Surgical treatment of liver and lung metastasis. New techniques and outcomes
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Outcome of thoracoscopic pulmonary metastasectomy evaluated by confirmatory thoracotomy

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Outcomes of thoracoscopic pulmonary metastasectomy

Introduction
Pulmonary metastases are frequently encountered in patients with solid tumours. Some solid tumours tend to produce only a few isolated lung metastases that are usually found peripherally in the lung parenchyma, frequently immediately subpleural. Examples of such tumours are: sarcomas, testicular tumours, renal cell carcinomas and less frequently, head and neck tumours, colorectal carcinoma, melanoma and endometrial carcinoma. In these cases, the surgical removal of metastases might be curative. After a total metastasectomy, 5-year survival may be as high as 30%. Although these data are derived from studies that were retrospective analyses of selected patient series, these results support the surgical resection of isolated lung metastases. A long-term remission will seldom be achieved when more than three metastases are found preoperatively. Unilateral located metastases are usually removed by a posterolateral thoracotomy. Bilateral tumours are excised by either a two-stage bilateral thoracotomy or by sternotomy. Peripherally located metastases enable complete removal by wedge resection with the stapling technique. Developments in thorascoscopic/laparoscopic instruments enable tissue stapling using a 12-mm port system. Unfortunately, thorascoscopic resection makes it impossible to examine the lung by palpation. Small lesions may then be difficult to find, and, if not seen on computed tomography (CT) scan, may easily be missed. It is not uncommon that more metastatic sites are found during a thoracotomy than anticipated by preoperative imaging techniques. When the disease is disseminated extensively, a cure will not be achieved by surgical procedures alone. A decision must then be made to resect if palliative goals can be met. The advantage of thorascoscopic removal of solitary metastases is the limited surgical trauma, which results in an improved postoperative recovery, shorter hospital stay and decreased long-term morbidity. These effects should be counterbalanced by the risk of incomplete resection of metastatic disease that is assured by thoracotomy and direct palpation. This study determined the feasibility, accuracy and outcome of thorascoscopic resection of solitary peripherally located pulmonary metastases.

Material and methods
Between November 1992 and October 1996, 28 patients (12 men and 16 women) with pulmonary nodules (found during follow-up by routine chest roentgenograms) that were considered to be metastases from the primary tumour, and for whom resection was considered as a therapeutic option, were eligible for this study. This study included thorascoscopic resection of all identified lesions evaluated by confirmatory thoracotomy. This study design was chosen as in 1992, thoracotomy with wedge resections of all suspicious lesions after careful palpation of the lung was considered standard treatment for pulmonary metastases. Furthermore, at the time, video-assisted operations were new and experimental. Further selection criteria included three or fewer solitary lesions with a diameter of three 3 cm or less, located in the periphery of the lung. No specific attempts were undertaken to
obtain preoperative cytological diagnosis. Patients were required to be fit enough to undergo the intended thoracotomy and pulmonary resection. If a pulmonary nodule appeared to be technically unresectable during the thoracoscopy, or if the nodules were benign or carcinoid, patients underwent a thoracotomy and were registered for this study but not included in the analysis.

Patients underwent the after standard work-up for surgery: CT scan (Siemens Somaton Plus CT scanner, Munich, Germany, single slice technique with slices of 7 mm without contrast), bronchoscopy, pulmonary function tests, and investigations to exclude loco-regional relapse or metastasis at other sites.

The end points for this study were the number of successful procedures, that is, the number of thoracoscopic resections for all lesions found on CT scan when no residual disease was demonstrable at confirmation thoracotomy; the number of technical failures; reoccurrence of the disease, either pulmonary or elsewhere; and survival.

The study was approved by the medical ethical committees of both the Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NCI-Avl) and the Academic Hospital Free University (AHFU). Patients were entered in the study after informed consent. Twenty-three patients were treated at the NCI/AvL and 5 at the AHFU.

**Surgical technique**

The 28 operations were performed by three surgeons (ER, FZ, SM). After the induction of general anaesthesia, patients were ventilated through a double-lumen endotracheal tube that allowed contralateral ventilation and ipsilateral collapse of the lung. Patients were positioned in a stable lateral position. Depending on the location of the metastases, three to four ports were introduced, usually 12 mm. After a careful inspection, all visible or "palpable" (by instrumentation) lesions were removed by the GIA stapling technique. Special care was taken not to clamp or sever the lesion. The specimen was then removed through one of the ports in a sterile bag and sent for frozen section analysis.

After the removal of all the recognized lesions and a histological examination by frozen section, a confirmatory thoracotomy was performed. The lung was then carefully examined for residual disease. Any suspicious palpable abnormality was excised, usually by GIA stapling technique. If the lesion was considered to be a second primary after frozen section histology, a formal lobectomy including lymph node sampling from the mediastinum was performed. Haemostasis was assured and air leaks were corrected before closure. Thoracotomy was closed over a chest tube.

**Statistical analysis**

The Fisher’s exact test was used to determine the relationship between the number of pulmonary metastases on CT scan and the result of thoracoscopic resection. An overall survival curve was constructed with the Kaplan-Meier method. The Clopper-Pearson method was used to determine the confidence interval of percentages. All statistical analyses were performed with the Statistical Package for the Social Sciences software, version 8.0 (SPSS, Chicago, IL).
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Table 1: Patients characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12 (43)</td>
</tr>
<tr>
<td>Female</td>
<td>16 (57)</td>
</tr>
<tr>
<td>Mean age at surgery (years)*</td>
<td>59 (35-72)</td>
</tr>
<tr>
<td>Previous disease</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>6 (21)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>8 (29)</td>
</tr>
<tr>
<td>Breast</td>
<td>4 (14)</td>
</tr>
<tr>
<td>Renal</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Others</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Preoperative CT scan finding</td>
<td></td>
</tr>
<tr>
<td>Number of lesions</td>
<td></td>
</tr>
<tr>
<td>one lesion</td>
<td>19 (68)</td>
</tr>
<tr>
<td>two lesions</td>
<td>3 (11)</td>
</tr>
<tr>
<td>three lesions</td>
<td>6 (21)</td>
</tr>
<tr>
<td>Diameter lesions (mm)*</td>
<td>17 (5-30)</td>
</tr>
</tbody>
</table>

*Values are mean (range). All other values in parenthesis are percentages.

Table 2: Perioperative findings

<table>
<thead>
<tr>
<th>Number of lesions on CT scan</th>
<th>1</th>
<th>&gt;1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>No thoracoscopic resection due to technical failure</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Thoracoscopic resection performed</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Thoracotomy not performed</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Confirmation thoracotomy (A)</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Thoracoscopic resection complete (B)</td>
<td>11</td>
<td>1</td>
</tr>
</tbody>
</table>

A vs. B: *P* = 0.010 Fisher exact test

Results

Table 1 lists patient characteristics. Table 2 shows the perioperative findings of all patients. It appeared technically impossible to perform a thoracoscopic metastasectomy in 10 patients (36%). In 7 patients the lesion was not visible because of pleural adhesions or a central location. In the 3 remaining patients, the lesion was visualized but complete thoracoscopic resection was impossible because of either the location or size of the lesion. These 10 patients underwent a thoracotomy.

One patient did not have a confirmatory thoracotomy because the lesion was diagnosed as a 1-cm carcinoid after analysis of the frozen section.
Seventeen of the 28 patients underwent a subsequent confirmatory thoracotomy. In 12 patients (71%) no visible or palpable abnormality was found after the thoracoscopic resection. In 5 patients (29%) residual disease (one to three nodules, range 2 to 5 mm) was found and removed. No residual tumour was found at the site of any of the thoracoscopic wedge resections.

Considering preoperative CT findings, the probability of a thoracoscopic resection being complete was higher in patients with one metastasis (11 of 12, 92%) than in patients with two or three metastases (1 of 5, 20%) \( p = 0.010 \); Fisher's exact test) (Table 2). In patients with one solitary metastasis the Clopper-Pearson confidence interval, which predicts the probability of a successful thoracoscopic resection, was 62% to 99%. The mean diameter of the lesions resected by thoracoscopy was 17 mm (range 7 to 30 mm).

The pathologic diagnoses of the resected lesions were benign (hamartoma; \( n = 1 \)), carcinoid (\( n = 1 \)), a second primary (\( n = 6 \)) and metastases of known primary (\( n = 20 \)). Five patients with a second primary were included in the 11 solitary deposits in which thoracoscopy was considered accurate.

The hamartoma could be visualized but not resected through thoracoscopy because of its central location in the nondeveloped fissure between the right upper and middle lobe.

There was no mortality associated with the procedure and there were no perioperative complications. Postoperatively, four complications occurred in 28 patients. These included
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pneumonia (n=1), prolonged air leak (n=1), subcutaneous emphysema (n=1), and transient respiratory failure (n=1).

Of the 20 patients with metastases, 6 have died to date, 7 are alive with disease and 7 are alive without demonstrable disease. The median follow-up of the 14 patients still alive is 42.5 months (range 2 to 71 months). Survival at 5-years is estimated to be 59% (SE 14%) (Fig 1). Among the 20 patients, 10 patients developed a recurrence of the disease within the chest: 3 patients in both lungs, 4 patients in the other lung, 2 patients in the same lung but in a different lobe, and 1 patient in the area of the wedge resection (port site).

Comment

This study shows that the thoracoscopic resection of solitary metastasis in the periphery of the lung is feasible. We demonstrated evidence that the success rate of the thoracoscopic resection is associated with the number of lesions found on CT. This finding is in contrast with a comparable study by McCormack and colleagues 12. In their series, additional malignant tumours were found at thoracotomy in 10 of 18 patients (56%) as compared with 5 of 17 (29%) in the present study. Even in patients with one lesion detected on CT, 7 of 14 patients (50%) had additional metastases found (one of 12 in this study). McCormack and colleagues concluded that cancer will be missed if thoracoscopy is used as the only technique because of the discrepancy between radiographic and surgical findings.

CT scan is known to underestimate the number of lesions found at thoracotomy. McCormack and colleagues 7 demonstrated that CT scan did not identify 42% of lesions. Lesions smaller than 1 cm are especially difficult to detect on CT. Munden and colleagues 13 reported that these small lesions, missed by CT scan but found during surgery, may not be ignored because many are malignant (58%). The current generation of helical CT screening 14 and positron emission tomography 15,16 may identify nodules in the 2 to 3-mm range and could be helpful in identifying metastases more accurately.

This study showed that known metastases could be resected with adequate margins by the video-assisted thoracoscopic wedge resection. However, lesions occult on CT scan but otherwise palpable may easily be missed by the thoracoscopic technique alone. The clinical consequence of this outcome is uncertain, as multiple lung metastases from solid tumours are very rarely cured by surgery alone. A long-term remission will seldom be achieved when more than three metastases are found preoperatively 3,6. Secondly, those “missed” nodules will emerge during follow up by chest roentgenogram or CT scan, and if solitary or limited in number, they will be accessible for surgical resection.

In our study, 10 of 28 patients (36%) underwent a thoracotomy because thoracoscopic resection was deemed technically impossible. This is in agreement with the experience from other series 17,18.

The favourable 5-years survival rate of 59% may be due to patient selection and the small numbers of patients. The two-stage procedure, thoracoscopy followed by a confirmatory
thoracotomy, does not seem to have a negative effect on the outcome. In this series, one patient had a port site recurrence diagnosed 20 months after thoracoscopic resection. This patient is described elsewhere. Port site recurrence is an uncommon but feared complication of thoracoscopy for malignant lesions. A number of precautions need to be taken to avoid port site recurrences. The use of thoracoports instead of tab incisions, atraumatic tissue handling, and the use of endoscopic specimen retrieval bags are factors that may reduce the risk of port site recurrence.

The advantage of thoracoscopy over resection through a thoracotomy is the limited surgical trauma with consequently reduced postoperative morbidity and pain. Additional benefits are an improved postoperative recovery, shorter hospital stay, and reduced medical costs.

Although this study was small, our evidence shows that the probability of a thoracoscopic resection being complete seems to be at least 62% for patients with a single metastasis on CT scan, given our selection criteria.

In conclusion, a thoracoscopic resection and a “wait and see” policy can be considered a viable treatment option for patients with solitary metastasis smaller than 3 cm, located in the periphery of the lung. Patients with multiple or centrally located lesions should be treated with thoracotomy because that technique allows palpation of the lung tissue and provides a better overview. Second primary tumours should be treated accordingly.

References
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