FULLY ENDOGRAPHIC MAJOR PULMONARY RESECTION FOR STAGE I BRONCHIAL CARCINOMA: INITIAL RESULTS

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KEYWORDS
Lobectomy; Segmentectomy; Video-assisted thoracic surgery; Fully endoscopic lobectomy

Summary
Introduction. — Several case-series studies of major pulmonary resection (MPR) by video-assisted thoracic surgery (VATS) for non-small-cell lung cancer (NSCLC) have been published, but fully endoscopic MPR is still very rarely performed. Our objective here was to report the outcomes in 71 patients recently managed using fully endoscopic MPR for NSCLC.
Methods. — From 2007 to 2009, 635 patients with NSCLC underwent MPR (pneumonectomy, lobectomy or segmentectomy). Among them, 71 (11%) had features strongly suggesting clinical stage I NSCLC and were managed by fully endoscopic MPR, with no utility incision. Lobectomy was performed in 63 patients and segmentectomy in eight patients. Conversion to thoracotomy was required in two (2.8%) patients, because of a fused fissure in one and tight pleural adhesions in the other. Radical lymphadenectomy was performed in all patients.
Results. — Of the 69 patients managed endoscopically, none died and none experienced intraoperative complications. Mean operating time was 226 ± 38 minutes (range, 137–307 minutes) and mean intraoperative blood loss was 111 ± 93 mL (range, 0–450 mL). The final histological examination showed stage I NSCLC in 52 patients, NSCLC with node involvement in nine patients (pN1 in 6 and pN2 in 3) and other types of malignancies in eight patients. Mean number of nodes removed was 21 ± 8 after right-sided lymphadenectomy and 23 ± 8 after left-sided lymphadenectomy and the mean number of dissected node sites was 3 (range, 2–5). The postoperative morbidity rate was 23%. Mean postoperative hospital stay length was 6.9 ± 2 days (range, 3–12).

Abbreviations: NSCLC, non-small-cell lung cancer; CRP, C-reactive protein; MPR, major pulmonary resection; T-MPR, major pulmonary resection by thoracotomy; VATS-MPR, video-assisted thoracic surgery major pulmonary resection; FE-MPR, fully endoscopic major pulmonary resection.

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Introduction

The surgical management of clinical stage I non-small-cell lung cancer (NSCLC) rests on anatomic pulmonary resection, usually a lobectomy and dissection of the mediastinal lymph nodes [1]. Although the optimal extent of lymphadenectomy remains controversial, most surgical teams advocate radical lymphadenectomy, i.e., removal of all the nodes and of the tissues adjacent to the node sites draining the tumor. Thoracotomy was long believed to be indispensable given the risk of intraoperative injury (most notably to the blood vessels) inherent in major pulmonary resection (MPR) and the difficulties sometimes encountered in performing adequate node dissection. Rib spreading and injury to the intercostal nerves are widely held to be the main factors responsible for postoperative pain and lung function impairment. Thus, regardless of the extent of the pulmonary resection, thoracotomy diminishes the forced expiratory volume in 1 second (FEV1) by 20% [2]. The adverse effects of conventional thoracotomy on respiratory function prompted evaluations of smaller incisions and of muscle-sparing procedures, which failed to demonstrate benefits [3]. This absence of measurable benefits may be ascribable to the key role in the postoperative symptoms of rib spreading and intercostal nerve injury, regardless of the type of thoracotomy [4]. Mini-incisions became possible with the development of endoscopy and video-assisted thoracic surgery (VATS). Recently, several groups reported large case-series studies of VATS lobectomy, which showed low morbidity rates and similar survival rates to those seen after open thoracotomy [5–9]. However, these techniques are still rarely used. Thus, it has been estimated that only 5% of the 40,000 lobectomies performed each year in the US are done using VATS [6]. During MPR by VATS, the dissection is done in part endoscopically and in part via a small utility incision. Although VATS offers advantages over conventional open surgery, the resection is not fully endoscopic. Fully endoscopic surgery is defined as surgery performed only using endoscopic instruments and a video display, with no opening of the chest. At present, fully endoscopic MPR is very rarely performed [10–13]. We report preliminary data on the feasibility, morbidity, and extent of lymphadenectomy in 71 patients with a presumptive diagnosis of clinical stage I NSCLC. These patients were treated over the last 2 years, which is too short to assess survival. The objective of our study was to determine whether fully endoscopic MPR for NSCLC was safe and met the criteria for oncological surgery, i.e., complete tumor removal via anatomic pulmonary resection, absence of tumor transgression during dissection, tumor-free resection margins, and mediastinal lymphadenectomy with node identification [14]. Although the 2007 recommendations issued by the American College of Chest Physicians (ACCP) indicate that the data comparing lymphadenectomy to node sampling are inconclusive [1], all patients in our case-series underwent radical lymphadenectomy, that is, the procedure that would have been performed had they been managed by open surgery.

Methods

From 1st January 2007 to 1st March 2009, 635 patients underwent MPR (pneumonectomy, lobectomy, or segmentectomy) for NSCLC at the chest surgery department of the Institut mutualiste Montsouris in Paris, France. Among them, 71 (10%) had a strong presumption of clinical stage I NSCLC and underwent fully endoscopic MPR. All procedures were done by the same surgeon (DG), without patient selection. A single patient with a clinical stage I tumor was unable to undergo fully endoscopic surgery, because of a history of thoracotomy. Of the 71 patients, 63 underwent lobectomy and eight segmentectomy. Segmentectomy was performed only in patients who had respiratory function impairments that contraindicated lobectomy. The histological diagnosis was obtained preoperatively by computed tomography (CT)-guided transcaneous fine needle aspiration in 25 patients and by bronchoscopy in two patients. This low preoperative diagnosis rate was ascribable to the small size and deep location of the tumors in many patients. In 30 of the 44 patients with no preoperative diagnosis, an intraoperative biopsy was obtained either by needle aspiration (Bard Monopty®, Covington, GA, USA) or by atypical resection (n = 4). In the remaining 14 patients, the diagnosis was achieved only upon examination of the histological specimen.

Technique

The principles of the technique have been described elsewhere [15,16]. General anesthesia and selective bronchial intubation are used. The patient is positioned on the side, as for open surgery. As with all thoracoscopic procedures, two monitors and a mechanical scope holder are used. The scope has a deflectable tip (from 0° to 100°; LTF, Olympus, Tokyo, Japan), a distal sensor and high-definition television (HDTV) signal quality [15]. Only instruments designed specifically for endoscopic surgery are used. The instruments are introduced via two or three trocar tubes depending on the dissection requirements. Hemostasis of the large blood vessels is achieved by endoscopic stapling and control of the smaller blood vessels (e.g., interlobar arteries) by clips, ultrasound coagulation (SonoSurg™, Olympus) or bipolar thermofusion coagulation (Ligasure™, Valleylab) as appropriate. Additional instruments 3 mm in diameter are used to perform local procedures or to improve exposure. Recently, exposure of the mediastinum and/or hilum has been achieved using dedicated spreaders that can be left inside the pleural cavity, thus diminishing the number of trocars. No utility incision is performed. At the end of the procedure, one of the port sites
Endoscopic lobectomy for lung cancer

Figure 1. Example of scars 1 month after middle lobectomy and mediastinal lymphadenectomy for lung adenocarcinoma. Thin arrows: trocar ports; thick arrow: trocar port enlarged at the end of the procedure to enable retrieval of the operative specimen.

is enlarged to 3—4 cm (Fig. 1) for extraction of the lobectomy specimen previously enclosed in a retrieval pouch. Extraction of the specimen did not require a spreader in any of our patients. Mediastinal lymphadenectomy is performed as during open surgery. Depending on the type of procedure, one or two pleural drains are inserted through the ports. Drain removal is decided based on the usual criteria, i.e., absence of air bubbles and less than 150 mL of drainage fluid per 24 h.

For postoperative analgesia, we followed the standard protocol used at our institution after thoracoscopy. On the first day, intravenous acetaminophen (1 g every 6 hours) was combined with subcutaneous morphine (5 mg every 4—5 h) depending on the pain scale score. Subsequently, acetaminophen (1 g tid) and tramadol (50 mg tid) were given, in combination with 5 mg doses of subcutaneous morphine depending on the pain scale score.

The following data were collected prospectively: operating time, intraoperative blood loss, postoperative complications, hospital stay length, number of removed node sites, number of removed nodes and final histological stage.

Results

There were 45 men and 26 women, with a mean age of 65 years (range, 44—85 years) and 11 (16%) patients older than 75 years. Conversion to open surgery was required in two patients:

• one of these patients had a fused interlobar fissure that was considered undissectable endoscopically and;

• the other had tight pleural adhesions whose release led to oozing of blood responsible for inadequate visibility.

The procedures in the remaining 69 patients are listed in Table 1. The predominance of tumors in the right lung and more specifically in the right upper lobe, was consistent with the usual topographic distribution [17]. Radical lymphadenectomy was performed in all patients.

No postoperative deaths occurred among the 69 patients managed by fully endoscopic surgery. None of these patients experienced intraoperative complications or tumor transgression during the dissection. Mean operating time was 226 ± 38 minutes (range, 137—307 minutes) (Fig. 2). Mean intraoperative blood loss was 111 ± 93 mL (range, 10—450 mL) and no patients required blood transfusions. Most of the 16 (23%) postoperative complications were minor (Table 2). Among them, four were directly related to the surgical procedure: recurrent nerve palsy occurred in two patients (one case on each side) and chylothorax in two patients, of whom one recovered spontaneously within 3 days and the other underwent thoracoscopic thoracic-duct ligation on postoperative day-5 with an uneventful subsequent course. Mean time to removal of the last drain was 4 ± 2 days (range, 2—9 days).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Pulmonary resection procedures performed in the 69 patients managed by fully endoscopic surgery.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection procedure</td>
<td>Number</td>
</tr>
<tr>
<td>Right upper lobectomy</td>
<td>27</td>
</tr>
<tr>
<td>Right middle lobectomy</td>
<td>8</td>
</tr>
<tr>
<td>Right lower lobectomy</td>
<td>9</td>
</tr>
<tr>
<td>Left upper lobectomy</td>
<td>9</td>
</tr>
<tr>
<td>Left lower lobectomy</td>
<td>8</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>8</td>
</tr>
<tr>
<td>Apical-posterior of right upper lobe (n = 2)</td>
<td></td>
</tr>
<tr>
<td>Apical of right lower lobe (n = 2)</td>
<td></td>
</tr>
<tr>
<td>Basal segments of right lower lobe (n = 2)</td>
<td></td>
</tr>
<tr>
<td>Lingula (n = 2)</td>
<td></td>
</tr>
</tbody>
</table>

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Table 2  Postoperative complications in the 69 patients managed by fully endoscopic surgery.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged air leak (&gt; 6 days)</td>
<td>3</td>
</tr>
<tr>
<td>Pneumothorax (repeat drainage)</td>
<td>2</td>
</tr>
<tr>
<td>Atelectasis (bronchoscopic aspiration)</td>
<td>2</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>5</td>
</tr>
<tr>
<td>Recurrent nerve palsy</td>
<td>2</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 3. Pleural drainage time and postoperative hospital stay length after fully endoscopic lobectomy or segmentectomy.

Mean hospital stay length after surgery was 6.9 ± 2 days (range, 3—12 days) (Fig. 3). The final histological diagnosis was stage I NSCLC in 52 patients and stage II NSCLC in nine patients (Tables 3 and 4). The remaining eight patients had the following types of cancer: lung metastases

Table 3  Final pathological stage in 69 patients with a presumptive preoperative diagnosis of clinical stage I non-small-cell lung cancer who were managed by fully endoscopic surgery.

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA</td>
<td>pT1N0M0</td>
<td>36</td>
</tr>
<tr>
<td>Stage IB</td>
<td>pT2N0 M0</td>
<td>24</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>pT1N1M0</td>
<td>3</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>pT2N1 M0</td>
<td>3</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>pT1N2 M0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>pT2N2 M0</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 4  Final histological diagnosis in 69 patients with a presumptive preoperative diagnosis of primary lung cancer who were managed by fully endoscopic surgery.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary adenocarcinoma</td>
<td>47</td>
</tr>
<tr>
<td>Squamous-cell carcinoma</td>
<td>6</td>
</tr>
<tr>
<td>Large-cell carcinoma</td>
<td>8</td>
</tr>
<tr>
<td>Carcinoid tumor</td>
<td>3</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Lung metastasis</td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 4. Total number of removed nodes on the right and left sides in patients managed with fully endoscopic surgery.

Figure 5. Number of nodes removed during right-sided dissection of groups 4R and 7.

Figure 6. Number of nodes removed during left-sided dissection of stations 5, 6, and 7.
Figure 7. Examples of node stations dissected during fully endoscopic surgery. a: appearance after dissection of station 4R; T: trachea; Ph: vagus nerve; Ph: phrenic nerve; Az: azygos arch; VCS: superior vena cava; BSD: right main bronchus; b: appearance after right-sided dissection of station 7; BSD: right main bronchus; BSG: left main bronchus; P: pericardium; Es: esophagus; c: appearance after dissection of stations 5 and 6; Ao: aorta; d: appearance after left-sided dissection of station 7; BSD: right main bronchus; BSG: left main bronchus; Es: esophagus.

(n = 2), carcinoid tumor (n = 3), pulmonary carcinosarcoma (n = 2) and lymphoma (n = 1). The margins were tumor-free in all patients. The mean number of hilar nodes (Group 10) removed during surgery or found in the operative specimen was two per patient (range, 0—9). The mean number of mediastinal nodes removed per patient was 21 ± 8 after right-sided dissection and 23 ± 8 after left-sided dissection. The mean number of dissected node stations per patient was 3.1 (2—5) (Figs. 4—7). All patients were reevaluated 1 month after surgery. The chest radiograph was considered normal in all patients. None of the patients experienced port site infection, chest wall complications or functional complications.

Discussion

Although VATS-MPR performed by experienced surgeons is now an accepted method for treating stage I or II NSCLC [1], it is still very rarely used. Jones et al. estimated that VATS-MPR was used for only 5% of lung cancer resection procedures in the US and 3% in the UK [5]. However, several large case-series studies of VATS-MPR for lung cancer showed very good morbidity and survival rates [6,7,9,18,19]. Several evaluations of postoperative C-reactive protein (CRP) and cytokine levels suggest better immune defense preservation after VATS than after conventional open thoracic surgery [2,20—22], in keeping with data obtained in other fields [23]. Although the potential clinical benefits of improved immune defense preservation are difficult to evaluate [24], VATS lobectomy is associated with short hospital stays. In our study, 42% of patients were discharged within 6 days after surgery and the longest stay was 12 days. In a retrospective study by Shigemura et al., hospital stay length was significantly shorter after fully endoscopic MPR than after VATS-MPR or conventional open MPR [18]. Although hospital stay length is not an outcome of major interest in patients with serious malignant diseases, a short stay indirectly reflects faster recovery [25]. In addition, VATS facilitated the delivery of adjuvant chemotherapy, allowing earlier treatment initiation and increasing the proportion of patients given the full planned protocol, compared to conventional open surgery [26]. However, several authors recently pointed out that, although promising, the results are difficult to interpret given the absence of standardized definitions of the procedures. Thus, substantial technical variations exist, most notably regarding the type and length of the incision and whether a rib spreader is used [27,28]. Our group and others [11—13,29,30] developed a technique that requires no utility incision. Instead
Feasibility

Very few reports of fully endoscopic MPR have been published and most come from Japanese groups [11,18,19,30]. Their data and ours show that, provided enough time and care are devoted to the dissection, conversion to open surgery is rarely required (2.8% of patients in our case-series and 1.6% in those reported by Shigemura et al.) [18]. Conversion to open thoracotomy was required in two of our patients, for tight pleural adhesions and a fused nondissectable fissure, respectively. In two other patients, fully endoscopic MPR was possible despite tight pleural adhesions, after a lengthy release phase. A fused fissure does not preclude endoscopic MPR, as shown by Nomori et al. [32]. Conversion to open surgery is required in patients with tight pleural adhesions whose release causes the oozing of blood in amounts that obscure vision. Importantly, conversion to open surgery is mandatory in patients with involved nodes adhering to vessels, whose dissection carries a risk of vessel injury.

Safety

The results reported here confirm earlier data indicating that fully endoscopic MPR has a satisfactory safety profile. No patients had bleeding events or complications that could not be managed endoscopically. Intraoperative blood loss was limited (111 mL on average), in keeping with earlier reports [18]. Blood loss at the upper end of the range observed in our study was related, not to the lung resection, but to dissection of the mediastinal nodes, which may be arduous by the endoscopic technique in overweight patients. In a case-series of patients with lung metastases managed by fully endoscopic MPR without mediastinal lymphadenectomy, we found that mean blood loss was only 55 mL [16].

Absence of an incision

We previously discussed the advantages of not performing a utility incision [15]. The fully endoscopic technique obviates the need for a utility incision, which does not improve safety and which, in many case-series, was closer to a mini-thoracotomy than to a simple parietal incision. Oda et al. even suggested dispensing with the retrieval incision by stapling the resection specimen then extracting it through one of the ports [11]. However, we do not recommend this method, given the need for a detailed histological examination of the specimen including identification of any pedicle nodes and accompanying parenchymatous lesions.

Mediastinal lymphadenectomy

Although recent recommendations do not indicate that radical lymphadenectomy is better than simple sampling [1], most surgeons feel that radical lymphadenectomy allows optimal staging and probably improves survival. Nevertheless, a recent study comparing radical lymphadenectomy to sampling in stage I NSCLC found no significant difference in survival [33]. Concern that fully endoscopic surgery (Table 4) might not allow satisfactory lymphadenectomy long prompted us to reserve this method for patients with benign lesions or metastases requiring no lymphadenectomy [16]. It has been suggested that the fully endoscopic method may not allow an oncologically radical procedure [34]. In our case-series, the mean number of removed nodes was 22 ± 7, which was similar or greater than the number removed by thoracotomy [33]. In a study comparing thoracotomy, VATS and fully endoscopic surgery for lobectomy, no statistically significant differences were found across the three groups regarding the number of removed nodes (25 ± 7 with thoracotomy, 22 ± 6 with VATS, and 23 ± 9 with fully endoscopic surgery) [18]. With sufficient experience, we found that stations 4R, 5, 6, 7, 8, and 9 were fairly easy to remove, whereas removal of group 7 via a left-sided approach was difficult in some patients, as with open surgery. To overcome this difficulty, we used appropriate instruments including a deflectable endoscope and, in some cases, we performed the lymphadenectomy as the first stage of the procedure, as recommended by Oda et al. [11]. Overall, with experience and appropriate equipment, fully endoscopic lymphadenectomy is equivalent to lymphadenectomy via open surgery.

Limitations of the fully endoscopic technique

The long operating time is a limitation in high-volume centers, together with the need for sophisticated equipment including a high-performance video system and for operating-room staff trained to use this equipment. Fully endoscopic MPR requires 226 minutes on average, whereas open lobectomy for a stage I tumor requires only half as much time [12]. We found no substantial decrease in the operating time with increasing experience (Fig. 2). In a study comparing fully endoscopic surgery, VATS, and open surgery for lobectomy, the mean operating time was significantly longer in the fully endoscopic group (246 ± 47 minutes versus 169 ± 27 minutes with VATS and 159 ± 27 minutes with open surgery) [18]. The long operating time reflects the need for set-by-step dissection and painstaking hemostasis, as even minimal bleeding impairs vision and therefore potentially compromises the safety of the dissection.

The reproducibility of fully endoscopic MPR has not been established. It has been reported that VATS-MPR for lung cancer can be taught safely [35]. Fully endoscopic MPR, however, requires highly specialized technical skills and sophisticated equipment, which limits the use of this technique. Although we have performed 142 fully endoscopic MRPs (including procedures for lung metastases and benign lesions), we still feel that this is not a routine procedure and we are not confident that it could be taught safely (Fig. 2). As underlined by Bollen et al., there is a long learning curve [10]. However, several factors can be expected to gradually improve the accuracy of fully endoscopic MPR.
One of these factors is the use of high-definition imaging systems and deflectable endoscopes [15] to facilitate orientation and close-up viewing [30]. Another factor is the use of instruments having multiple degrees of freedom [29], which improve dissection accuracy. Finally, CT angiography with 3D reconstruction facilitates the intraoperative detection of blood vessels, most notably in patients with variant anatomy [36].

**Use of fully endoscopic surgery in patients with stage II cancer**

The large case-series of VATS-MPR included patients with stage II and even stage IIIA cancer [7]. Only patients with clinical stage I cancer were included in our study and in previous studies of fully endoscopic MPR. Whether increasing experience will lead to expanded use of fully endoscopic surgery is unknown, but several arguments suggest that this method may be best reserved for stage I tumors. First, a tumor that is large and/or that involves a neighboring organ may be difficult to expose, which may lead to tumor transgression. Second, blood vessel dissection may be difficult and hazardous in patients with N1 or N2 nodes. In our experience, the unexpected identification of nodes in the pedicle and/or fissure was associated with difficulties such as the oozing of blood and adhesions.

In sum, our results in this preliminary cohort of 55 patients, together with previously published data, indicate that fully endoscopic MPR allows oncological radical surgery as defined in the introduction: anatomic resection without tumor transgression, tumor-free margins, and radical mediastinal lymphadenectomy. Whether the indications of fully endoscopic MPR will expand as experience accumulates and technology improves remains unclear. At present, we feel that fully endoscopic MPR is best suited to the management of patients with stage I lung cancer.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

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