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Determination of the timing for thoracic imaging prior to pulmonary metastasectomy: an analysis on surgical planning and lesion detection

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ABSTRACT

Aims: The aim of this study is to reveal the relationship between the timing of thoracic computed tomography (CT) imaging conducted prior to surgery and the pre-surgical period in patients planned for pulmonary metastasectomy (PM), and to determine a safe pre-surgical timing for thoracic CT.

Methods: This study is a retrospective cohort study examining the data of patients who underwent pulmonary metastasectomy (PM). The research includes 96 patients who underwent PM between January 2017 and July 2022. Patients' demographic data, primary malignancy diagnoses, type of operation, sizes of masses requiring anatomical resection, the number of lesions detected in thoracic CT, the number of lesions identified during surgery, and the timing of thoracic tomography were recorded. The timing of thoracic CT imaging was compared with the number of lesions detected preoperatively and postoperatively.

Results: The study included 96 patients, comprising 49 females and 47 males. The most common primary pathological diagnosis was colon cancer at 36.5%, followed by breast cancer at 12.5%. 66.6% of the patients were operated on with thoracotomy, 29.1% with video-assisted thoracoscopic surgery (VATS), and 4.2% with rethoracotomy. The average number of lesions detected in preoperative thoracic tomography was 1.67±0.96, while the average number of lesions detected during surgery was 2.03±1.41. In patient groups where thoracic CT was performed 10 days or less before the operation, no significant difference was found between the number of lesions detected during surgery and the number of lesions in the CT. However, in patients where thoracic CT was performed more than 10 days before the operation, the number of lesions detected during surgery was significantly higher than the number of lesions detected in the CT.

Conclusion: In this research, it was concluded that for patients planned for PM, repeating thoracic CT after the 10th day following the initial detection of metastases in the pre-surgical phase may contribute to the detection of more lesions.

Keywords: Pulmonary metastasectomy, thoracic computed tomography, number of lesions, metastatic disease

INTRODUCTION

Cancer is characterized by the uncontrolled growth and spread of certain cells to other body parts. According to the World Health Organization (WHO) 2020 report, cancer is a leading cause of death globally, accounting for approximately 10 million deaths in 2020.[1] About 30% of patients with malignant diseases develop pulmonary metastasis, which is the spread of cancer cells from the primary tumor to distant organs, significantly contributing to cancer morbidity and mortality.[2-5] Pulmonary metastases commonly originate from colon, rectum, kidney, breast, prostate, and oropharyngeal carcinomas, among others.

The management of pulmonary metastases includes various strategies such as surgery, radiotherapy, and chemotherapy, with surgery recommended for patients in the oligometastatic stage who can tolerate the procedure.[6] Pulmonary metastasectomy (PM) has been established as a treatment that can prolong survival in patients with metastatic lung cancer from various primary solid tumors.[7] However, the decision to proceed with metastasectomy is influenced by several factors including the ability to completely resect metastatic disease and the number of pulmonary metastases.[8] Preoperative assessment with thoracic computed tomography (CT) is crucial for operation planning, aiming to minimize residual disease post-surgery.[9] The timing of thoracic CT imaging prior to surgery is pivotal, as earlier detection of metastases can lead to

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more comprehensive resection and potentially improved long-term outcomes.[10]

This study aims to explore the relationship between the timing of thoracic CT imaging conducted prior to surgery and the outcomes in patients planned for PM, seeking to establish a safe pre-surgical timing for thoracic imaging.

METHODS

Ethical approval for this study was obtained from Kartal Dr. Lütfi Kırdar City Hospital Clinical Researches Ethics Committee (Date: 27.04.2023, Decision No: 2023/514/248/14), adhering to the ethical guidelines of the Declaration of Helsinki for medical research involving human subjects.

This retrospective cohort study analyzed patients who underwent PM surgery in the thoracic surgery clinic of Kartal Dr. Lütfi Kırdar City Hospital from January 2017 to July 2022. Inclusion criteria were patients above the age of 18 who had undergone PM, while exclusion criteria included patients with incomplete medical records, and patients with contraindications to thoracic surgery due to other health conditions.

Data were meticulously gathered from hospital records and medical files, encompassing demographic details (age, gender), clinical parameters (CT scan dates, number of lesions detected), and surgical techniques employed. Specific attention was given to documenting the thoracic CT technical criteria, including scan resolution, contrast use, and slice thickness, ensuring a standardized approach across all patients.

The thoracic CT imaging, as depicted in Figure, is instrumental in our preoperative assessment, providing high-resolution insights into the number, location, and characteristics of pulmonary nodules. Thoracic CT scans were interpreted by a radiologist who experience in thoracic imaging, ensuring consistency and accuracy in identifying metastatic nodules. The radiological appearance of metastatic nodules was defined based on size, density, and contrast enhancement patterns, aiming to differentiate metastatic lesions from benign nodules.

Statistical Analysis

In the descriptive statistics of the data, mean, standard deviation, median, minimum, maximum, frequency, and ratio values were used. The distribution of variables was measured with the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for the analysis of quantitative independent data. The Wilcoxon test was used for the analysis of dependent quantitative data. Spearman's correlation analysis was used for correlation analysis. SPSS 28.0 (Version 29, Chicago, IL, USA) software was used for the analyses. Results were considered statistically significant for $p<0.05$.

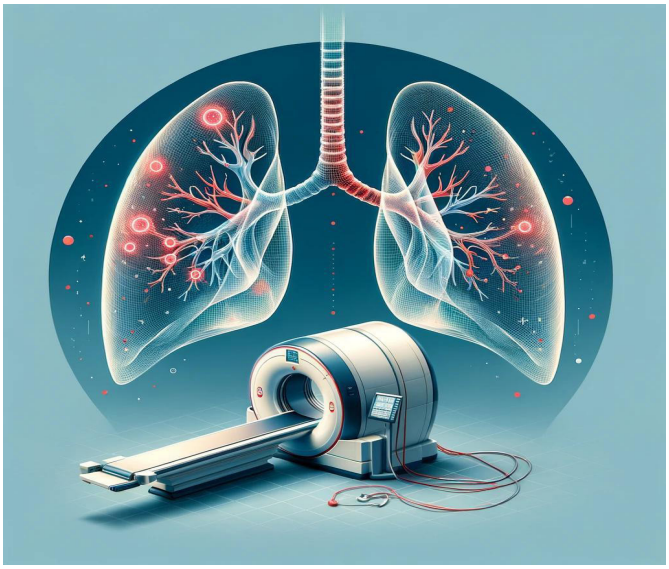

Figure. Illustration of thoracic CT imaging in pulmonary metastasectomy assessment

RESULTS

In this study, the primary malignancies of patients undergoing PM surgery were examined in detail. The total number of patients is n=96. The ages of the patients in our study range from 6.0 to 79.0 years, with a median age of 56.0. This reflects a heterogeneous age distribution prior to surgical intervention. The gender distribution of patients is balanced, with 51.0% females and 49.0% males. The dates of patients' thoracic CT scans are spread over a wide range (1.0-30.0 days), with a median CT date of 10.0 days. This indicates that patients were assessed at different times for medical imaging. There is a statistically significant increase in the number of lesions during the operative period ($p<0.05$) (Table 1).

Table 1. General characteristics of the patients

Variables	Min-Max	Median	Mean±sd/n-%
Age	6.0 - 79.0	56.0	55.3 ± 13.2
Gender Woman			49 51.0%
Time between thoracic CT and operation (days)	1.0 - 30.0	10.0	11.4 ± 8.5
CT lesion count	1.0 - 6.0	1.0	1.7 ± 1.0
Operative lesion count	1.0 - 8.0	1.0	2.0 ± 1.4
Increase in lesion count	0.0 - 3.0	0.0	0.4 ± 0.7
Mass size (mm)	2.0 - 8.0	3.0	3.9 ± 1.4

CT: Computed tomography

According to the findings, the most common histopathological type of primary tumor in 36.5% (n=35) of these patients is colon cancer. Breast cancer is

the second most frequent, accounting for 12.5% (n=12) of cases. Other common malignancy types include 7.3% (n=7) renal cell carcinoma (RCC), 8.3% (n=8) rectum cancer, and 5.2% (n=5) osteosarcoma. Among the rare types are mandibular malignant melanoma, mesenchymal tumor, stomach cancer, pancreatic cancer, uterine sarcoma, and ureteral carcinoma, each constituting 1.0% (n=1) of cases. These results show a heterogeneous distribution of primary malignancies in patients undergoing pulmonary metastasectomy. Data on surgical techniques used for metastasectomy interventions in a total of 82 patients are as follows: Video-assisted thoracoscopic surgery (VATS) was the method of choice in 35.4% (n=34) of all interventions. Thoracotomy emerged as a surgical technique used in 60.4% (n=58) of patients. Rethoracotomy was used in 4.2% (n=4) of the total interventions.

The procedures performed were 75.0% (n=72) wedge resections, 5.2% (n=5) lower left lobectomies, 3.1% (n=3) lower lobe superior segmentectomies, 2.1% (n=2 each) upper lobe anterior segmentectomies and upper lobe posterior segmentectomies, and 1.0% (n=1 each) for lower lobe basal segmentectomy, lower lobe posterior segmentectomy, apical segmentectomy, apicoposterior segmentectomy, right lower bilobectomy, right middle lobectomy, right upper lobectomy, and left upper lobectomy. These results indicate that the wedge resection technique is commonly preferred for the removal of metastatic lesions, with other specific lobectomy types being used at lower rates (Table 2).

In the study, the Wilcoxon test was used to evaluate the differences between the number of lesions in thoracic CT and the number of lesions during surgery. It was found that the difference between the CT lesion count and the operative lesion count was statistically significant ($p<0.05$). The Wilcoxon test indicates that these changes signify an increase in the number of lesions from the CT period to the operative period. The number of lesions during the operative period showed a significant increase ($p<0.05$) compared to the CT period. No significant difference ($p>0.05$) was observed in the number of lesions during the CT period between the groups with <10 days post-CT and >10 days post-CT. No significant difference ($p>0.05$) was observed in the number of lesions on the day of surgery between the groups with <10 days post-CT and >10 days post-CT. In the group with <10 days post-CT, the number of lesions during the operative period showed a significant increase ($p<0.05$) compared to the CT period. In the group with >10 days post-CT, the number of lesions during the operative period showed a significant increase ($p<0.05$) compared to the CT period. The increase in the number of lesions in the group with >10 days post-CT was significantly ($p<0.05$) higher than in the group with <10 days post-CT (Table 3).

Table 2. Types of surgical operations performed on patients

Variables	Surgical methods	n	%
Implemented intervention	VATS	34	35.4%
	Thoracotomy	58	60.4%
	Rethoracotomy	4	4.2%
Types of lobectomies	Lower lobe basal segmentegtomy	2	2.1%
	Lower lobe posterior segmentegtomy	1	1.0%
	Lower lobe superior segmentegtomy	3	3.1%
	Apical segmentegtomy	2	2.1%
	Apiko posterior segmentegtomy	1	1.0%
	Right lower bilobectomy	1	1.0%
	Right middle lobectomy	1	1.0%
	Right upper lobectomy	2	2.1%
	Left lower bilobectomy	1	1.0%
	Left lower lobectomy	5	5.2%
	Left upper lobectomy	1	1.0%
	Upper lobe anterior segmentegtomy	2	2.1%
	Upper lobe posterior segmentegtomy	2	2.1%
	Wedge resection	72	75.0%

VATS: Video-assisted thoracoscopic surgery

Table 3. Timing of thoracic tomography in pulmonary metastases

Number of lesions	After thorax CT <10 day			After thorax CT >10 day			p	
	Mean±sd		Median	Mean±sd		Median		
Detected on preoperative thoracic CT	1.70	1.13	1.00	1.62	0.63	2.00	0.422	m
Detected during surgery	1.95	1.56	1.00	2.15	1.16	2.00	0.078	m
Increase in the number of lesions	0.25	0.66	0.00	0.54	0.76	0.00	0.006	m
Intra-group variation		0.010	W		0.000	w		

m: Mann whitney u test, w: Wilcoxon test, CT: Computed tomography

DISCUSSION

According to the findings of this study, in patient groups where thoracic CT was performed 10 days or less before the surgery, no significant difference was observed between the number of lesions detected during surgery and the number of lesions in the thoracic CT. However, in patients where thoracic CT was performed more than 10 days before the surgery, the number of lesions detected during surgery was significantly higher than the number of lesions detected in the thoracic CT. This suggests that the time elapsed before pulmonary metastasectomy may influence the number of lesions detected during surgery, and thoracic CT taken a longer time before could contribute to detecting more lesions. This important observation should be considered in clinical decision-making and operation planning.

Looking at recent developments in many types of cancer, aggressive pulmonary resection, R0 resection, or curative resection in lung metastases arising in these patients has become a standard strategy for addressing pulmonary metastasis when it can be achieved in addition to systemic chemotherapy and surgical treatment.[11,12]

When examining recommendations, for patients undergoing PM, a longer disease-free interval between the treatment of the primary tumor and the emergence of metastatic disease is desired, and there is no absolute time frame, including the synchronous presentation of metastatic disease, that is considered too short to contemplate PM.[13,14] However, especially for the detection of synchronous metastases, it is recommended to repeat lung CT six to eight weeks after the recognition of pulmonary metastases, to ensure that no additional target lesions (or too many target lesions) have emerged.[15] Yet, in our literature review, we did not find any specific recommendations on how long before surgery thoracic CT imaging should be performed in patients with planned primary operations. Nevertheless, the decision-making process for PM is dynamic and requires close follow-up.[16]

In our research, when examining the demographic data of patients undergoing PM, we found it to be consistent with the literature.[17] Similar to our study, many authors have also found no statistically significant difference in long-term survival between male and female patients after pulmonary metastasectomy.[18,19] Research has shown that accurate preoperative assessment and operation planning with sectional imaging can reliably detect nodules as small as 2 to 3 mm.[20] In this research, similarly, nodules as small as 2 mm were detected, with an average size of 3.9 mm. Among the poor prognostic factors identified through multivariate analysis using a broad cohort are the number and size of tumors.[21] Studies particularly investigating the relationship between tumor sizes and recurrence stand out, with research showing that recurrences are more frequent in metastases larger than 2 mm.[21,22] Similarly, the inverse relationship between the number of metastases and survival is likely due to multiple factors. As the number of pulmonary metastases increases, the likelihood of incomplete resection, the burden of widespread occult disease in the lungs, and the probability of recurrence in the lung are higher.[23,24] Consistent with the literature, in this research, the number of nodules is between 1-2.[21] Outcomes are better with fewer metastases. However, among thoracic surgeons, there is no consensus on what burden of disease constitutes an insurmountable barrier for patients with multiple metastases. The important factor is not the absolute number of metastases, but the feasibility of resecting all disease areas.

Colon malignancies are the most common primary tumors in patients undergoing PM, followed by RCC, breast cancer, ENT (ear, nose, and throat) cancers, and uterine malignancies.[25] Consistent with these data, our study also found that the most frequent primary malignancy was colon malignancy.

In PM, several standard lung resection techniques characterized by the amount of lung tissue removed (e.g., wedge resection, segmentectomy, lobectomy) can be used to resect pulmonary metastases, either through an open thoracotomy incision (anterior thoracotomy, posterior thoracotomy) or using minimally invasive techniques. The choice between VATS or open thoracotomy approach depends on the characteristics of the metastases, including their locations, numbers, and sizes, as well as lesion stability assessed in thoracic CT scans.[26] Open thoracotomy has traditionally been the standard for the resection of pulmonary metastases to allow for bimanual palpation of the lungs. However, VATS is gaining popularity with advanced imaging techniques that can more accurately detect smaller lesions.[27] In our study as well, thoracotomy has an advantage over VATS. Similarly, in our research, nearly all patients were aimed for complete resection using both methods. This is thought to be due to the ongoing debate over the safety of VATS in PMs.[28] Despite advancements in imaging technology, occult lesions continue to be a source of concern.[29] The method used for PM in the patients included in the study is Wedge Resection. Wedge resection for pulmonary metastasis is now considered an appropriate procedure due to its reduced invasiveness and ability to preserve lung function.[7] Therefore, it is the most commonly used procedure for resecting pulmonary metastases from various types of malignancies.[30]

There is no direct evidence addressing how soon before metastasectomy a chest CT scan should be performed.[9] Limited data suggest that patients with tumor doubling

times of <20 to 40 days have poor outcomes after metastasectomy and are less likely to be considered realistic candidates for metastasectomy.[31] Similarly, a study found better survival in patients with metastatic colorectal carcinoma resected within a month compared to those who had resection more than a month after the initial detection of isolated pulmonary metastases.[32] Therefore, although the data are limited, some studies suggest that delaying resection after the discovery of a metastasis offers no significant benefit and recommend proceeding with metastasectomy as soon as patient assessment is complete, based on well-designed comparative series that directly address the question.[9] Hence, in this study, the boundary for thoracic imaging was set at 10 days, comparing two groups, and it was considered that thoracic CT imaging within 10 days prior to surgery could affect the number of lesions detected during surgery, and thoracic CT taken a longer time before could contribute to detecting more lesions. Similarly, it was thought that performing a new thoracic imaging 10 days after the first detection of a metastasis could be appropriate, akin to the recommendation of conducting a CT scan within 4 weeks post-metastasectomy unless the tumor doubling time is exceptionally short or long.

Limitations

This study has some limitations. The retrospective analysis of data carries the risk of missing or erroneous information. The patient sample used in the study is limited, which could restrict the generalizability of the findings. The research is based on data obtained from a single center, which may limit the level of representation of the general population. Future studies involving larger participant groups, prospective designs, and data collection from different clinical settings could help to mitigate these limitations.

CONCLUSION

In this research, it was concluded that for patients planned for PM, repeating thoracic CT after the 10th day following the initial detection of metastases in the pre-surgical phase may contribute to the detection of more lesions.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Kartal Dr. Lütfi Kırdar City Hospital Clinical Researches Ethics Committee (Date: 27.04.2023, Decision No: 2023/514/248/14).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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