Hand-Assisted Thoracoscopic Surgery for Pulmonary Metastasectomy through Sternocostal Triangle Access: Superiority in Detection of Non-Imaged Pulmonary Nodules

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Hand-Assisted Thoracoscopic Surgery for pulmonary metastasectomy through sternocostal triangle access allows manual palpation of both lungs, thus permitting effective treatment of lung metastases. In our research, 62 patients from November 2001 to January 2012 underwent our Hand-Assisted Thoracoscopic Surgery procedures for pulmonary metastasectomy. Clinical data, including the number of pulmonary metastases determined by Computed Tomography/Positron Emission Tomography-Computed Tomography, surgical findings and survival data of these patients were collected. We found that the median follow-up time was 23.7 months (range 2.4 to 85.6 months). 30 cases of them had post-operative recurrences and the median disease-free survival period was 27.4 months. For Computed Tomography scan, the overall sensitivity for proved metastases was 63% (115/182). 67 non-imaged malignant nodules were palpated and removed in 14 cases. For Positron Emission Tomography-Computed Tomography scan, the overall sensitivity was 66% (79/120). 41 non-imaged malignant nodules were palpated and removed in 12 cases. This study show that the Hand-Assisted Thoracoscopic Surgery provides an easier way for routine bilateral pleural exploration, and thus is critical and effective in detection of non-imaged malignant pulmonary metastases, which might contribute to long-term disease-free survival.

Complete resection of pulmonary metastases remains the standard treatment for selected patients with isolated pulmonary metastases from extra-thoracic primary malignancies, which is associated with a 5-year survival rate of 21% to 68%.

When video-assisted thoracic surgery (VATS) was introduced as a minimally invasive surgery, it was quickly utilized in metastasectomy. Some new approaches, such as the transthoracic hand-assisted thoracoscopic surgery (HATS) developed by Mineo and Detterbeck as well as the trans-diaphragmatic HATS developed by Wright, have been used in this field. We also developed a HATS procedure for bilateral lung metastasectomy through sternocostal triangle access, which has been reported previously.

Some authors suggest that the sensitivity of a Computed Tomography (CT) scan is insufficient, and therefore complete manual exploration during thoracotomy should be considered for patients undergoing pulmonary metastasectomy. In addition, without manual palpation, the high rate of missing occult metastases during VATS procedures is unacceptable. This study assessed the reliability of our HATS approach in detecting occult metastases when comparing to preoperative helical CT and Positron Emission Tomography-Computed Tomography (PET-CT), and analyzed the survival of the patients who underwent this procedure.

Results

62 patients with pulmonary nodules and a history of solid organ malignancy underwent 65 HATS procedures for pulmonary metastasectomy by the same group of surgeons. Three patients underwent more than one pulmonary
metastasectomy for recurrence. The characteristics of the procedures are shown in Table 1. The histological information of primary tumors was demonstrated in Table 2.

Median follow-up of HATS for bilateral lung metastasectomy through sternocostal triangle access patients was 23.7 months (range 2.4 to 85.6 months). No patient was lost of follow-up. Post-operative recurrences were found in 30 cases. The routine examinations in the follow-up included chest X-ray performed every three months with chest CT scan every six months for five years. Abdominal CT scan was done every six months to twelve months depending on the status of the patients and the classification of primary cancer. Five-year disease-free survival rate in our cohort was shown in Figure 1. One-year, Two-year, Three-year and five-year disease-free survival rates were 84.4%, 61.8%, 44.3% and 31.9%, respectively. Mean disease-free survival time was 40.5 months (log-rank, 95% confidence interval, 32.03 to 48.94). Median disease-free survival period was 27.4 months.

CT scans were performed before 62 HATS procedures. The median interval between metastasectomy and the examination was 13 days (range, 2–52 days). Based on the information of CT scans, 111 pulmonary nodules that were not identified in the images preoperatively were found in 26 cases, and 67 non-imaged malignant nodules were palpated and removed in 14 cases. 29 (29/42) cases who had predicted unilateral metastases at CT scan were confirmed to be unilateral. While if we change the definition into the high metabolic nodules, 76 pulmonary nodules that were not imaged preoperatively were found in 19 cases, and 43 non-imaged malignant nodules were palpated and removed in 12 cases. 18 (18/25) of the cases who had been predicted to have unilateral metastases were confirmed to be unilateral. Sensitivity and positive predictive value for CT/PET-CT are shown in Tables 3.

**Discussion**

Accurate thoracic imaging brings reliable prediction of the metastatic disease. It is very important to select those patients who would
benefit from resection, and palliate those patients who would not\(^1\). Technological progress has resulted in the widespread availability of helical CT scanners\(^1\), which has demonstrated superior detection rates compared to conventional CT\(^1\). Overlapping image reconstruction may enhance the number of visible nodules and reduce the number of false-positive nodules attributable to cross sections of pulmonary vessels\(^1\). Therefore, some researchers suggested that helical CT should be the better choice than the palpation of lungs\(^1\). Unfortunately, recent studies have compared helical CT prediction to surgical exploration and reported a high risk of missing lesions in CT scan\(^1\).

VATS has been widely used in thoracic surgery in the last decade. Although it is a minimally invasive surgery, VATS makes the palpation of the lungs difficult and incomprehensive, and therefore might be not suitable for pulmonary metastasectomy. The previous studies of VATS showed unsatisfactory results in detection of pulmonary metastatic lesions when compared to our HATS procedure (Table 4)\(^8,14\). Indeed, VATS is suitable for diagnosis of most undefined peripheral pulmonary nodules including pulmonary metastasis\(^1\). However, the role of therapeutic VATS metastasectomy remains largely unknown\(^1\).

The standard approach of metastasectomy is to palpate the lungs at the time of resection in order to completely remove all metastatic deposits\(^1\). Some researchers recommended sternotomy or thoracotomy\(^1\). Studies of these conventional procedures have found that the sensitivity of helical CT in detection of pulmonary metastatic lesions

### Table 3 | Nodules Revealed at Surgery and on Computed Tomography/Positron Emission Tomography- Computed Tomography

| Procedures enrolled to the analysis (N = 65) | Surgery | TRUE Positive | FALSE Negative | Sensitivity | FALSE Positive | PPV |
|--------------------------------------------|---------|---------------|----------------|-------------|----------------|-----|
| Nodules                                    | 252     | 139           | 113            | 55%         | 21             | 87% |
| Metastases                                  | 183     | 126           | 57             | 69%         | 33             | 79% |

| Procedures with CT scan (N = 62) | Surgery | TRUE Positive | FALSE Negative | Sensitivity | FALSE Positive | PPV |
|----------------------------------|---------|---------------|----------------|-------------|----------------|-----|
| Nodules                          | 246     | 135           | 111            | 55%         | 5              | 96% |
| Metastases                       | 182     | 115           | 67             | 63%         | 15             | 88% |

| Procedures with PET-CT (N = 43) | Surgery | TRUE Positive | FALSE Negative | Sensitivity | FALSE Positive | PPV |
|---------------------------------|---------|---------------|----------------|-------------|----------------|-----|
| Nodules                         | 169     | 93            | 76             | 55%         | 1              | 99% |
| Metastases                      | 120     | 79            | 41             | 66%         | 8              | 91% |

| Procedures with CT & PET (N = 40) | Surgery | TRUE Positive | FALSE Negative | Sensitivity | FALSE Positive | PPV |
|-----------------------------------|---------|---------------|----------------|-------------|----------------|-----|
| Nodules                           | 163     | 104           | 59             | 64%         | 5              | 95% |
| Metastases                        | 118     | 78            | 40             | 66%         | 18             | 81% |

PPV: Positive Predictive Value.

### Table 4 | Sensitivity of Helical CT in Detecting Pulmonary Metastases

| Approaches | Study | N  | No. of metastases | Sensitivity (%) |
|------------|-------|----|-------------------|-----------------|
| Thoracotomy| Kayton et al 2006\(^{16}\) | 54 | 209               | 87.6            |
| Thoracotomy| Nakajima et al 2007\(^{14}\) | 34 | 130               | 85.4            |
| Thoracotomy| Kang et al 2008\(^{17}\) | 27 | 198               | 77              |
| Thoracotomy| Pfannschmidt et al 2008\(^{18}\) | 125 | 331              | 83.7            |
| Thoracotomy| Ellis et al 2011\(^{9}\) | —  | 73                | 88.3            |
| Thoracotomy| Chung et al 2011\(^{19}\) | 120 | 368              | 26.7% (32/120) have occult metastases |
| VATS       | McCormack et al 1999\(^{8}\) | 18 | 19                | *               |
| VATS       | Nakajima et al 2007\(^{14}\) | 79 | 120               | 90              |
| VATS       | Ellis et al 2011\(^{9}\) | —  | 35                | *               |
| Transxiphoid HATS | Mineo et al 1999\(^{3}\) | 13 | 21                | 76.2            |
| Transxiphoid HATS | Ambrogi et al 2000\(^{10}\) | 22 | 49                | 84              |
| Transxiphoid HATS | Mineo et al 2001\(^{24}\) | 29 | 60                | 81.7            |
| Substernal HATS | Detterbeck et al 2004\(^{4}\) | 16 | 18.8% (3/16) have occult metastases |
| Transxiphoid HATS | Mineo et al 2007\(^{25}\) | 71 | 178               | 87.1            |
| Mix 1      | Parsons et al 2004\(^{11}\) | 41 | 88                | 78              |
| Mix 2      | Parsons et al 2007\(^{7}\) | 60 | 135               | 60              |
| Our HATS   | Current study | 62 | 182               | 22.6% (14/62) have occult metastases |

N: Number of cases.

—: No data obtained.

\(^*\): The number of pulmonary nodules palpated and removed is less than the number of pulmonary nodules detected on CT scan.

Mix1: The approaches consists of sternotomy (n = 19), unilateral thoracotomy (n = 11), VATS with a substernal handport (n = 11).

Mix2: The approaches consists of sternotomy (n = 30), unilateral thoracotomy (n = 19), VATS with a substernal handport (n = 11).
vastly curative treatment, which is associated with long-term survival. These studies also demonstrated that the sensitivity of PET-CT varies from 64.3% to 67.5% (Table 5)13,20,21, while our figure was 66%. The above results demonstrated that our HATS procedure, which may be more minimally invasive compared with sternotomy or thoracotomy, had similar ability in detection of occult pulmonary metastases.

Although the mortality of conventional thoracotomy is low1, there is increasing effort devoted to new approaches that may reduce the morbidity. Under this circumstance, the HATS procedure, which allows bilateral pleural exploration with a hand, would be an appropriate technique for patients undergoing metastasectomy with curative intent2–4. Mineo, Wright and Detterbeck have reported their HATS approaches that allow bilateral manual palpation of the lung in 1999, 2003 and 2004, respectively2,5,6. The above three HATS approaches demonstrated analogous results in detection of occult pulmonary metastatic lesions (Table 4). As an improvement for HATS, we have some variation in this surgical procedure to overcome some limitations of previous ones. For example, the change of resection from xiphoid appendix to sternocostal triangle access reduced the morbidity of intraoperative rhythm disturbance. Furthermore, keeping the integrity of diaphragm may reduce the risk of post-operative diaphragmatic hernia.

The analysis of 5,206 patients with pulmonary metastasis confirmed that complete removal of all metastatic deposits was a potentially curative treatment, which is associated with long-term survival1. The survival data of VATS, obtained from patients with fewer metastases, did not illustrate a frustrating result compared with conventional thoracotomy or HATS procedure (Table 6)2,5,12,13,20,21. The DFS of metastatic tumors treated with conventional thoracotomy or other HATS procedures, both of which allowed palpation of the lungs, were reported from less than 10 months to 29 months in the literatures (Table 6), while the figure in our cohort was similar (27.4 months). There is only one study that reported a better DFS than ours. In this study only the patients with lung metastasis of colorectal cancer were enrolled. In addition, the mean number of pulmonary lesions was 1.73, which was much less than ours (3.88). Therefore, the primary tumors with better prognosis and fewer lung metastases would contribute to the better survival23.

There are several limitations in this study. First, all the data were retrospectively collected. Second, although the radiographic images were reviewed by the same thoracic surgeon and consultant radiologist, the operative findings were recorded according to the operation notes and pathologic reports. Third, the involvement of different surgeons throughout the time of the study may bring in some bias, even though they were all trained in the same group. For example, results of finger palpation or the findings of additional metastatic lesions may not be consistent in all cases. A further well-controlled prospective study is needed to verify the value of our HATS approach in detection of occult pulmonary metastases and the survival data of patients with pulmonary metastases.

In conclusion, our HATS approach provides an easier way for routine bilateral pleural exploration similar to conventional sternotomy or thoracotomy regardless of unilateral or bilateral nodules on preoperative radiographic imaging. Using this HATS approach, we detected and removed occult pulmonary metastases, which might contribute to long-term DFS.

### Methods

This study was approved by the institutional review board of Sun Yat-sen University Cancer Center (SYSUCC) and informed consent was obtained from each participant. Chart review was performed on 62 consecutive patients who suffered from pulmonary metastases and underwent 65 HATS procedures through sternocostal triangle access between November 2001 and January 2012. Patients clinical and pathological data were obtained. Patients undergoing our HATS procedures were selected according to two mandatory prerequisites: (a) complete control of the primary tumor; (b) absent or resectable extrapulmonary metastases. Exclusion criteria were a history of pleuritis or pleurodesis, or the presence of cardiomegaly or arrhythmia.

CT examination were performed in 62 cases before metastasectomy, while PET-CT examination in 43 cases. The Philips twin flash CT was used from 1995 to 2005 with 10-mm slice collimation and 10-mm reconstruction. The Philips Brilliance 16 CT (Philips Healthcare, Andover, MA) with 5-mm slice collimation and 5-mm reconstruction was introduced in 2005. A Toshiba Aquilion 64 CT scanner (Toshiba

### Table 5 | Sensitivity of PET-CT in Detecting Pulmonary Metastases

| Approaches | Study | N  | No. of metastases | Sensitivity(%) |
|------------|-------|----|-------------------|----------------|
| Thoracotomy | Fortes et al 2008[20] | 104 | 154 | 67.5 |
| Thoracotomy | Cerfolio et al 2009[13] | 57 | 67 | 64.3 |
| Thoracotomy | Cerfolio et al 2011[21] | 152 | 21.1% (32/152) have occult metastases | 66% |
| Our HATS | Current study | 43 | 116 | 27.9% (12/43) have occult metastases |

N: Number of cases.

### Table 6 | Disease-free survival of metastasis tumor

| Approaches | Study | N  | DFS (months) | Survival Rate |
|------------|-------|----|-------------|---------------|
| Thoracotomy | Mutsaerts et al 2002[22] | 19 | <10 | 1-year: —, 2-year: 42, 3-year: —, 5-year: — |
| Thoracotomy | Nakajima et al 2008[2] | 71 | 27 | 57.6 |
| Thoracotomy | Carballo et al 2009[15] | 135 | 24.8 87.4 | —, 26.2 67.9 |
| Thoracotomy | Nakas et al 2009[12] | 27 | 29 | —, —, —, —, — |
| VATS | Mutsaerts et al 2002[22] | 16 | <10 | 1-year: —, 2-year: 50, 3-year: —, 5-year: — |
| VATS | Nakajima et al 2008[2] | 72 | 23.8 64.6 | —, 42.6 34.4 |
| VATS | Carballo et al 2009[15] | 36 | 25.6 91.7 | —, 69.6 69.6 |
| VATS | Nokes et al 2009[12] | 25 | 20 | —, —, —, —, — |
| Transxiphoid HATS | Mineo et al 2001[24] | 29 | 19 | —, —, —, —, — |
| Transxiphoid HATS | Mineo et al 2007[25] | 71 | 12 | —, —, —, —, — |
| Our HATS | Current study | 65 | 27.4 84.4 | 1-year: 61.8, 2-year: 44.3, 3-year: 31.9 |

N: Number of cases.

—: No data obtained.
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Author contributions

H.L. and L.J. designed and performed most experiments. L.J. and Y.B.L. wrote the main manuscript text. D.R.S.T. and Y.Z. collected the clinical data. L.J., Y.G.Z. and G.W.M. performed data analysis. H.L. designed and directed the overall project.

Additional information

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