Long-term follow-up of video-assisted talc pleurodesis in malignant recurrent pleural effusions

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Abstract

Objective: Recurrent pleural effusion is a common condition and often presents a challenge for treatment. The aim of this report is to evaluate the long-term follow-up of thoracoscopic management of malignant recurrent pleural effusions.

Methods: From July 1st, 1992 to February 28th, 2001, out of 2311 VATS procedures performed at our Institution, 690 patients (29.85%) underwent videothoracoscopy (VATS) for recurrent pleural effusion. Of these 611 (88.55%) were treated for a malignant pleural effusion. There were 374 male and 237 female, with a mean age of 61.2 years. In all patients VATS was performed under general anaesthesia. The pleural effusion was carefully aspirated; fibrinous adhesions were taken down while dense fibrous adhesions were selectively divided; some limited decortications were also performed. Multiple pleural biopsies were always performed. Pleurodesis was performed with 5 g of sterile purified talc insufflated through a talc atomizer. One chest tube was left in situ for 3–5 days.

Results: Operative mortality was 0.81% (five cases). Postoperative complications occurred in 19 cases (3.1%). Specific histologic diagnosis was obtained in all patients. Follow-up was available for 602 patients (98.5%). After a median follow-up of 64 months (range 5–105 months), talc pleurodesis was successful in controlling recurrence of effusion in 92.7% (558 out of 602) of patients. The success rate did not show any statistically significant difference between patients who underwent postoperative adjuvant therapy and patients who did not. In two patients with failure of talc pleurodesis a redo-VATS was performed.

Conclusions: VATS represents the method of choice for both diagnosis and treatment of malignant recurrent pleural effusions. Talc poudrage is safe and effective in obtaining pleurodesis. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Video-assisted thoracic surgery; Pleural effusion; Recurrent pleural effusion; Pleurodesis; Treatment

1. Introduction

Recurrent pleural effusions occur commonly in cancer patients, especially in those with tumours of the lung and breast which account for 75% of all malignant pleural effusions [1], with the remaining 25% represented by malignant pleural mesothelioma, carcinoma of the stomach, ovary, lymphoma and other neoplastic diseases. Benign conditions, such as tuberculosis, pneumonia, rheumatoid pleurisy, congestive heart failure, pulmonary embolism, systemic lupus erythematosus, liver cirrhosis, sarcoidosis, may be also associated with pleural effusions.

The evidence of a pleural effusion require early evacuation of the fluid in order to relief symptoms, such as dyspnea, othopnea, and cough, and to allow for re-expansion of the lung; furthermore diagnosis should be obtained as soon as possible. Treatment options include needle thoracocentesis or tube thoracostomy. Recurrent or persistent pleural effusions in oncologic patients represent a challenge for treatment and need for a reliable, safe and definitive treatment. Videothoracoscopy (VATS) represents the gold standard for recurrent pleural effusions either for obtaining a diagnosis or for palliation of the effusion. The aim of this report is to evaluate the results and the long-term follow-up of 611 patients treated by videothoracoscopic talc poudrage for malignant recurrent pleural effusions.

2. Patients and methods

From July 1st 1992 to February 28th 2001, out of 2311 VATS procedures performed at our Institution, 690 patients (29.85%) underwent VATS for recurrent pleural effusion. Of these, 611 (88.55%) were treated thoracoscopically for a malignant pleural effusion. There were 374 (61.2%) males...
and 237 (38.8%) females. Their mean age was 61.1 years (range 23–83 years). Surgical criteria were: (1) need for diagnosis after histologically/cytologically negative thoracentesis, fiberoptic bronchoscopy, and/or fine needle aspiration biopsy: 153 patients (25.1%); (2) histologically/cytologically proven malignant recurrent pleural effusion non-responding to chemotherapy therapy and to corticosteroid: 247 patients (40.4%); (3) need for diagnosis and non-responding recurrent pleural effusion: 211 patients (34.5%).

Of the 611 patients, 491 (80.3%) had a history of previous malignancy. Forty-two patients developed pleural effusion following surgical treatment of lung neoplasm.

All patients underwent preoperative bronchoscopy to exclude endobronchial obstruction, and chest CT scan. In 97.8% (598 out of 611) of the patients one or two preoperative needle thoracentesis (with a mean of 1250 ml of evacuated pleural fluid) were performed in order to evaluate the possibilities of the lung to re-expand following evacuation of the pleural cavity and to obtain diagnosis. In 82% of the patients (501 out of 611) three or four thoracentesis were performed. VATS was performed in all patients under general anaesthesia. A 10.5-mm camera port and one or two 5.5-mm instrumentation ports were inserted. The pleural effusion was carefully aspirated; fibrinous adhesions were taken down while fibrous adhesions were divided with diathermy coagulation. A thorough assessment of the pleura and lung surface was made, and multiple (at least 6–7 samples) biopsies were taken from appropriate areas. The degree of lung expansion was ascertained with sustained positive pressure ventilation (25 cm of H2O). If lung expansion was not adequate to fill the hemithorax (trapped lung syndrome), a decortication was undertaken by removing the visceral cortex from the underlying lung by combined blunt dissection and traction from forceps in the same way as in open surgery [2]. Pleurodesis was performed with 5 g of sterile purified talc powder insufflated through a talc atomizer under direct vision. At the end of the procedure one (occasionally two) the chest tube was left in situ. The drain was removed when the volume collected remained under 200 ml for at least 48 h, usually 3–5 days.

Before being discharged from the hospital the patients were interviewed and a chest roentgenogram was obtained. Outpatients were followed-up by clinical interviews and chest X-ray after 1, 3, and 6 months, and every 8 months. Follow-up ended 1 September 2001. The effectiveness of talc pleurodesis was ascertained on relief of symptoms, and recurrence of pleural effusion by roentgenogram. A satisfactory result was defined as the improvement of symptoms with no detectable fluid on chest X-ray or evidence of residual fluid only in the costophrenic angle. In case of no-symptomatic improvement or recurrence of pleural fluid, the result was judged unsatisfactory.

3. Statistical analysis

Multiple comparisons were made with Fisher’s test. Differences were considered significant when the P value was less than 0.05.

4. Results

The average duration of VATS talc pleurodesis only was 16 min (±6 min). In 29 patients (4.7%) with a trapped lung syndrome, a thoracoscopic decortication was performed before talc pleurodesis; in such cases the duration was 79 min (±18 min). In an additional 15 patients with a trapped lung syndrome, thoracoscopic decortication was not performed because of the very poor performance status. All patients were weaned from mechanical ventilation in the operating theatre. Intraoperative complication occurred in one patient (0.14%) and consisted of damage to the mammary artery which was resolved thoracoscopically. Operative (30-day) mortality was 0.81% (five cases): there were two pulmonary embolisms, one pulmonary oedema, one myocardial infarction and one acute renal failure. Postoperative complications occurred in 19 cases (3.1%) (Table 1). Diagnosis was obtained in all patients. The pathology for all patients is shown in Table 2. The mean hospital stay was 5.8 days (range 4–31 days). Follow-up data was available for 602 (98.5%) of the 611 patients. Following surgery, 521 patients (85.3%) underwent adjuvant (chemo/hormono/and/or radiotherapy) therapy. Ninety patients (14.7%) received no treatment. Nine patients (1.5%) were lost at follow-up. After a median follow-up of 64 months (range 5–105

Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft tissue emphysema + prolonged air leak</td>
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</tr>
<tr>
<td>Prolonged air leak</td>
<td>5</td>
</tr>
<tr>
<td>Perforated gastric/duodenal ulcers</td>
<td>2</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
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Table 2

<table>
<thead>
<tr>
<th>Pathology of 611 malignant pleural effusion</th>
<th>No.</th>
<th>%</th>
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</thead>
<tbody>
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</tr>
<tr>
<td>Breast cancer</td>
<td>101</td>
<td>16.6</td>
</tr>
<tr>
<td>Malignant pleural mesothelioma</td>
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<td>8.9</td>
</tr>
<tr>
<td>Lymphoma</td>
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</tr>
<tr>
<td>Ovary cancer</td>
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<tr>
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<td>1.8</td>
</tr>
<tr>
<td>Sarcoma</td>
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<td>1.1</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>6</td>
<td>0.9</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>Uterus cancer</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>3</td>
<td>0.4</td>
</tr>
<tr>
<td>Oesophageal cancer</td>
<td>1</td>
<td>0.1</td>
</tr>
</tbody>
</table>
months), videothoracoscopic talc pleurodesis was successful in controlling recurrence of effusion in 92.7% of patients (558 out of 602). The success rate of the procedure was 93.0% (482 out of 518) in the group of patients who underwent adjuvant therapy, and 90.4% (76 out of 84) in the group of patients who received no adjuvant therapy. There was no statistical significant difference between the two groups of patients \( (P = \text{NS}) \). In the group of patients who underwent thoracoscopic decortication plus talc poudrage the success rate was 96.6% (28 out 29). In the group of patients with trapped lung syndrome who underwent talc poudrage only the success rate was 13.3% (2 out of 15).

The difference between the groups was statistically significant \( (P < 0.0001) \). In two patients with failure of videothoracoscopic talc pleurodesis for malignant effusion (malignant pleural mesothelioma in both cases), a redo-VATS was performed, respectively, 12 and 14 months after the primary VATS treatment; in both patients the redo-treatment was effective in controlling pleural effusion.

5. Discussion

Thoracocentesis is an essential first step in the diagnosis and treatment of recurrent pleural effusions. Anyway, repeated thoracocentesis may only provide temporary relief and can be associated either with the recurrence of pleural effusion (90% of patients will develop recurrence of effusion within 30 days) \( [3] \) or to iatrogenic pneumothorax, pleural fluid loculation or contamination with subsequent empyema. Simple large-bore (28F–36F) or small-bore (7F–16F) chest tube drainage often provide reliable drainage of the pleural cavity, although around 80% of patients show recurrence of their effusion within 30 days after removal of the tube \( [4,5] \). Drainage and pleurodesis by instillation of sclerosing agents has been shown to be an effective procedure for palliation of these patients. Among sclerosing agents, asbestos-free talc has proved to be superior to other commonly used agents, such as irritant chemothrapeutics agents, with a success rate ranging from 81 to 100% \( [6–8] \), compared to the 70–75% success rate shown by Tetracycline \( [9] \). Furthermore with asbestos-free talc there is no increased risk of mesothelioma and no significant impaired respiratory function \( [10–12] \). Some authors \( [14] \) show concern regarding the reported incidence of ARDS following talc poudrage. Such a complication, which has never been observed in our large experience, has not yet been clarified and maybe it could be related to various coexisting factors. In the light of the enormous experience gained worldwide, VATS has proved to be a safe procedure with a very low mortality and morbidity rate. At our institution, out of 2311 VATS procedures performed from July 1992 to February 2001, the overall mortality was 0.25% (six cases). Video-assisted thoracoscopy with talc poudrage has replaced conventional instillation of talc slurry through tube thoracostomy as the procedure of choice to achieve pleurodesis. As a matter of fact, VATS offers the advantage of complete evacuation of the pleural cavity, and visualization of the pleural surface allowing multiple biopsies to be performed with 100% diagnostic accuracy. Furthermore, adhesions may be broken up with confirmation of complete lung expansion, and appropriate distribution of the nebulized talc under direct vision and apposition of the pleural surfaces. To be as much effective as possible the lung should be completely re-expanded during the process of pleurodesis. If the lung is not able to re-expand, this results in increased intrapleural negative pressure and promotes filling of the pleural cavity ex vacuo until the balance of hydrostatic pressure is restored, resulting in a variable-sized pleural effusion. In the ‘lung trapped syndrome’ a prerequisite for successful pleurodesis is represented by a thoracoscopic decortication, which is commonly associated with an higher morbidity \( [2] \). An alternative is represented by the insertion of a pleuroperitoneal shunt \( [9] \), which has never been used in the present series. The operative mortality rate (0.81%) reported in the present series of 611 patients looks to be higher if compared to the 0.25% reported in the overall series of 2311 VATS performed at our institution. However, the series of pleural effusion includes patients with advanced malignancy which seem to be at much higher risk than those of the overall series. The goal of treatment in patients with pleural effusion is a successful palliation which should be assessed in terms of relief of symptoms and no recurrence of effusion on chest X-ray. The successful rate reported in our series of patients with malignant pleural effusion, 92.7% (558 out of 602), seems to be in agreement with figures reported by different authors. Schulze \( [13] \) and de Campos \( [14] \) reported a successful rate of 93% in a series of 105 VATS talc poudrage, and 93.4% in a series of 393 VATS talc poudrage, respectively. It should be adequately stressed that patients with malignant pleural mesothelioma have a high risk of tumoral seeding at the site of thoracoscopy ports. We as well as others recommend local radiotherapy, usually 30 Gy in ten daily fractions, in all of these patients \( [15] \).

In patients with trapped lung syndrome, thoracoscopic decortication represents the procedure of choice to achieve long-term pleurodesis with a statistically significant difference compared to talc poudrage only \( (P < 0.0001) \). Pleuroperitoneal shunts have been claimed by some authors \( [9] \) for trapped lung syndrome but we do not have any experience with such devices.

Adjuvant postoperative treatment (chemo/hormono and/or radiotherapy) does not statistically modify the success rate of talc poudrage in our experience.

The analysis of our 44 failed VATS talc poudrage pointed out that in at least 14 (31.8%) of these, the operating surgeon judged the lung to be trapped; of these only one patient belonged (2.27%) to the group of thoracoscopic decortications while the remaining 13 patients with trapped lung syndrome did not undergo thoracoscopic decortication.
because of a poor performance status. Two patients who showed a late recurrence of pleural effusion with a free lung underwent a redo-VATS talc poudrage. We believe that in case of early recurrence of effusion there is no rationale for a successful redo-pleurodesis. Only patients who show late recurrence (at least one year in our series) and good performance status, may probably benefit from a redo-treatment. Alternatives for patients with early recurrence include chest tube or pleuropertitoneal shunt insertions.

In conclusion, videothoracoscopic talc poudrage represents a safe and reliable method to obtain pleurodesis in patients with malignant recurrent pleural effusion non-responding to corticosteroid therapy and or to chemotherapy, or in cases in which the diagnosis has not been ascertained. The long-term results show a very high successful rate (92.7%). A more effective pleurodesis is likely if videothoracoscopic talc poudrage is performed early after the diagnosis and the lung is free to re-expand. At least one needle thoracocentesis is recommended before surgery in order to evaluate the compliance of the lung. Adjuvant therapy does not improve the success rate of talc poudrage. In trapped lung syndrome the failure rate of talc poudrage alone is very high so that a thoracoscopic decortication should be added. An alternative procedure is represented by the insertion of a pleuropertitoneal shunt [9]. Regarding the side effects of talc poudrage, no increased risk of malignant pleural mesothelioma, no significant deterioration of lung function, and no significant evidence of ARDS has been reported in controlled clinical trials and in our series [10–14].

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References


Appendix A. Conference discussion

Professor A. Yim (Shatin, Honk Kong): I have one question and one comment.

Talc pleurodesis has been shown to be highly effective from your results and from the published literature. Therefore I do not understand why you have to give additional postoperative radiation to your patients.

We reported a few years ago a randomized, prospective study comparing talc slurry with VATS talc insufflation for patients with malignant pleural effusion (Ann Thorac Surg 1996;62:1665–58) and found no differences between groups. We therefore advocate talc slurry for these patients who do not have trapped lungs. Not every patient needs to have surgery, and VATS although generally safe, is certainly not free from complications.

Dr Cardillo: Regarding the question, we use radiotherapy only in patients with malignant pleural mesothelioma, because we and others have seen the diffusion of the tumour along the trocar, at the point in which the ports are inserted. So the only reason to give local radiotherapy in patients with mesothelioma is to avoid local dissemination of the tumour.

Regarding talc slurry, I know that some institutions prefer talc slurry instead of talc poudrage. Our experience, and we think in this approach, is a little bit different, but, of course, the issue is open.

Dr H. Hauck (Vienna, Austria): Two questions. The first, do you have experience in this procedure on both sides, and the second question, what do you do if the lung did not expand fully?

Dr Cardillo: We have seen patients with effusion in both sides and in some cases we have treated it simultaneously, but it depends on the patient’s condition. Sometimes we do a staged procedure, sometimes we do a one-stage procedure.

As to the second question, as I showed in one of my slides, a thoracoscopic decortication should be added to the procedure, otherwise, the talc poudrage is ineffective. An alternative is represented by the pleuropertitoneal shunt, but we have never used it.

Dr D. Blyth (Durban, South Africa): What I would like to ask you about is your management of tuberculosis. Certainly we would see so very much more pleuropulmonary tuberculosis, in other words, a lot of lung destruction. Did you see this with your cases, did you follow them up with CT scan, say, later on to determine extent of damage, or was that your definitive treatment, or did you have to go on to surgery at a later stage and did the pleurodesis then complicate your surgery?

Dr Cardillo: We have seen some patients with tuberculosis, as I showed in my slides, but usually before doing the operation we do a CT scan to...
ascertain the condition of the lung, and in patients with a destroyed lung, as you asked me, I think talc poudrage is ineffective. We have to choose the type of surgery very, very carefully in these patients, and then to decide the operation with the pulmonologist. So it is a big problem. You cannot solve this problem with just talc poudrage.

**Mr A. Mearns (Bradford, UK):** Two questions. One a question, the other a comment. The first one is the talc varies throughout the world and it depends which pit they are taking it out of in your country. Some of it causes patients to have very serious reactions. What is your pharmacist doing to the talc before you get in theatres so that all the pyrogens have gone, because it can be very pyrogenic?

But number two, I would like to challenge the concept that you treat mesothelioma effusions with talc. Mesothelioma effusions accumulate very slowly when they are drained and very few of the patients feed a second drainage. The tragedy of mesothelioma is the effusion space is very quickly obliterated by the progress of the tumour, and you don’t need a bulk of talc in smothering a tumour space that is about to be obliterated by the progression of the disease, because this is not a cure, and very few patients actually need a talc poudrage. You need a diagnosis, I agree, and that you pick themselves out by having a significant respiratory problem with a second or third accumulation of fluid. Far too much talc is going on unnecessarily in the patient with mesothelioma because doctors feel they must do something. Don’t do it.

**Dr Cardillo:** Regarding the need of talc poudrage in mesothelioma, personally we disagree with you. We have treated 54 patients with mesothelioma, and this is a huge number. The great majority of these patients were treated because there was no diagnosis. In patients with mesothelioma it is very difficult to ascertain the diagnosis only with a cytological examination. Usually pathologists ask for a biopsy in mesothelioma, and in most of the patients we have done the operation not only for palliation of the effusion but for diagnosis, and moreover, most of our patients started effusion sometime before surgery and we see that the recurrence was very quick to come back of the effusion. So that was the reason we did talc poudrage in mesothelioma.

So the message is, in mesothelioma you have to carefully stage the patient, and I think that VATS is the most important procedure to stage the patient. You can see how is the mediastinal pleura, the diaphragmatic pleura. So it is important.

**Dr Mearns:** My problem is not the thoracotomy or the adequacy of the biopsy. That is mandatory. The question is whether you actually need to leave some talc in as a mark that you have been there. You must drain the effusion, correct, and you must get an adequate biopsy, correct, but why do you need the talc in everybody? That is what I am saying. There is too much talc going in. Everybody can have a biopsy, everybody can have a drainage, a first-time drainage of their effusion. That’s good surgery. It’s the talc signature I challenge.

**Dr O. Kshivets (Siauliai, Lithuania):** These are patients that are very difficult to treat and any success in this field should be appreciated. My question is, did you try to combine talc with intrapleural chemotherapy?

**Dr Cardillo:** Really, we didn’t in this group of patients, absolutely, we didn’t try to give intrapleural chemotherapy plus talc poudrage.