Thoracoscopic or Open Surgery for Pulmonary Metastasectomy: An Observer Blinded Study

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Background. **Video-assisted thoracic surgery (VATS) resection of pulmonary metastases has long been questioned because radiologically undetected parenchymal lesions may be missed when bimanual palpation is restricted to the portholes. Technology, however, has improved and advanced VATS resections are now performed routinely worldwide. This prompted us to conduct a prospective observer-blinded study on pulmonary metastasectomy.**

Methods. **Eligible patients with oligometastatic pulmonary disease on computed tomography (CT) underwent high-definition VATS, with digital palpation by 1 surgical team and subsequent immediate thoracotomy during the same anesthesia by a different surgical team, with bimanual palpation and resection of all palpable nodules. Preoperative CT evaluations and surgical results were blinded. Primary endpoints were number and histopathology of detected nodules.**

Results. **During a 3-year period 89 consecutive patients, with newly developed nodules suspicious of lung metastases from previous cancers in colon-rectum (n = 59), kidney (n = 15), and other malignancies (n = 15) were included, with a total of 140 suspicious nodules visible on CT. During VATS, 122 nodules were palpable (87%). All nodules were identified during thoracotomy, where 67 additional and unexpected nodules were also identified; 22 were metastases (33%), 43 (64%) were benign lesions, and 2 (3%) were primary lung cancers.**

Conclusions. **In patients operated for nodules suspicious of lung metastases, a substantial number of additional nodules were detected during thoracotomy despite advancements in CT imaging and VATS technology. Many of these nodules were malignant and would have been missed if VATS was used exclusively. Consequently, we considered VATS inadequate if the intention is to resect all pulmonary metastases during surgery.**

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The indications of pulmonary metastasectomy are constantly evolving [1]. Previously, before effective chemotherapy was introduced many patients with pulmonary metastases from germ cell tumors and sarcomas were referred for metastasectomy; today, the majority of patients have metastases from colorectal cancer. Currently, there are no published randomized trials that can guide thoracic surgeons in this field and the level of evidence to support the many aspects of pulmonary metastasectomy is limited to case series and metastasectomy registries [2].

We know that preoperative computed tomographic (CT) scans do not always demonstrate every metastasis in the lung that is subsequently detected during thoracotomy [3, 4]. Yet, video-assisted thoracoscopic surgery (VATS) is also used for pulmonary metastasectomy despite its inherent limitation in digital palpation that is restricted to the portholes. We previously reported preliminary data demonstrating that although the VATS technology has improved tremendously in recent years a substantial number of nodules are still missed during a VATS procedure [5]. In the present study we present data from 3 consecutive years of investigating if the surgical approach matters in pulmonary metastasectomy.

Material and Methods

This study was approved by the Regional Ethics Committee of Southern Denmark (approval number: S-20100033) and written informed consent was obtained from all patients. Preliminary data from this study were published earlier [5] and this study includes patients after additional 26 months of accrual. Thus, during a 38-month period (November 2010 to January 2014) 127 patients with a suspicion of limited pulmonary metastatic disease as seen on CT scan and considered eligible for therapeutic surgical resection were referred to our department. All had undergone positron emission tomography-CT to exclude widespread disseminated disease and were routinely scheduled for endobronchial ultrasound-guided transbronchial fine-needle aspiration (EBUS-FNA) 4 days prior to metastasectomy to exclude metastatic disease in the mediastinal lymph nodes, in which case they were considered inoperable and referred for oncologic treatment.

Prior to metastasectomy 2 surgical teams separately evaluated the patient's chest CT scan used for referral, which was always less than 6 weeks old and always a multislice CT scan with a slice thickness of 3 to 5 mm

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depending on the referring physician's preference. All CT scans were viewed by scrolling on a digital monitor, which is known to increase sensitivity [6], and the number of visible nodules was recorded and blinded for the other surgical team before surgery was commenced.

The VATS and thoracotomy were performed during the same anesthesia by 2 different surgical teams selected at random from 8 board-certified and dedicated general thoracic surgeons who then performed 1 of both procedures assisted by junior staff. During general anesthesia with single lung ventilation, patients were positioned in a lateral decubitus position and the operating table was flexed to widen the intercostal spaces. Three small skin incisions for the thoracoscope and for digital palpation or instrumentation were placed at the VATS surgeon's preference. Digital palpation included use of a grasping instrument to bring the lung parenchyma toward the palpating finger in any manner the VATS surgeon preferred. The number of palpable nodules considered resectable in the lung parenchyma including a clear description of which lobes were involved was recorded at this point but the nodules were not resected during VATS in order to provide a virgin field for subsequent open bimanual palpation. After the VATS surgeon had left the operating table a thoracotomy was subsequently performed immediately by a new and different surgeon who connected the 2 most appropriate portholes from the VATS procedure, allowing for complete inspection and bimanual palpation of the whole lung. All palpable nodules were then resected by simple parenchymal sparing wedge resection using a mechanical stapler, always leaving a clear safety margin of at least 1 cm. Finally, mediastinal lymph node dissection was performed. At this time the findings of the second surgeon were recorded. Prior to closure of the thoracotomy the VATS surgeon entered the operating room and revealed his findings to exclude a possibility that he or she had identified a nodule that was not discovered during thoracotomy. All specimens were sent for histologic evaluation and the histopathology report from each resected nodule was compared with the perioperative findings. Primary endpoints were the number of visible nodules on the patient's CT scan and number of palpable nodules during each of the 2 subsequent surgical procedures, their anatomic location, and histopathology of resected nodules.

Results

During the 38-month period, 127 patients were referred but 38 were excluded from this trial. Eighteen patients had disseminated disease and were consequently referred for oncologic treatment; 17 of these patients had metastatic mediastinal lymph node involvement discovered during EBUS and 1 patient had pleural carcinomatosis discovered during the VATS procedure. Another 14 patients were excluded because they had more than 3 suspicious nodules in the same lung on chest CT scan which we did not consider as limited metastatic disease and in 6 patients the nodules were located too deep in the lung parenchyma that they were not considered eligible for a VATS resection.

All patients had a history of primary cancers in the colon-rectum (n = 59), gastrointestinal stromal tumor (n = 1), kidney (n = 15), breast (n = 2), gynecologic (n = 2), malignant melanoma (n = 4), esophagus (n = 1), oncocytoma (n = 1), urothelial (n = 1), and small intestine (n = 3). As shown in Table 1 both surgical teams each identified exactly 140 nodules suspicious of metastatic disease on the patient's preoperative chest CT and 122 of these nodules (87%) were palpated during the VATS procedure. Table 1 also demonstrates that during the subsequent immediate thoracotomy an additional 67 nodules were identified. Case-by-case match of the anatomic location of these 67 nodules revealed that 22 (33%) were unexpected metastases, 43 (64%) were benign lesions, and 2 (3%) were primary lung cancers. Malignant nodules were found in all but 2 patients who had sarcoidosis. One of the patients with lung cancer had a subcarinal lymph node metastasis (station 7) detected during thoracotomy despite preoperative EBUS-FNA. In total, 189 nodules were resected during the thoracotomy; 135 were malignant and 54 were benign nodules. Of the 189 nodules, 122 (65%) were identified during the VATS procedure (Table 1), and 111 nodules (91% of the 122 identified nodules or 59% of all 189 nodules) were identified in the same lobe as the malignant nodule, which was resected during thoracotomy. Thus, not all nodules palpated during VATS corresponded with the ones palpated and resected during thoracotomy. Of the 67 additional nodules, 16 were located in the right upper lobe, 3 in the middle lobe, 18 in the right lower lobe, 12 in the left upper lobe, and 18 in the left lower lobe. When we analyzed each lung separately and compared the location

Table 1. Results of 2 Surgical Teams Separately Evaluating the Patient's Chest Computed Tomographic (CT) Scan

Variable	Chest CT Scan	Surgical Approach	Scenario	Malignant Nodules	Benign Nodules
1. Surgeon		VATS			
Number of nodules detected	140	122	Best case	111	11
			Worst case	79	43
2. Surgeon		Thoracotomy			
Number of nodules detected	140	189		135	54
Difference in the number of nodules detected with VATS and thoracotomy		67		24	43

The numbers represent the number of nodules detected with each modality and a purely hypothetical "worst-case" and "best-case" scenario depending if the additional 43 nodules that were detected during thoracotomy were or were not among the nodules palpated during video-assisted thoracic surgery (VATS).