Long-term Survival After Videothoracoscopic Lobectomy for Stage I Lung Cancer*

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Study objectives: The aim of this study was to evaluate our personal experience and survival curves after video-assisted thoracic surgery (VATS) lobectomies for stage I lung cancer, in comparison with the results reported in existing literature.

Design: Retrospective analysis of our experience and an overview of literature.

Setting: Department of Surgery, San Giuseppe Hospital, University of Milan.

Patients: From October 1991 to December 2001, of 257 patients with clinical stage I lung cancer, 193 patients underwent VATS lobectomy, 7 patients were declared inoperable at thoracoscopic exploration, and 57 patients were converted (18 patients for oncologic reasons and 39 patients for technical reasons).

Results: We observed no intraoperative mortality and no recurrence. Survival data were analyzed with the Kaplan-Meier method along with a log-rank test for statistical significance. The global survival rates at 3 years and 5 years were 77.7% and 63.64%, respectively. T1N0 patients had a better survival curve at 3 years and 5 years (83.50% and 70.21%, respectively) compared to T2N0 patients (71.13% and 56.12%). Patients < 70 years of age had better 3-year and 5-year survival rates (82.37% and 73.32%, respectively) than those > 70 years of age (57.49% and 37.09%). This difference was statistically significant (p < 0.01).

Conclusions: Our results after the VATS approach match the “best” results reported in literature following conventional surgery. Minimally invasive surgery seems to imply reduced tissue damage and decreased impairment of immunologic function. VATS lobectomy permits radical oncology as accurately as lobectomy by thoracotomy, provided that long-established standards are respected. In spite of technical difficulties, it could therefore become a valid alternative in treating stage I lung cancer.

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Key words: bronchogenic carcinoma; pulmonary lobectomy; survival; video-assisted thoracic surgery; video-assisted thoracic surgery lobectomy

Abbreviations: CI = confidence index; IL = interleukin; NSCLC = non-small cell lung cancer; VATS = video-assisted thoracic surgery

Lobectomies are undoubtedly the most difficult operations to perform thoracoscopically. Ten years after the first video-assisted thoracic surgery (VATS) resection,1–3 concern regarding the potential for intraoperative accidents and, above all, regarding oncologic validity have limited the development and acceptance of this kind of operation. Postoperative pain and hospital stay are apparently reduced, daily activities are resumed more rapidly, and cosmetic results are better.4–8 As most of these procedures are performed for malignancies, these advantages weigh little in the overall considerations regarding oncologic problems.

The oncologic validity of VATS pulmonary resections is certainly unproven, although most authors admit to using precisely the same methods and criteria generally employed in conventional oncologic surgery. A few preliminary reports9–12 at 3 years and 5 years of follow-up show that results are sometimes superior to those obtained with conventional open surgery. This improved outcome could be due to the reduced trauma and consequent immunologic advantages.13 If proven, this would be a further incentive for the surgical community to adopt thoracoscopic techniques.

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Patients and Methods

From October 1991 to December 2001, of 2,306 VATS procedures carried out in the same institution, 257 patients with clinical first-stage lung cancer underwent surgery for an intended VATS lobectomy. All of these patients, who were eligible for curative surgery on the basis of traditional staging (chest radiographs, and thoracic, abdominal, and brain CT, and bronchoscopy), were submitted to a VATS exploration as the first step of the operation. This preliminary step enables the surgeons to decide between thoracoscopic or thoracotomic resection. Preliminary thoracoscopy can also reveal an unexpected cause of inoperability, as it did in seven patients of our series (six pleural carcinomatosis without pleural effusion, and one mediastinal invasion). Indication criteria for VATS lobectomy established at the beginning of our experience are as follows: (1) T1N0 and T2N0 lung cancers < 3 cm in size; (2) no intrabronchial lesion or bronchoscopic evidence of infiltration of the lobar bronchi; (3) no atelectasis; and (4) no evidence of infiltration of the parietal pleura during VATS exploration.

The technical aspects of VATS lobectomy have already been described in our previous articles.2,14–17 The procedure was converted to thoracotomy in 57 patients (18% of the cases). The conversions were due to absence of the fissure in 2 cases, invasion of the parietal pleura in 2 cases, and failure of the lung to collapse in 2 cases. VATS lobectomy was successfully carried out in 193 patients. All types of resection were undertaken (Table 1). The histologic type is detailed in Table 2. Postoperative histology confirmed the preoperative staging in 165 patients (87 T1N0 and 78 T2N0) but revealed pathologic lymph nodes in 28 patients (N1 in 22 cases and N2 in 6 cases).

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The global Kaplan-Meier survival rates at 3 years and 5 years were 77.7% (95% confidence interval [CI], 7.3) and 63.6% [95% CI, 9.4], respectively. T1N0 patients had a better survival curve at 3 years and 5 years (83.5% [95% CI, 8.9] and 70.2% [95% CI, 12.4], respectively) compared to T2N0 patients (71.1% [95% CI, 11.6] and 56.1% [95% CI, 14.2]) [Fig 1]. However, there was no statistical difference between survival rates for stage IA and stage IB patients (Fig 2). The histologic type of tumor,

Table 1—Type of Resection Among 193 VATS Lobectomies (October 1991 to December 2001)*

<table>
<thead>
<tr>
<th>Type of Resection</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right upper lobectomies</td>
<td>45</td>
</tr>
<tr>
<td>Right lower lobectomies</td>
<td>43</td>
</tr>
<tr>
<td>Middle lobectomies</td>
<td>22</td>
</tr>
<tr>
<td>Bilobectomy</td>
<td>1</td>
</tr>
<tr>
<td>Left upper lobectomies</td>
<td>36</td>
</tr>
<tr>
<td>Left lower lobectomies</td>
<td>43</td>
</tr>
<tr>
<td>Lingulatectomies</td>
<td>3</td>
</tr>
</tbody>
</table>

*Single institution series.

Results

We recorded no intraoperative mortality. Two patients (1.03%) died within 60 postoperative days: one patient due to contralateral pneumonia, and the other patient due to rupture of the heart 15 days after a myocardial infarction. Long-distance follow-up was carried out by outpatient examination every 6 months and every year. Official death certificates produced by the Office of Vital Statistics were obtained in order to verify causes of death. Fifteen patients found at postoperative histology to have a carcinoid tumor and 2 patients with small cell lung cancer were excluded from the analysis of survival, even though they were alive after 5 years. Data were analyzed using the Kaplan-Meier method. The statistic significance of Kaplan-Meier curves was been analyzed with the log-rank test.

The average age was 63.08 years (range, 11 to 78 years), and male patients outnumbered female patients with a ratio of 3.1 to 1. No recurrence of disease was discovered at follow-up in the lung, mediastinum, or trocar insertion or utility thoracotomy sites. Four patients had metachronous lung cancers. During the follow-up, we registered 41 deaths: 25 deaths were due to progression of the disease, and 4 deaths were due to different diseases (two acute myocardial infarctions and two strokes); two patients died of bone metastases within 3 months postoperatively, and five patients died of other cancers (prostate, pancreas, kidney, etc.). In five patients, the cause of death could not be ascertained.

The global Kaplan-Meier survival rates at 3 years and 5 years were 77.7% (95% confidence interval [CI], 7.3) and 63.6% [95% CI, 9.4], respectively. T1N0 patients had a better survival curve at 3 years and 5 years (83.5% [95% CI, 8.9] and 70.2% [95% CI, 12.4], respectively) compared to T2N0 patients (71.1% [95% CI, 11.6] and 56.1% [95% CI, 14.2]) [Fig 1]. However, there was no statistical difference between survival rates for stage IA and stage IB patients (Fig 2). The histologic type of tumor,
whether squamous (68.9% [95% CI, 13.5] at 3 years, 63.3% [95% CI, 14.5] at 5 years) or adenocarcinoma (83.9% [95% CI, 8.3] at 3 years, 63.3% [95% CI, 13] at 5 years), also showed no statistically significant influence (Fig 3). There was a statistically significant difference ($p < 0.01$) between patients < 70 years or > 70 years of age. In the 90 patients who were < 70 years of age, the 3-year and 5-year survival rates were 82.3% [95% CI, 8.7] and 72.3% [95% CI, 11.3], respectively, compared to the 45 patients aged > 70 years, in whom survival rates were 57.5% [95% CI, 16.4] and 37.1% [95% CI, 18] (Fig 4).

**Discussion**

Although different authors\(^3\)–\(^5\),\(^7\),\(^8\),\(^10\),\(^12\),\(^14\) have adopted VATS for staging and treating stage I lung cancer, this approach is still widely debated. Minimally invasive surgery has gradually and widely replaced conventional surgery as the procedure of choice for benign chest disease. This has not occurred for treating malignancy, due to technical reasons (still inadequate instrumentation, lack of three-dimensional vision, and the possibility of manually palpating the lesion) and, even more impor-
tantly, due to oncologic concerns. The possibility of carrying out a major VATS lung resection in selected cases has been described since the 1990s, but has not gained wide acceptance, and still only a few centers worldwide carry out these operations routinely. VATS lung resections are undoubtedly more technically demanding than the same conventional procedures. Faced with these objective difficulties, questions have arisen on the need for learning a new technique or carrying out technical acrobatics in order to accomplish a procedure that is simple to learn and carry out with a conventional approach. This is particularly true in cases of stage I lung cancer. A number of reasons have contributed to establishing a rather negative opinion particularly in surgeons who are accustomed to conventional criteria and results, not only regarding thoracoscopic lobectomies, but also regarding thoracoscopy in general when applied to lung cancer. An improperly increased number of thoracoscopic wedge resections carried out instead of conventional lobectomies, “unorthodox” simultaneous stapling techniques proposed to overcome difficult dissections, and concerns on tumor seeding have all contributed to these perplexities.

At present, no randomized study has proven the advantages of VATS lobectomies over conventional lobectomies. However, the advantages would appear to include reduced postoperative pain and hospital stay, faster resumption of regular activities, and improved cosmetic result. An inquiry regarding thoracoscopic procedures carried out by Mack et al in 1997 revealed that videothoracoscopic approach for complex procedures such as VATS lobectomies...
were considered by most surgeons as “investigative” or “unacceptable.” When we carried out the first VATS lobectomy for cancer in October 1991, we were fascinated by this technology, but strongly believed that the indications and codified surgical steps and oncologic principles had to be respected even with VATS approach.

In our series, one of the most emphasized aspects was the intraoperative evaluation of lymph nodes. Fourteen patients in whom N1 or N2 nodes were discovered during the operation were converted. Nevertheless, postoperative histology findings unexpectedly revealed N1 nodes in 22 patients (11.4%) and N2 nodes in 6 patients (3.1%).

The possibility of tumor seeding on the trocar insertion site or minithoracotomy through which the specimen is removed has been described in the early phases of literature, but is seldom encountered presently. In our opinion, seeding and recurrence on the surgical resection margins can be the consequence of technical mistakes or incorrect indications for thoracoscopy. In our series of 1,010 consecutive patients with lung cancer undergoing thoracoscopy to achieve a true surgical staging of the neoplasm, and among whom 327 patients finally underwent a thorascopic resection (193 lobectomies, 6 pneumonectomies, and 128 wedge resections), we have never observed any seeding on the trocar site insertion or on the resection margins. The crucial steps are careful manipulation, avoidance of
tumor damaging, and employment of a plastic bag, when necessary. However, cases of tumor invasion in the trocar insertion sites have been described in literature despite the use of a plastic bag.5

Another main aspect that causes doubts and concerns regarding VATS lobectomies for cancer is the limited literature available on patient survival. Data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) show relative survival rates for stage I non-small cell lung cancer (NSCLC) diagnosed in the United States in 1992 and 1993 of 57.8% after 3 years and 46.9% after 5 years. More recent data concerning 38,652 patients with stage I NSCLC diagnosed in 1994 and 1995, reported by 1,633 US hospitals for the National Cancer Data Base, showed a 5-year survival rate of 36.89%.24,25

For stage I lung cancers, the largest historical series26–30 available in the literature indicate that survival of patients treated with conventional approach ranges between 54% and 83% for stage IA (T1N0), and between 37% and 65% for stage IB (T2N0). At present, still only a few articles5,8–12,19,31 report survival curves in patients with stage I lung cancer following VATS lobectomy (Table 3). A comparison among series of VATS lobectomies shows significant differences between different authors.11,18

In our experience, the survival of patients with stage I lung cancer following VATS lobectomy reaches the global rate of 77.7% at 3 years and 63.64% at 5 years. In patients > 70 years old, the survival rate was 57.49% at 3 years and 37.09% at 5 years, also due to the age-factor mortality. But in patients < 70 years old, the survival rates are 82.37%
at 3 years and 72.32% at 5 years. Statistical analysis has proven that this difference is highly significant (p < 0.01). No survival difference has been recorded for different histologic types (Fig 3).

The good results described in the literature could be determined by a number of factors. Undoubtedly, it must be borne in mind that the very strict selection criteria for thoracoscopic lobectomy determine a further understaging in the variable group that make up stage I lung cancer. This could represent a selection bias of patients with better prognostic factors, which are not clearly identifiable due to the limited number of patients available. Furthermore, the criteria for selecting the patients to be submitted to VATS lobectomy are different in the different series.

Different articles\textsuperscript{13–36} have sustained the possibility of a more favorable immunologic response after VATS, with reduced tissue damage and consequent reduction of stress hormones. Reduction of IgG levels, lower levels of C-reactive protein interleukin (IL)-6, tumor necrosis factor and cortisol, a better preservation of cell-mediated immunity, and a reduced postoperative release of inflammatory and antiinflammatory cytokines have been demonstrated. Even more important, a reduced release of tumor necrosis factor-α, IL-1β, IL-6, and IL-10 (antiinflammatory cytokines) have been observed.\textsuperscript{13,31,37}

We can therefore argue that, in spite of the technical difficulties, VATS lobectomy for lung cancer could become a valid alternative to conventional treatment of stage I lung cancer if carried out in qualified centers. Videothoracoscopy permits oncologic radicality as accurately as thoracotomy lobectomy, provided that long-established standards are respected. Survival curves in literature are extremely encouraging, but they do not unquestionably prove the superiority of VATS lobectomies for stage I lung cancer, even though the data are without doubt on par with the “best” data obtained after conventional surgery.

**References**


