206 cases. J Thorac Cardiovasc Surg 1997;113:37-49.
7. Lien HH, Lindsköld L, Fosså SD, Aass N. Computed tomography and conventional radiography in intrathoracic metastases from non-seminomatous testicular tumor. Acta Radiol 1988;29:547-9.
8. Kayton ML, Huvos AG, Casher J, Abramson SJ, Rosen NS, Wexler LH, et al. Computed tomographic scan of the chest underestimates the number of metastatic lesions in osteosarcoma. J Pediatr Surg 2006;41:200-6.
9. Güven T, Sırmalı M, Türüt H, Fındık G, Gezer S, Kaya S, et al. Outcomes of metastasectomy in secondary tumors of the lung: A retrospective analysis of 74 patients. [Article in Turkish] Türk Göğüs Kalp Damar Cer Derg 2006;14:216-21.
10. Sawada S, Suehisa H, Ueno T, Sugimoto R, Yamashita M. Monitoring and management of lung cancer patients following curative-intent treatment: clinical utility of 2-deoxy-2-[fluorine-18]fluoro-d-glucose positron emission tomography/computed tomography. Lung Cancer (Auckl) 2016;7:45-51.
11. Mineo TC, Ambrogi V, Tonini G, Nofroni I. Pulmonary metastasectomy: might the type of resection affect survival? J Surg Oncol 2001;76:47-52.

12. Molnar TF, Gebitekin C, Turna A. What are the considerations in the surgical approach in pulmonary metastasectomy? J Thorac Oncol 2010;5:140-4.
13. Downey RJ, Bains MS. Open Surgical Approaches for Pulmonary Metastasectomy. Thorac Surg Clin 2016;26:13-8.
14. Eckardt J, Licht PB. Thoracoscopic or open surgery for pulmonary metastasectomy: an observer blinded study. Ann Thorac Surg 2014;98:466-9.
15. Carballo M, Maish MS, Jaroszewski DE, Holmes CE. Video-assisted thoracic surgery (VATS) as a safe alternative for the resection of pulmonary metastases: a retrospective cohort study. J Cardiothorac Surg 2009;4:13.
16. Nakas A, Klimatsidas MN, Entwisle J, Martin-Ucar AE, Waller DA. Video-assisted versus open pulmonary metastasectomy: the surgeon's finger or the radiologist's eye? Eur J Cardiothorac Surg 2009;36:469-74.
17. Kuritzky AM, Aswad BI, Jones RN, Ng T. Lobectomy by Video-Assisted Thoracic Surgery vs Muscle-Sparing Thoracotomy for Stage I Lung Cancer: A Critical Evaluation of Short- and Long-Term Outcomes. J Am Coll Surg 2015;220:1044-53.
18. Pfannschmidt J, Klode J, Muley T, Dienemann H, Hoffmann H. Nodal involvement at the time of pulmonary metastasectomy: experiences in 245 patients. Ann Thorac Surg 2006;81:448-54.
19. Mutsaerts EL, Zoetmulder FA, Meijer S, Baas P, Hart AA, Rutgers EJ. Outcome of thoracoscopic pulmonary metastasectomy evaluated by confirmatory thoracotomy. Ann Thorac Surg 2001;72:230-3.
20. Cangel G, Turna A, Demirkaya A, Tuzun H, Kaynak K, Demirhan O. Results of resection of pulmonary metastasis and prognostic factors. Turk Gogus Kalp Dama 2014;22:354-62.
21. Internullo E, Cassivi SD, Van Raemdonck D, Friedel G, Treasure T. Pulmonary metastasectomy: a survey of current practice amongst members of the European Society of Thoracic Surgeons. J Thorac Oncol 2008;3:1257-66.