

# Early Outcome of Minimal Access Surgery to Mesothelioma

Hassan S. Hassan, Hany A. Eldomiaty, Ramy M. Samir\*

Department of Cardiothoracic Surgery, Suez Canal University, Egypt

## Abstract

**Background:** Malignant pleural mesothelioma (MPM) is a rare and aggressive malignancy arising from the mesothelial cells lining the pleural cavity. Treatment options include surgery, chemotherapy, radiation, and multimodality treatment. **Objective:** This study is designed to identify the short terms benefits and risks of surgical options for patients of mesothelioma with pleural effusion. **Patients and Methods:** This study was held at Suez Canal university hospitals and designed as a randomized control clinical trial all patients with proven diagnosis of mesothelioma with pleural effusion were included and randomized over 3 groups; Group A: patients underwent evacuation with a chest tube and pleurodesis by talc powder slurry. Group B: patients underwent VATs evacuation and pleurodesis. Group C: patient undergone VATs partial pleurectomy with decortication. **Results:** The patients were predominantly males; the pain scale was from 4 to 8 on a visual analogue scale with a mean of 6.315 patients (42.9%) undergone evacuation with a chest tube and pleurodesis while 10 patients (28.6%) underwent VATS pleurodesis with talc pou-drage also 10 patients (28.6%) undergone VATs partial pleurectomy from which 6 (17.1%) patients required decortication for trapped lung. with mean 7 days and the post-operative pain ranged on VAS scale from 2 to 9 with a mean of 4 while postoperative air leak occurred in 5 patients (14.3%) and postoperative wound infection in a total of 13.4%. **Conclusion:** VATs partial pleurectomy seems to be a good method in the management of mesothelioma as it operatively allows the benefit of managing lung entrapment and allows better lung expansion and is postoperatively associated with superior control on effusion recurrence.

**Keywords:** mesothelioma, VATs, pleurectomy, pleurodesis

## Introduction

Malignant pleural mesothelioma (MPM) is a rare and aggressive malignancy arising from the mesothelial cells lining the pleural cavity. There is a clear association between occupational or environmental asbestos and mineral fiber exposure and the development of MPM<sup>(1)</sup>. Malignant mesothelioma is an aggressive, treatment-resistant

tumor, which is increasing in frequency throughout the world. Although the main risk factor is asbestos exposure, a virus, simian virus 40 (SV40), could have a role.. Cytopathology of mesothelioma effusions or fine-needle aspirations is often sufficient to establish a diagnosis, but histopathology is also often required. Patients typically present with breathlessness and chest pain with pleural effusions. Median

\*Corresponding Author: ramy\_abdelrahman@med.suez.edu.eg

survival is now 12 months from diagnosis<sup>(2)</sup>. In 2015, about 60,800 people had mesothelioma, and 32,000 died from the disease. Rates of mesothelioma vary in different areas of the world. Rates are higher in Australia, the United Kingdom, and lower in Japan. It occurs in about 3,000 people per year in the United States. It occurs more often in males than females. Rates of disease have increased since the 1950s. Diagnosis typically occurs after the age of 65 and most deaths occur around 70 years old<sup>(3)</sup>. In Egypt retrospective study by Akl et.al 2007 was done there were 584 cases diagnosed as MPM on a histopathological basis during the period from January 1998 to December 2007. Full epidemiological data were only available for 165 cases due to the absence of a reliable registration system<sup>(4)</sup>. Treatment options for the management of malignant mesothelioma include surgery, chemotherapy, radiation, and multimodality treatment. Surgery in patients with disease confined to the pleural space is reasonable. The histopathological classification of a patient's malignant mesothelioma plays a pivotal role in treatment decisions. Patients whose mesotheliomas are sarcomatoid or biphasic (having both epithelioid and sarcomatoid features) have a worse prognosis and are generally not candidates for surgical intervention<sup>(5)</sup>. Tri-modality therapy involves a combination of all 3 standard strategies: surgery, chemotherapy, and radiation. In a study, patients undergoing a tri-modality approach involving extra-pleural pneumonectomy followed by combination chemotherapy and radiotherapy had an overall median survival rate of 24% at 2 years<sup>(6)</sup>. The role of surgery in malignant pleural mesothelioma remains a contentious issue. So the meso-vats trial was conducted as randomized control trial compared two palliative interventions: cytoreductive surgery in term of Vats partial pleurectomy versus talc pleurodesis in

patients with suspected or confirmed malignant mesothelioma and pleural effusion. The authors hoped to show an improvement in survival for video assisted thoracic partial pleurectomy (VAT-PP) and compare cost and symptom control in both interventions<sup>(7)</sup>.

## Patients and Methods

The study was held at thoracic surgery unite at Suez Canal University hospitals the main thoracic surgery center at east of Egypt which drain patients from 5 provinces including Suez Canal and Sinai territories. This study was designed as a randomized control clinical trial and all patients proven diagnosis of mesothelioma with pleural effusion were included and randomized over 3 groups. *Group A:* patients undergone evacuation with chest tube and pleurodesis by talc powder slurry. After insertion of chest tube according to radiology assessment , gradual evacuation started till complete evacuation and insurance of lung expansion by x ray and when drain output was less than 100 /24hour slurry mixture prepared by injection of local anesthetic through chest tube followed by talc-saline mixture then clamping the tube 6-12 hours after that release clamp and tube removal. *Group B:* patients undergone VATs evacuation and pleurodesis by talc powder poudrage. We used either general anesthesia or local anesthesia+ sedation, we prefer 2 port technique one for camera and the other for suction then used to introduce insufflator then talc powdered in chest cavity followed by closure in layer leaving small bore chest drain for the next 12-24 hours. *Group C:* patient undergone VATs partial pleurectomy with decortication. Classic 3 port VATs technique used as and 5<sup>th</sup> space utility port, camera port at 7<sup>th</sup> or 8<sup>th</sup> space and 3<sup>rd</sup> port ant scapular line, we started evacuation then partial

pleurectomy done +/- decortication as needed and after completion 2 drains left and removed after stoppage of drainage and air leak. Randomization was done with numerical sequence fashion. Patients were assessed for age, gender, smoking, history of asbestos exposure, symptoms, the tumor (type and stage), and post intervention for hospitalization, post-operative complications recurrence of effusion or empyema formation, the patient satisfaction from the procedure and quality of life improvement at the end point of the study at 3 months.

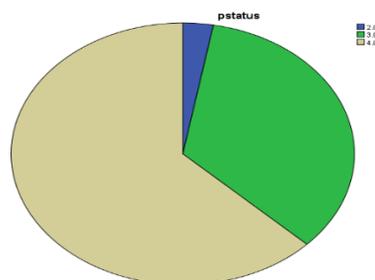
### Statistical Analysis

Data was collected and Statistical analysis was done by statistical package for social science (SPSS) version 22. Chi square was used to compare different frequencies. T test is similarly used for mean correlation and F test for comparison between different means. The level of significance (p value of 0.05. results to be statistically significant if value was < 0.05.

### Results

The patients were predominantly males (85.7%) with mean age 59.4 years youngest was 40years and oldest was 80 years. pain was the most frequent symptom in all patients with scale from 4 to 8 on visual analogue scale with mean 6.3 and cough is second to pain (60% of patients) the patients performance status according to Eastern Cooperative Oncology Group grading 62.9 % at the 4<sup>th</sup> grade as shown in figure 1. The epithelioid subtype was the most common by 80 % of the patients and the stage at presentation was 57.1 stages 3 and 42.9 stage 4 as shown in figure2. Fifteen patients (42.9%) undergone evacuation with chest tube and pleurodesis while 10 patients (28.6%) underwent VATS pleurodesis with talc poudrage also 10 patients (28.6%)

underwent VATs partial pleurectomy from which 6 (17.1%) patients required decortication for trapped lung as shown in figure 3.



**Figure 1: patients' performance status**

Post-operative hospitalization ranged from 4 days to 14 days with mean 7 days and the post-operative pain ranged on VAS scale from 2 to 9 with mean 4 while post-operative air leak occurred in 5 patients (14.3%) post-operative wound infection in total 13.4 % of the patients. Despite there was statistical significance in the presence of air leak in patients in group B and group C (p-value = 0.05) as shown in table 1 there was no statistical significance in total hospitalization between 3 groups (p-value 0.69). There was no statistical significance for empyema development post-intervention in group A (p-value 0.41) as shown in table 2. There was statistical significance for effusion recurrence at the end point of the study in group A (p-value =0.05) (table 3). Applying independent T-test, no statistical significance between the 3 groups regarding post-operative wound infection and hospitalization was seen. But there is high statistical significance in patient satisfaction at the end point of the study in favor of group C as globally 74.3 of the patients were satisfied at the end point of the study. There was no post-operative mortality to the end point of the study.

### Discussion

In our study The patients were predominantly males (85.7%) with mean age 59.4

years youngest was 40 years and oldest was 80 years, pain was the most frequent symptom in all patients with scale from 4 to 8 on visual analogue scale with mean 6.3 and cough is second to pain (60% of patients) the patients performance status according to Eastern Cooperative Oncology Group grading 62.9% at the 4<sup>th</sup> grade and the epithelioid subtype was the most common by 80% of the patients and the stage at presentation was 57.1 stage 3 and

42.9 stage 4. and data collected show the same pattern as in the meso-vats trial The VAT-PP and talc pleurodesis groups were generally balanced for age (mean, 69 years in both), sex (86% male in both), tumor type (epithelioid in 84% and 83%), International Mesothelioma Interest Group stage (e.g., III in 49% and 43%, IV in 27% and 35%), Eastern Cooperative Oncology Group performance status (0 in 24% and 19%, 1 in 60% and 62%)<sup>(7)</sup>.

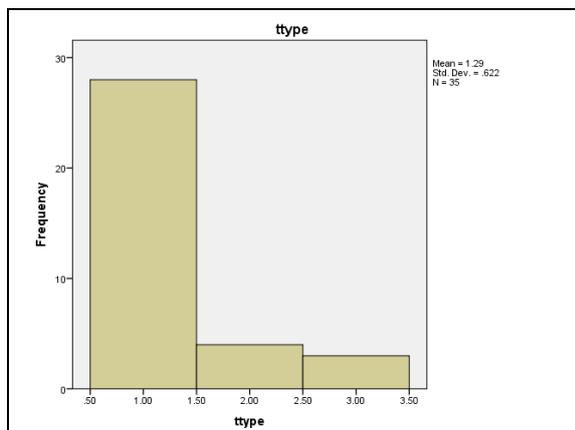


Figure 2: Mesothelioma pathology histogram

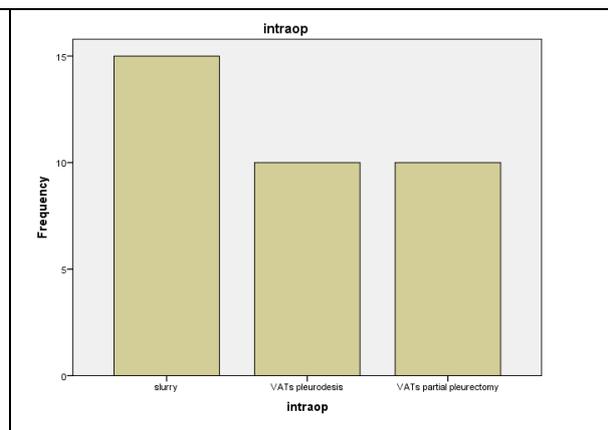


Figure 3: Frequency of 3 groups of intervention

Table 1: Relation between intraoperative intervention and postoperative air leak			
	Air leak		p value
	Yes	No	
Intra operative intervention			0.05
Slurry	0	15(42.85%)	
VATs pleurodesis	2(5.7%)	8(22.85%)	
VATs partial pleurectomy	3(8.57%)	7(20%)	
Total	5(14.28%)	30(85.71%)	

Table 2: Relation between intraoperative intervention and postoperative empyema				
	empyema		Total	p value
	yes	no		
Intraoperative intervention				0.41
Slurry	1 (2.85%)	14 (40%)	15 (42.85%)	
VATs pleurodesis	0	10 (28.57%)	10 (28.57%)	
VATs partial pleurectomy	0	10 (28.57%)	10 (28.57%)	
Total	1 (2.85%)	34 (97.14%)	35 (100%)	

Table 3: Relation between intraoperative intervention and recurrence after 3 months				
	Recurrence after 3 months		Total	p value
	yes	No		
Intraoperative intervention				0.05
Slurry	5 (14.28%)	10 (28.57%)	15 (42.85%)	
VATs pleurodesis	0	10 (28.57%)	10 (28.57%)	
VATs partial pleurectomy	0	10 (28.57%)	10 (28.57%)	
Total	5 (14.28%)	30 (85.71%)	35 (100%)	

Also, in fysh et al study of the 494 cases of mesothelioma recorded, 478 patients had proven MPM. Of these, 390 (86% men, mean (SD) age 70 (10.4) years)<sup>(8)</sup> and Phillips et al study there was 70 patients with mean age 68 years and the pathology was Epithelioid 68%; sarcomatous 7%; biphasic 25%<sup>(10)</sup> and same data from Aelony et al who included 26 patients with pathology Epithelial 88%; sarcomatoid 12%<sup>(11)</sup>. In our study 15 patients (42.9%) undergone evacuation with chest tube and pleurodesis while 10 patients (28.6%) underwent VATS pleurodesis with talc poudrage also 10 patients (28.6%) undergone VATs partial pleurectomy from which 6 (17.1%) patients required decortication for trapped lung. In larger trail as meso-Vats operative groups included 87 patients for VATs parietal pleurectomy and 188 patient talc pleurodesis group. (7) While in fysh and et al Pleurodesis was attempted in 165 patients (42.3%), either by surgery (n=78) or bedside instillation of talc (n=86) or bleomycin (n=1). Surgical pleurodesis was performed during video-assisted thoracoscopy (VATS) (n=64), pleuroscopy (n=3) or thoracotomy (n=11); all surgical pleurodesis procedures included talc poudrage and, in addition, 12 had pleurectomy<sup>(8)</sup> and Phillips et al Fifteen patients received only diagnostic direct pleural biopsy, 40 had video-assisted thoracoscopic, pleural biopsy and talc pleurodesis while 15 patients underwent thoracotomy and pleurectomy for disease

confined to the pleura<sup>(10)</sup>. In our data post-operative hospitalization ranged from 4 days to 14 days with mean of 7 days and the post-operative pain ranged on VAS scale from 2 to 9 with a mean of 4 while post-operative air leak occurred in 5 patients (14.3%) post-operative wound infection in total 13.4 % of the patients and there was no postoperative mortality to the endpoint of the study. Despite there is high statistical significance in the presence of air leak in patients in VATS pleurodesis and VATs partial pleurectomy ± decortication (p value= 0.05) there was no statistical significance in total hospitalization between 3 groups (p-value 0.69), and there was no statistical significance for postoperative empyema development but there was statistical significance regarding recurrence and 3 months post-intervention in talc slurry group. In meso-Vats trail Surgical complications were significantly more common with VAT-PP, occurring in 24 (31%) of 78 patients completing VAT-PP vs 10 (14%) of 73 completing talc pleurodesis (P = .019); respiratory complications (24% vs 15%, P = .22) and air-leak beyond 10 days (6% vs 1%, P = .21) were non significantly more common with VATs parietal pleurectomy. Median hospital stay was 7 vs 3 days (P <.0001).(7) also complications were significantly more common after VAT-PP than after talc pleurodesis, occurring in 24 (31%) of 78 patients who completed VAT-PP versus ten (14%) of 73 patients who completed talc

pleurodesis ( $p=0.019$ ), as were respiratory complications (19 [24%] vs 11 [15%];  $p=0.22$ ) and air-leak beyond 10 days (five [6%] vs one [1%];  $p=0.21$ ), although not significantly so. Median hospital stay was longer at 7 days in patients who received VATs parietal pleurectomy compared with 3 days (2-5) for those who received talc pleurodesis ( $p<0.0001$ ).<sup>(8)</sup> Survival after limited surgical management of malignant mesothelioma is comparable to a previously reported more radical surgical approach.<sup>(10)</sup> thoracoscopic talc pleurodesis remains a safe, low-morbidity, inexpensive primary palliative treatment option for malignant pleural mesothelioma and a valid control arm option for therapeutic trials<sup>(11)</sup>

## Conclusion

Despite being with more complication VATs partial pleurectomy seems to be good method in management of mesothelioma as it is operatively allowed benefit of managing lung entrapment and allow better lung expansion and post operatively associated with superior control on effusion recurrence and better patients satisfaction and better quality of life in comparison to talc slurry.

## References

1. Carbone M, Ly VH, Dodson RF, et al. Malignant mesothelioma: facts, myths, and hypotheses. *J Cell Physiol.* 2012; 227:44–58.
2. Robinson BW, Musk AW, Lake RA. Malignant mesothelioma. *Lancet.* 2005 Jul 30-Aug 5;366 (9483): 397-408
3. GBD 2015 Disease and Injury Incidence and Prevalence, Collaborators. (8 October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". *Lancet.* 388 (10053): 1545–1602.
4. Akl Y, Kaddah S, Abdelhafeez A, et al. Epidemiology of mesothelioma in Egypt. A ten-year (1998-2007) multicentre study. *Arch Med Sci.* 2010;6(6):926–931. doi:10.5114/aoms.2010.19303
5. Ryan CW, Herndon J, Vogelzang NJ. A review of chemotherapy trials for malignant mesothelioma. *Chest.* 1998 Jan. 113(1 Suppl):66S-73S
6. Batirel HF, Metintas M, Caglar HB, et al. Trimodality treatment of malignant pleural mesothelioma. *J Thorac Oncol.* 2008 May. 3(5):499-504.
7. Rintoul RC. The MesoVATS trial: is there a future for video-assisted thoracoscopic surgery partial pleurectomy? *Future Oncol.* 2015;11 (24 Suppl):15-7.
8. Fysh ETH, Tan SK, Read CA, et al. Pleurodesis outcome in malignant pleural mesothelioma. *Thorax* 2013; 68:594-596.
9. Taioli E, van Gerwen M, Mihalopoulos M, et al. Review of malignant pleural mesothelioma survival after talc pleurodesis or surgery. *J Thorac Dis.* 2017 Dec;9(12):5423-5433.
10. Phillips PG, Asimakopoulos G, Maiwand MO. Malignant pleural mesothelioma: outcome of limited surgical management *Interact Cardiovasc Thorac Surg.* 2003 Mar;2 1):30-4.
11. Aelony Y, Yao JF. Prolonged survival after talc poudrage for malignant pleural mesothelioma: case series. *Respirology.* 2005 Nov;10 (5):649-55.