

# Video-Assisted Thoracoscopic Wedge Resection of T1 Lung Cancer in High-Risk Patients

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## Objective

This study assessed the reliability and safety of VATR for treatment of peripheral T1 lung cancer in high-risk patients.

## Summary Background Data

Surgical resection is the best therapy for stage I lung cancer. Patients with poor cardiopulmonary status or those who are elderly (> 75 years of age) are considered to be at high risk from thoracotomy and are frequently referred for radiation therapy or expectant palliative management. Data from previous studies suggest that survival with wedge resection is similar to that with lobectomy. The authors propose VATR, which is minimally invasive, as a therapeutic option in patients considered to be at high risk for resection by thoracotomy.

## Methods

Between November 1990 and November 1992, more than 400 thoracoscopic lung resections were performed. Thirty patients with poor pulmonary function (forced expiratory volume [FEV<sub>1</sub>] < 1 L or < 35% predicted; arterial oxygen tension [PaO<sub>2</sub>] < 60 mmHg on room air; diffusion capacity [DCO] < 40%) underwent 31 VATRs (1 patient had a staged procedure for bilateral synchronous lung cancers). All patients had T1 peripheral lesions with no bronchoscopically visible lesions. Computed tomography of the chest revealed no evidence of mediastinal disease in all patients.

## Results

Patients had a mean FEV<sub>1</sub> value of 0.9 L (38% predicted) and a mean age of 71 years. Tumors were located in left upper lobe (LUL) in 13 patients, in right lower lobe (RLL) in 7 patients, in right upper lobe (RUL) in 6 patients, in left lower lobe (LLL) in 4 patients, and in right middle lobe (RML) in 1 patient. Computed tomography-guided wire localization, methylene blue surface injection, and intraoperative ultrasonography were used to assist in defining difficult lesions. All lesions were successfully resected without converting to thoracotomy. One patient died on the 34th postoperative day of myocardial infarction (operative mortality rate of 3%). Five patients had prolonged air leaks (< 5 days), with a median chest tube time of 3 days. Two patients experienced pneumonia.

## Conclusion

The authors concluded that VATR is a safe and reliable procedure for treatment of peripheral T1 lung cancer in high-risk patients. Long-term follow-up will be required to determine the efficacy of this procedure regarding survival and locoregional recurrence.

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Surgical resection is considered the best therapy for stage I lung cancer. Patients who are deemed unfit for surgery because of limited pulmonary function, cardiac status, or general health status are usually treated expectantly or with radiation therapy. Patients with clinical and radiologic stage I non-small cell lung cancer (NSCLC) receiving radiation therapy have a 5-year survival rate between 5% and 21%.<sup>2-5</sup> This low disease-free survival rate has stimulated interest in offering these patients surgery in the form of limited resection. Recently, video-assisted thoracoscopic resection (VATR) has emerged as a novel method for the resection of peripheral lung tumors.<sup>6,7</sup> This technique offers excellent visualization and the ability to localize and remove lesions in a patient-friendly manner, possibly with minimal stress and pain. This article reviews the early experience with VATR performed at three hospitals for peripheral T1 lung cancer in high-risk patients.

## PATIENTS AND METHODS

From November 1990 to November 1992, more than 400 thoracoscopic lung resections were performed. Thirty patients with peripheral T1 non-small cell lung cancer who fulfilled one or more of the following criteria were considered to be at high risk for thoracotomy and were offered lung resection through the VATR technique: forced expiratory volume (FEV<sub>1</sub>) in 1 second of less than 1 L or less than 35% predicted; arterial oxygen tension (PaO<sub>2</sub>) of less than 60 mmHg on room air; diffusion capacity (DCO) of less than 40% predicted; or an age of 75 years or older with poor general health status.

All patients had computed tomography of the chest indicating the absence of mediastinal lymph node involvement. All patients underwent bronchoscopy with no visible evidence of endobronchial disease. The mean age of these patients was 70.8 ± 6.4 years (median age, 71.5 years; age range, 56 to 83 years). The FEV<sub>1</sub> value for these patients was 1 ± 0.3 L or 39.5% ± 13.8% predicted.

Indications for VATR were a low FEV<sub>1</sub> value in 21 patients, age older than 75 years in 7 patients, a low PaO<sub>2</sub> value in 7 patients, and a low DCO value in 6 patients. Patients who had a low PAO<sub>2</sub> value were receiving continuous home oxygen with at least 2 L/min of oxygen administered through a nasal prong. The mean age of patients undergoing VATR because of their age was 78.4 ± 4.1 years. Patients who were operated on because they

had a low DCO value had a mean of 32.2% ± 4.6% predicted. Patients who were admitted for a low FEV<sub>1</sub> value had a mean of 0.9 ± 0.17 L or 33.2% ± 13.8% predicted FEV<sub>1</sub>.

Of the 31 procedures performed on 30 patients, lesions were identified pathologically as adenocarcinoma in 23, as squamous cell carcinoma in 6, and as large cell carcinoma in 2. Tumors were located in the left upper lobe on 13 occasions, in the right lower lobe on 7, in the right upper lobe on 6, in the left lower lobe on 4, and in the right middle lobe on 1. In order to assist in the intraoperative localization of these lesions, computed tomography-guided wire localization together with methylene blue lung surface injection was used on 18 occasions. Intraoperative ultrasonography was used on 7 occasions.

## RESULTS

All lesions were successfully identified intraoperatively. On 13 occasions, this was done using the conventional techniques of indirect inspection and palpation. On the other 18 occasions, the lesions were small and were in a location that was thought to be difficult to visualize, or were associated with extensive interstitial lung disease requiring the use of additional perioperative and intraoperative localization techniques.

All patients tolerated one lung ventilation reasonably well. With patience and time, most lungs deflated well and allowed proper inspection of the pleural cavity. Introduction of a suction catheter into the bronchus of the operative site facilitated deflation of the lung on a few occasions. None of the patients required carbon dioxide insufflation. Intraoperative sampling of ipsilateral hilar and N2 nodes was attempted routinely. All lesions were successfully resected without the need for conversion to thoracotomy. The resections were performed using mostly the Endo-GIA (Auto-Sutures, US Surgical Instruments). Nd:YAG laser and electrocautery together with autoclips were used on a few occasions to complete the resection or to perform the whole resection as described by Perlman. Fibrin glue (Tisseel, IMMUNOCANADA) was sprayed over the resection margins to minimize airleak when electrocautery or laser dissection was performed on five occasions. No significant complications occurred intraoperatively.

One patient died on the 34th postoperative day. This 62-year-old man, who had an FEV<sub>1</sub> value of 1.06 L (32% predicted), underwent wedge resection of a left upper lobe adenocarcinoma. He suffered a prolonged airleak (chest tube removed on the 20th postoperative day) and myocardial infarction on the 8th postoperative day. Despite maximal medical treatment, he had an expanding myocardial infarction associated with cardiogenic shock and died on the 34th postoperative day.

Presented at the 113th Annual Scientific Session of the American Surgical Association, Baltimore, Maryland, April 1-3, 1993.

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Accepted for publication April 15, 1993.

Chest tubes were removed at  $5.5 \pm 6.8$  days after operation (median, 3 days; range, 1 to 30 days). Five patients had prolonged airleak of more than 5 days ( $18.4 \pm 8.6$  days) (median, 14 days; range, 7 to 30 days). Two patients had pneumonia and required intravenous antibiotic therapy. Patients were discharged at a mean of  $8.6 \pm 7.6$  days after surgery (median, 6.5 days; range, 3 to 34 days).

## DISCUSSION

Over the last three decades there has been a marked increase in the incidence of lung cancer, from 40/100,000 to 70/100,000 population.<sup>8</sup> Most patients will have advanced lung cancer and only a small percentage will have clinical T1NOMO disease at the time of diagnosis.<sup>1,9</sup> In surgically staged NSCLC, only 152 of 1121 patients (35%) were reported to have T1N0 disease by the Lung Cancer Study Group. These patients had an expected 5-year survival rate of 68% and locoregional recurrence occurred in 28% of them, with the highest initial failure in the ipsilateral hemithorax.<sup>8-12</sup>

Despite the less than ideal results of surgery in stage I lung cancer, it remains the most effective treatment modality. Thirty-five years ago, a debate existed among surgeons as to whether a lobectomy, a less radical operation than a pneumonectomy, was an adequate procedure for patients with stage I lung cancer. Today, and based on numerous retrospective reports, a more limited resection in the form of segmentectomy or wedge resection appears to offer as good a survival outcome as a lobectomy.<sup>13-15</sup> A recent prospective Phase III study by the Lung Cancer Study Group compared the outcome of limited resection (segmentectomy or wedge resection) with that of lobectomy for peripheral T1N0. Despite careful intraoperative assessment of lymph node stations and resection margins, there was a 2.7-fold higher rate of locoregional recurrence in the limited resection arm than in the lobectomy arm. More disturbing was the observation that wedge resection had an even higher (3.5-fold) local recurrence rate as compared to lobectomy. Notwithstanding the smaller number of patients undergoing wedge resection (40 undergoing wedge resection, 110 undergoing segmentectomy, and 150 undergoing lobectomy), no survival difference could be observed between the three groups at 5 years (all being approximately 60%).<sup>15</sup>

Patients who are deemed unfit for surgery because of limited pulmonary function, cardiac disease, old age, or poor general health status are either treated expectantly or with radiation therapy. Such patients with stage I NSCLC receiving radiation therapy have an expected 5-year survival rate between 5% and 21%.<sup>2-5</sup> It appears that continuous and higher dosage radiation therapy (60 Gy)

results in better survival than fractionated and lower dosage radiation therapy (< 50 Gy). The disease-free survival rate was disturbingly low in patients receiving radiation therapy who had incomplete or no response. A major limitation to the interpretation of such radiation therapy studies is the less than adequate lymph node staging of patients enrolled and hence the chance of dealing with patients with higher than stage I lung cancer. Nevertheless, meta-analysis of such data indicates that surgical resection by wedge resection or segmentectomy continues to offer the best local control and survival rate (40% to 75%) in patients with peripheral T1 NSCLC.<sup>1,13-16</sup>

Thoracoscopic surgery, an old technique practiced for nearly a century, has benefitted from the technology acquired by the general and gynecological surgeons performing laparoscopic surgery. While initially video-assisted thoracoscopic surgery was indicated for the diagnosis and management of pleural disease, the availability of excellent visual tools together with the development of endostapling devices allowed for the expansion of its indications to the diagnosis and management of pulmonary, pericardial, and mediastinal disease.<sup>6</sup>

In this study, we reviewed our initial experience with VATR of peripheral T1 NSCLC in high-risk patients who would have been denied surgery otherwise because of poor lung function, general health status, or old age. A preoperative workup of these patients, which included chest x-rays, computed tomography, and bronchoscopy, confirmed these lesions to be clinically T1NOMO. Mediastinoscopy was not performed, accepting a 5% risk of false-negative mediastinal lymph node involvement.

In this group of 30 consecutive patients, VATR was well tolerated with no intraoperative complications. The operative mortality rate in this series was 3% and the only significant complication was that of prolonged airleak in five patients. Since we have adapted the routine application of Fibrin glue on the raw surface of the resection margins, we have not encountered the problem of prolonged airleak anymore. While comparisons are not available, it is the perception of the treating teams that these patients had less pain, better pain control, and shorter hospital stays than those patients undergoing open thoracotomy for the same indications.<sup>17</sup>

Our report indicates that VATR can be successfully applied for the resection of peripheral T1 lung cancer in high-risk patients. The procedure is patient-friendly and is associated with a low morbidity rate. We are concerned about the recent reports of a higher incidence of locoregional recurrence after wedge resection alone compared with a formal lobectomy. Nevertheless, in this group of high-risk patients, a more radical operation such as lobectomy is not feasible. These patients would be offered expectant treatment, radiation therapy, or

surgery. We believe that surgery offers the best option for the prompt removal of the tumor, together with a low morbidity rate and a better chance of survival. We are currently on the verge of starting an intergroup study that will examine in a randomized Phase III design the efficacy of adding local cone down radiation therapy to the resection margins after limited surgical resection in high-risk patients with peripheral T1 NSCLC.

Regarding the biology of lung cancer, we believe that it is likely that therapeutic modalities successfully applied to breast and rectal cancer can be implemented with similar efficiencies for lung cancer, just as the argument for Halstedian techniques of radical surgery have given way to less extensive procedures. It is possible that wedge resection with staging with or without radiation therapy based on the stage of cancer may prove to be the procedure of choice not only for patients at high risk from radical surgery, but also for all patients with T1NO lung cancer. Until carefully designed studies address these issues and prove them, we would recommend wedge resection by video-assisted thoracoscopic techniques only in patients who would not otherwise be eligible for major lung resection.

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## Discussion

DR. JAMES B. D. MARK (Stanford, California): Dr. Shennib, I enjoyed your presentation. I think it is worth noting that this series of patients came from several institutions.

Dr. Shennib, Dr. Landreneau, Dr. Mack, and others have done this with several kinds of problems treated by thoracoscopy. I think it is quite worthwhile because in that way they can gather a larger number of patients over a shorter period of time and bring more information to us quickly.

There is no question that thoracoscopy is upon us. In about one-third of our patients who go to the operating room, thoracoscopy is at least part of that operation. Sometimes it replaces an open technique such as an open lung biopsy. Sometimes it is a supplement to other techniques.

Now we have to decide just when and where to use it. Remember, you are comparing it to limited thoracotomy in high-risk patients that, as you note, has been carried out over the years with significant success. And it is going to have to be that good. I think it is not a leap forward to consider this an adequate operation for patients who are good risks and who have stage 1 lung cancer.

I'd like to ask Dr. Shennib what he does if on computed tomography scanning he finds that there are enlarged mediastinal nodes with a small peripheral lung cancer.

Additionally, I'd like to ask if you have carried out this operation for lesions that turned out not to be lung cancer? Clearly, some of the small lesions are not going to be diagnosed preoperatively. I think a long hospitalization and an air leak up to 30 days wouldn't be good for these benign lesions.

A third question is, has there ever been tumor contamination of the exit wound when you pull that specimen out through a small incision?

Again, I enjoyed the presentation and I appreciate the privilege of discussing the paper.

DR. JOSEPH MCLAUGHLIN (Baltimore, Maryland): (Slide) During a similar period over the past 2 years, we have performed video-assisted thoracoscopy on 143 patients. Sixty of these patients at our institution had resection of pulmonary tissue for a variety of reasons, 20 because of pulmonary nodules that we were unable to diagnose specifically preopera-