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REVIEW ARTICLE

Thoracoscopy and talc pleurodesis for malignant pleural effusions

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ABSTRACT

Malignant pleural effusion (MPE) is the result of the direct infiltration of the pleura by neoplastic cells and affects more than 15% of cancer patients. The incidence of this type of effusion is increasing in parallel with the rising incidence of cancer, with patients experiencing an increasing survival rate due to diagnostic and therapeutic advances. This article aims to review two fundamental aspects of the diagnostic and therapeutic management of MPE: medical thoracoscopy as a fundamental tool for the direct exploration of the pleural cavity, and pleurodesis with talc to achieve adhesion of the two pleural layers, thereby preventing re-accumulation of fluid and reducing the symptoms in these patients.

Keywords: Pleurodesis. Talc. Thoracoscopy

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INTRODUCTION

Malignant pleural effusion (MPE) is the result of the direct infiltration of the pleura by neoplastic cells[1,2]. It affects more than 15% of cancer patients. The incidence of this type of effusion is increasing in parallel with the rising incidence of cancer, and these patients experience an increasing survival rate due to diagnostic and therapeutic advances.

MEDICAL THORACOSCOPY

Medical thoracoscopy, or pleuroscopy, contrary to what may be assumed, predates surgical thoracoscopy. The first article describing the clinical application of medical thoracoscopy was published in 1910[3]. This technique is simply a safe and straightforward method in the hands of expert personnel, enabling exploration of the pleural cavity. Since then, until 1955, its primary use was inducing pneumothorax by lysing pleural adhesions as a therapeutic measure for pulmonary tuberculosis management. In 1955, its diagnostic utility began to be emphasized. Subsequently, in 1990, exclusively surgical thoracoscopy emerged to conduct minimally invasive video-assisted interventions, following the trend of laparoscopic surgery[4]. In recent decades, pleuroscopy has gained significant relevance and recognition, driven not only by technological advances but also by its diagnostic and therapeutic role in managing diseases affecting the pleural cavity. These diseases constitute 25% of the cases seen by pulmonologists, with 20–25% of pleural effusions remaining undiagnosed despite repeated thoracentesis and closed needle biopsies[5]. Currently, medical thoracoscopy is the gold standard in diagnosing pleural effusion[6], with the diagnostic yield for malignant pleural effusion reaching 95%[7,8]. From a therapeutic perspective, pleuroscopy is commonly employed for draining pleural fluid and performing pleurodesis in malignant pleural effusions, with a success rate of up to 90%[9]. In recent years, pleuroscopy has also become a fundamental tool for investigating pleural pathophysiology, particularly in neoplastic pathology, owing to a better understanding of tumor biology and the development of more sensitive molecular diagnostic techniques[10].

The technique of the procedure today is, surprisingly, very similar to that described at the time by Hans Christian Jacobaeus[11]. It is a minimally invasive technique, performed in an interventional pulmonology office by a pulmonologist (Fig. 1). It is performed under local anesthesia and superficial sedation, with the patient breathing spontaneously and under cardiovascular and respiratory monitoring. The patient is placed in lateral decubitus on their healthy side, with a pillow under the thorax and the arm ipsilateral to the affected hemithorax positioned upwards and forwards. This makes it easier to identify the intercostal spaces. A previous thoracic ultrasound is recommended to locate the pleural fluid chamber and identify the best entry point for the trocar (Fig. 2). After locating the entry point, local anesthesia is instilled in the area. Adequate anesthesia in this area will allow for a more careful exploration of the pleural space and will also be better tolerated. Subsequently, a dissection by planes is performed down to the pleura

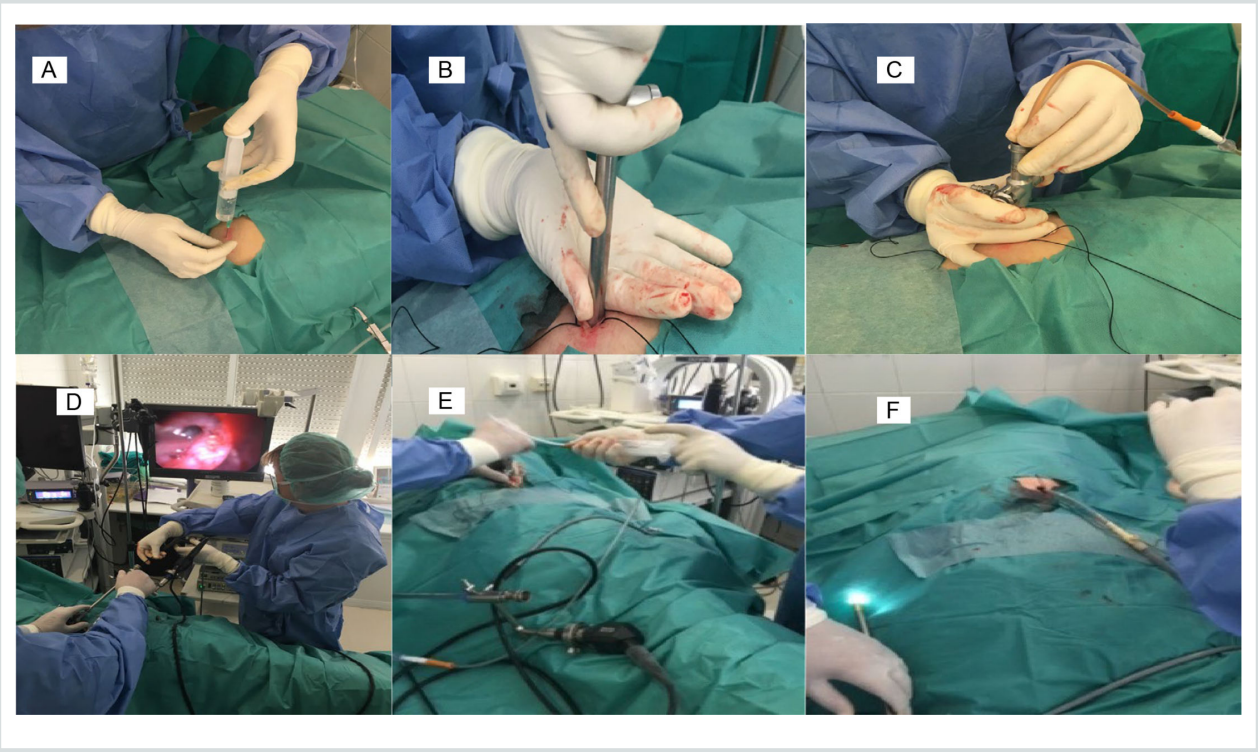

Figure 1. Thoracoscopy technique. **A:** instillation of local anesthesia. **B:** introduction of the trocar. **C:** evacuation of pleural fluid. **D:** exploration of the pleural cavity and taking of biopsies. **E:** talc poudrage. **F:** placement of thoracic drainage after exploration.

from a 1–2 cm skin incision located in the mid-axillary line between the fourth and seventh intercostal spaces. In patients with pleural effusion, approximately 200–300 ml of fluid is aspirated, and a pneumothorax is subsequently induced, allowing the lung to collapse and move away from the chest wall, creating a space for trocar insertion. However, in the presence of a larger amount of pleural fluid, the procedure can also be performed directly under ultrasound guidance.

Additional accesses can be created, although standard pleuroscopy tends to use a single-access approach. The diameter of the incision is between 7 and 11 mm, while the diameter of the optics is between 6 and 10 mm and the diameter of the biopsy forceps is between 4 and 6 mm. After establishing the entry point, the pleural fluid is aspirated to allow for a proper examination. Once all the pleural fluid has been evacuated, the thoracoscope is introduced. It is important to have a good view to avoid damaging any structures. The following must be identified: the diaphragmatic pleura, the posterior parietal pleura from the posterior costophrenic angle to the apex of the cavity, and the anterior face, which is examined in reverse by passing over the lung. The entire visible lung surface and the explorable part of the mediastinum are explored. The exploration of the pleural cavity must be performed carefully, and the findings can vary significantly depending on

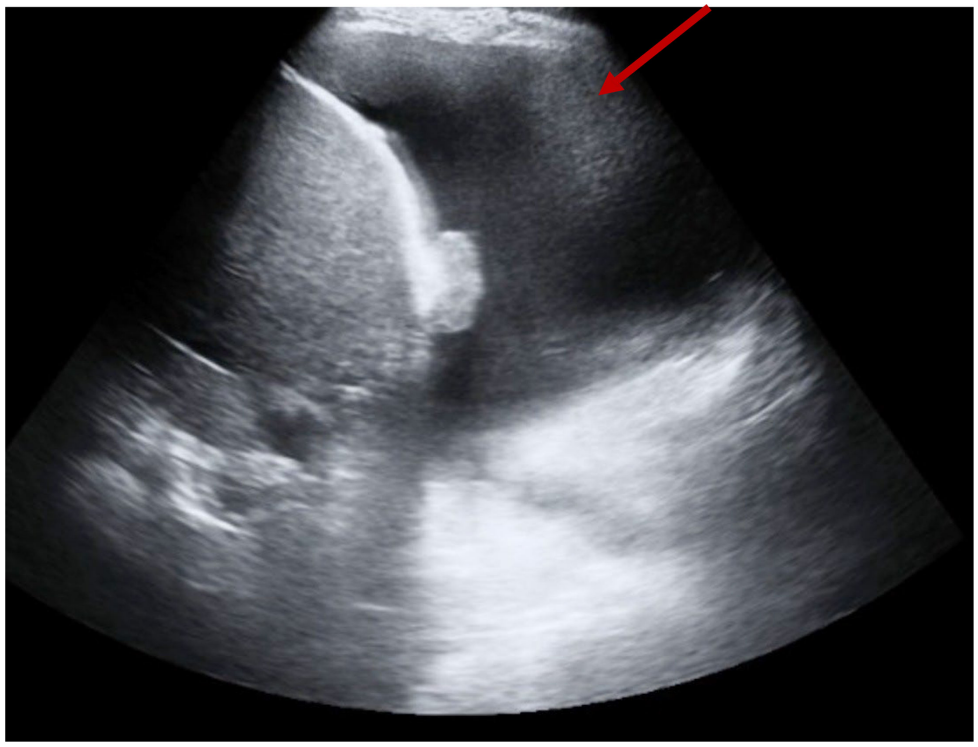

Figure 2. Thoracic ultrasound prior to thoracoscopy allows for the quantification of the amount of pleural fluid and selection of the best entry point. In this case, there is an implant at the diaphragmatic level, and the red arrow indicates the best entry point.

the patient's pathology (Fig. 3). This exploration allows the selection of the area to be biopsied (Fig. 4).

Once the biopsies have been performed, if the instillation of talc is necessary, it is administered over the entire pleural cavity. At the end of the technique, a thoracic drainage tube is introduced through the entry point, directing it towards the most basal and posterior area, subsequently removing the trocar. After completion of the exploration, the chest drain is connected to a collection vessel (air and fluid are discharged). The drainage is removed when the debit is less than 150 mL/day, after which the wound is closed, and the patient can be discharged from the hospital.

Pleuroscopy can be performed with a rigid or semi-rigid instrument. Pleuroscopy performed with rigid endoscopic equipment requires a light source, an endoscopic camera attached to a telescope, and a trocar. Rigid telescopes are 27–31 cm in length and 7–12 mm in diameter; they have angles that allow either a straight (0°) or oblique (30° or 50°) view. The trocars are made of single-use plastic or stainless steel with a variable diameter of 5–13 mm[12,13]. The semi-rigid pleuroscope (Olympus LTF 160 or 240) measures 7 mm external diameter and 27 cm in

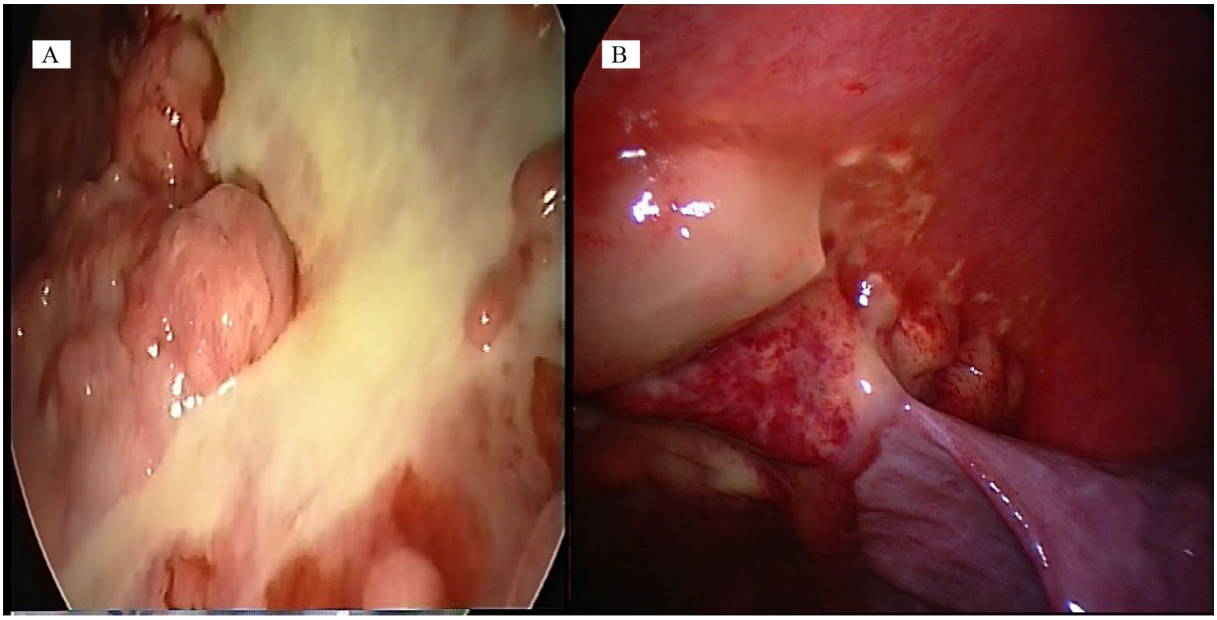

Figure 3. Thoracoscopy images. **A:** pleural mesothelioma. **B:** metastases of ovarian adenocarcinoma.

length and functions like a flexible bronchoscope. The flexible tip allows 160° upward and 130° downward angulation and has a 2.8 mm working channel to accommodate various accessories[14]. When using the semi-rigid pleuroscope, a single 1 cm skin incision is sufficient, into which a disposable flexible trocar with an inner diameter of 8 mm fits.

The main difference between the two instruments undoubtedly lies in the superior ability of the semi-rigid pleuroscope to explore a larger area of the pleural cavity due to the easy maneuverability of its agile tip around adhesions and, consequently, the ease of performing biopsies. In addition, with the rigid pleuroscope, it is very common to exert pressure and angulation on the periosteum, which can be painful. On the other hand, the image quality is significantly better with the semi-rigid pleuroscope, also called flexirigid[15]. However, the main disadvantage of semi-rigid pleuroscopy is the small working channel, which may limit adequate biopsies. To overcome this limitation, Thomas et al.[16] used cryoprobes to sample the parietal pleura, which could be introduced through the working channel of the semi-rigid pleuroscope, with a diagnostic yield of 90%, comparable to conventional biopsies[16]. A drawback of flexible forceps is the lack of mechanical strength needed to obtain samples from fibrous or thickened pleurae. In contrast, the more robust, rigid biopsy forceps facilitate larger and deeper biopsies and are more effective at breaking adhesions. To overcome this problem, Sasada et al.[17] proposed the use of a new technique

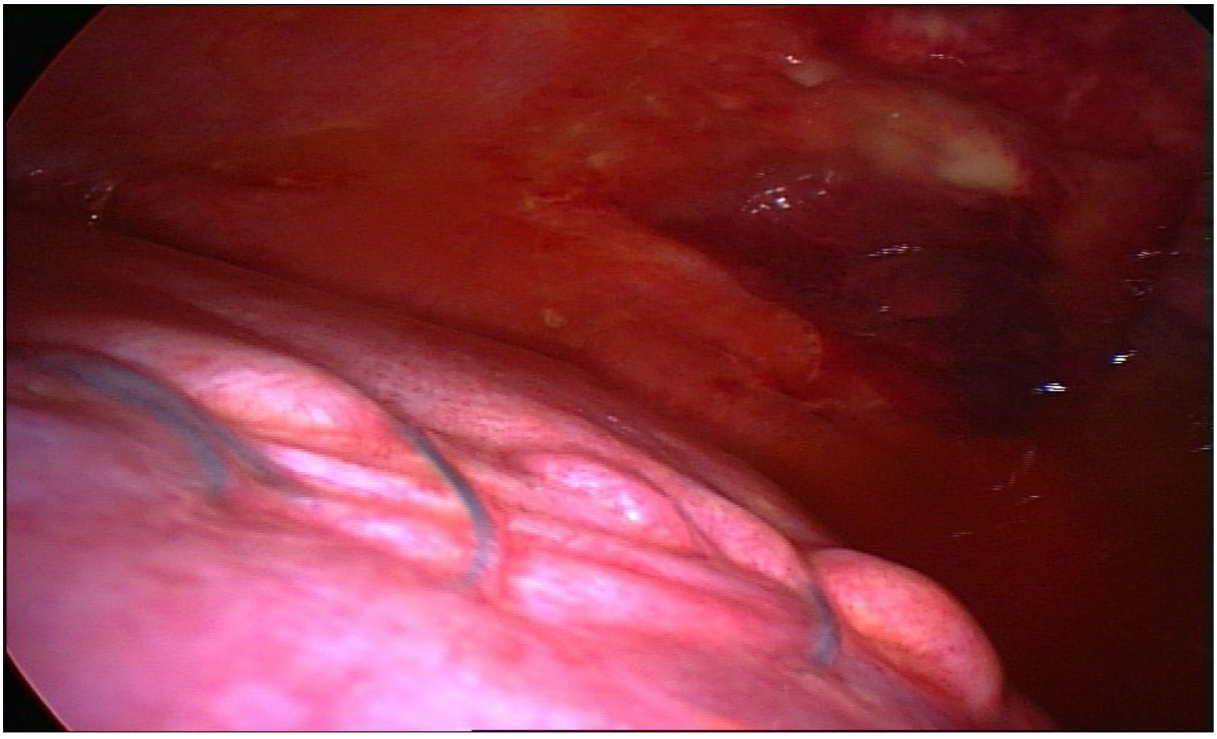

Figure 4. Intercostal vessels. The examination must be performed very carefully to avoid damaging the vascular structures.

of electrocautery through the working channel of the semi-rigid pleuroscope, increasing the diagnostic yield to 85% compared to 60% with standard flexible forceps. Even in the diagnosis of malignant pleural disease, where rigid pleuroscopy achieves a diagnostic yield of 95%[18], there are no results to suggest that smaller biopsies result in lower diagnostic accuracy. In a prospective study of 66 patients, mostly with neoplastic pathology, a similar diagnostic yield was obtained between semi-rigid and rigid pleuroscopy (92.3% vs. 96.3%)[19]. Rozman et al.[20] published the first randomized study with 84 patients, demonstrating a very comparable diagnostic yield despite the considerably higher specimens obtained with rigid forceps.

PLEURODESIS

The fundamental function of pleurodesis is to adhere to the two pleural layers (parietal and visceral) so that the lung always remains expanded, thus avoiding the accumulation of liquid in the pleural space. Its main indications are recurrent MPE, spontaneous pneumothorax, and recurrent pleural effusions of benign etiology. In this article, we will focus on recurrent MPE.

To achieve pleurodesis, there are two methods:

1. Mechanical/physical methods that produce direct inflammation at the level of the pleural surface (e.g., mechanical abrasion, laser/argon electrocoagulation).

2. Intrapleural administration of agents (mostly chemical) that produce inflammation at the level of the pleural surfaces with activation of the coagulation system, secondary fibrosis, and symphysis of the pleural space (chemical pleurodesis).

Several biological processes are necessary to achieve pleural symphysis. Mesothelial cells are thought to be the most important element in the development of pleurodesis. In response to sclerosing agents, these cells secrete a variety of mediators, including chemokines such as interleukin-8 (IL-8) and monocyte chemoattractant protein-1 (MCP-1), as well as growth factors: vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), and transforming growth factor-β (TGF-β). Numerous data suggest that intact mesothelial cells and these cytokines play a crucial role in the initiation and maintenance of different pathways of pleural inflammation and pleural space obliteration. In addition to mesothelial cells, some inflammatory cells recruited from the blood, mainly neutrophils and mononuclear cells, are known to play an important role. Fibroblast proliferation in the pleural space is also essential for the pleurodesis process, and there is evidence that talc stimulates the production of fibroblast growth factors by mesothelial cells. One of the main phenomena that occurs after the instillation of a symphyseal agent is the activation of the coagulation cascade in the pleural space[21,22]. Agrenius et al.[23] were the first to demonstrate an increase in coagulation at the pleural level and a decrease in fibrinolytic activity after the instillation of a sclerosing agent. Rodriguez-Panadero et al.[24] demonstrated that successful pleurodesis was associated with a significant reduction in fibrinolytic activity, expressed as D-dimer concentration in pleural fluid, 1 day after talc powder administration ($p < 0.001$).

The relationship between pleurodesis and the activation of systemic coagulation was evaluated by Montes-Worboys et al.[25] in 231 patients with MPE undergoing talc poudrage. Higher IL-8 levels were observed in patients with early mortality after pleurodesis, but the difference was not statistically significant.

In patients with recurrent pleural effusion, pleurodesis is a symptomatic treatment that controls dyspnea secondary to the re-accumulation of fluid in the pleural space. The effect of pleurodesis in these patients is evident early after pleurodesis. In recurrent spontaneous pneumothoraces; however, pleurodesis has a more delayed effect, as it is not used to treat the current episode of pneumothorax but rather to prevent future episodes of recurrence.

Symptomatic treatment of MPE is the most frequent indication for pleurodesis in our Pleural Pathology Units (mainly malignant pleural effusions).

To know when to perform pleurodesis in a patient with MPE, the following questions must be answered:

1. **Is the patient's symptomatology, mainly dyspnea, directly attributable to pleural effusion or to the underlying pulmonary involvement?** Although it is not always easy to answer this question, a favorable response to pleurodesis can be expected when dyspnea improves on evacuating thoracentesis. However, it should not be forgotten that in most cases of MEP, the lung is macroscopically or microscopically diffusely affected (multiple metastases and/or carcinomatous lymphangitis); therefore, these data should be used as a guide only when improvement of symptoms after thoracentesis is very evident.

2. **Is MPE recurrent?** Given the foreseeable evolution of MPE toward its increase and, consequently, an increase in the associated symptoms, current guidelines consider pleurodesis to be considered early in these effusions. This would avoid future discomfort for the patient and would favor a better outcome, as it would be performed before the lung becomes trapped.

3. **Is the lung capable of re-expanding after complete evacuation of the pleural effusion?** If the lung surface is completely covered by tumor lesions or by a layer of fibrin, or if the main bronchus is obstructed by a tumor mass, it is unlikely that complete pleural symphysis will be achieved. When complete expansion of the lung cannot occur after evacuative thoracentesis, we are dealing with a trapped lung. Various ways of predicting its existence have been proposed: pleural manometry, M-mode chest ultrasound, and patient symptoms during evacuation. However, there is not enough evidence to recommend any of these methods in isolation in our daily practice[26]. We believe that their combined use is the most advisable approach for predicting their existence. In nonexpandable lungs, there is a greater decrease in pressure when the volume is removed. Pleural elastance, a change in pleural pressure divided by the change in the volume of pleural fluid drained, has shown to accurately differentiate nonexpandable lungs from normal lungs, with a cutoff of 14.5 cm H_2O/l as the upper limit of normal. If pleural elastance is elevated (≥18 cm H_2O/l), the probability of pleurodesis failure is high[27-29].

Numerous agents have been used throughout history to attempt chemical pleurodesis. Currently, the sclerosing agent of choice for pleurodesis in MPE is talc. Its symphyseal effect is well established (average efficacy 93%), and it is inexpensive and widely available[30]. It is now known that talc is not carcinogenic if applied free of impurities (especially asbestos). To minimize the risk of complications, it is therefore required that talc is free of contaminants and that its particle size is larger than 15 µm[31,32] (Fig. 5). The average dose of talc administered is 4 g. It has been shown that results do not improve when more than 5 g are used. A meta-analysis published in 2021, reviewing 26 studies with 4482 patients undergoing pleurodesis with talc, concludes that talc is a safe and effective sclerosing agent. The most frequent

complications reported were pain (20% of cases), fever (14%), and transient dyspnea (13%). The percentage of cases of respiratory failure and distress was 0%[33]. These results have significant interest because, in the past, the safety of this agent was questioned by some articles that associated its use with the appearance of distress; in these articles, the talc used had irregular particles, some with a very small diameter (less than 5 µm); hence, the talc currently used particles with a larger diameter.

Talc can be administered as poudrage (thoracoscopic route) or as a suspension via a chest drain (slurry). In 2020, the results of a clinical trial (Talc pleurodesis: a randomized trial of poudrage vs. slurry in malignant pleural effusion, TAPPS study) comparing the two administration techniques were published. A total of 482 patients (slurry, n = 240; poudrage, n = 242) were included in the final analysis for the study. Following a per-protocol analysis, whereby patients with trapped lungs were excluded, a significant difference (p = 0.045) was found, favoring talc poudrage, although this effect disappeared when only patients who were alive at 30 days (talc slurry, n = 130; talc poudrage, n = 152) were included. They found no difference in the failure rate of pleurodesis in the two treatment arms (22% in the talc poudrage group vs. 25% in the talc slurry group).

This study had some important limitations. The trial entry criteria specified that patients be sufficiently fit to undergo local anesthetic thoracoscopy under light sedation, which may make the results less applicable to those patients presenting with a greater degree of frailty. Furthermore, the trial was conducted on an open-label basis, which may have influenced the results of patient-reported measures, such as pain or breathlessness. It is also probable that the clinicians responsible for recruitment and trial interventions were required to assess patients for pleurodesis failure, introducing the potential for bias. In addition, the TAPPS trial excluded the analysis of patients who survived more than three months, which may also affect the final results[34].

Another factor that can influence the outcome of pleurodesis is the patient's tumor type. Bielsa et al.[35] investigated the impact of tumor type on the efficacy of bedside doxycycline and thoracoscopic talc poudrage pleurodesis. In the talc group, patients with lung cancer and mesothelioma had significantly lower complete response rates (63 and 61%, respectively) compared with breast cancer (77%) and other metastatic effusions (74%, p = 0.012). Regression analysis identified pleural tumor burden and tumor type as independent predictors of pleurodesis failure in the talc group[35].

When comparing the results of pleurodesis with talc poudrage vs. talc slurry, it should also be considered that, in thoracoscopy, the talc is powdered under direct visual control, allowing for a more uniform distribution throughout the pleural cavity. However, in the case of talc slurry, the distribution is less uniform, which can facilitate the appearance of loculations and, therefore, incomplete pleurodesis[36]. Rodríguez Panadero et al.[13] indicate that in assessing the results of pleurodesis with talc, most of the talc administered in slurry form might eventually

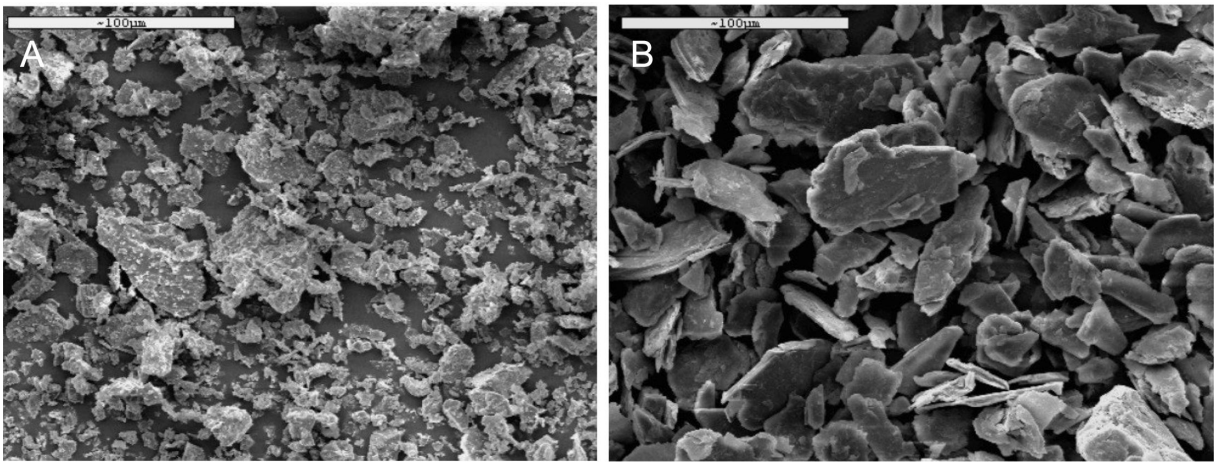

Figure 5. Scanning electron microscopy images of two types of talc. **A:** talc with irregular particles (not recommended)—mean 18.5 ± 14.2 µm. **B:** talc with large particles (recommended)—mean 25.3 ± 16.5 µm (*modified from Arellano-Orden et al., 2013*[82]).

leave the pleura through the chest tube after the drain is unclamped and suction is applied[13].

We believe that further studies comparing the two forms of talc administration are needed, taking into account the factors discussed previously.

In recent years, the tunneled indwelling pleural catheter (TIPC) has been included in the treatment algorithm for recurrent MPE. TIPC placement is an alternative to chemical pleurodesis that offers patients the possibility of regular home drainage of pleural fluid and is also the treatment of choice in patients with trapped/nonexpandable lungs, failed pleurodesis, or loculated effusion[30]. Multiple trials in recent years have reported an improvement in dyspnea and quality of life with the use of TIPC. A systematic review of 19 studies reported symptomatic improvement in 96% of patients after TIPC insertion[37]. Spontaneous pleurodesis rates after TIPC have also been reported to range from 20% to 50%. There are many studies comparing TIPCs with talc slurry. The TIME2 trial (Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomised controlled trial) randomized patients to TIPC vs. talc slurry and observed an improvement in dyspnea with TIPC at six months, a reduction in hospital stays, and a reduced need for further procedures, although with an increase in complications[38]. The AMPLE study (A multicenter pleural effusion study of the efficacy of indwelling catheters) also randomized patients to TIPC vs. talc slurry and demonstrated that TIPC patients had a shorter hospital stay and required fewer subsequent pleural interventions[39]. It is important to determine the optimal drainage regimen via TIPC in these patients. The multicentre ASAP trial (A study of symptom control and

pleural symphysis" trial, comparing the effects of different drainage regimens with TIPC to improve pleurodesis outcomes) demonstrated that daily drainage compared to alternate day drainage in patients with TIPC resulted in higher rates of spontaneous symphysis (47% vs. 24%; $p = 0.003$)[40]. Similar rates of spontaneous pleurodesis were also demonstrated in the AMPLE2 trial comparing daily drainage with symptom-based drainage (44.2% vs. 15.9%; $p = 0.004$), although no difference in dyspnea control was observed between the two groups[41].

TIPC can also be placed in patients undergoing diagnostic thoracoscopy and subsequent talc poudrage (with complete or partial lung re-expansion) or in patients undergoing thoracoscopy in whom a nonexpandable lung is observed on examination. Suzuki et al.[42] observed a spontaneous pleurodesis rate of 53% in patients undergoing TIPC after thoracoscopy vs. 28% in patients undergoing TIPC placement by a standard technique. Considering these results, we believe that the combination of the two therapies (talc poudrage and TIPC) may have a synergistic effect in the control of pleural effusion. This was particularly relevant in the subgroup of patients with loculated pleural effusion undergoing thoracoscopy with lysis of adhesions and TIPC placement (pleurodesis rate 67% vs. 21%). In patients with suspected recurrent or symptomatic MPE, TIPC insertion by thoracoscopy may be considered in two circumstances, regardless of lung expandability: (1) concurrent need for pleural biopsies and (2) pleural effusion with numerous adhesions and loculations demonstrated by CT scan and chest ultrasound.

At present, therefore, we have different techniques for pleurodesis in MEP with similar efficacy according to published studies: talc poudrage, talc slurry, and TIPC, which can be used alone or in combination depending on the patient's characteristics and preferences.

ETHICAL DISCLOSURES

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

REFERENCES

1. Heffner JE. Diagnosis and management of malignant pleural effusions. Respirology. 2008;13:5–20.
2. Asciak R, Rahman NM. Malignant pleural effusion: from diagnostics to therapeutics. Clin Chest Med. 2018;39:181–93.
3. Jacobaeus HV. Ur die moglichkeitdie zystoskopie bei untersuchung seroser hohlungen anzuwenden. Munch Med Wochenschr. 1910;57:2090–2.

4. Marchetti GP, Pinelli V, Tassi GF. 100 years of thoracoscopy:Historical notes. Resp. 2011;82(2):187–92.
5. Lee P, Colt HG. Rigid and semirigid pleuroscopy: the future is bright. Respirology. 2005;10:418–25.
6. Froudarakis ME. New challenges in medical thoracoscopy. Resp. 2011;82(2):197–200.
7. Froudarakis ME. Diagnostic work-up of pleural effusions. Respir. 2008;75:4–13.
8. Metintas M, Ak G, Dundar E, Yildirim H, Ozkan R, Kurt E, et al. Medical thoracoscopy vs CT scan-guided abrams pleural needle biopsy for diagnosis of patients with pleural effusions: a randomized, controlled trial. Chest. 2010;137:1362–8.
9. Rodríguez-Panadero F. Medical thoracoscopy. Respir. 2008;76(4):363–72.
10. Anevlavis S, Froudarakis ME. Advances in pleuroscopy. Clin Respir J. 2018;12:839–47.
11. Jacobaeus HC. The practical importance of thoracoscopy in surgery of the chest. Surg Gyn Obstet. 1922;34:289–96.
12. Loddenkemper R. Medical thoracoscopy/pleuroscopy. In: Ernst A, Herth F, editors. Principles and practice of interventional pulmonology.New York: Springer; 2013. p. 605–21. doi: 10.1007/978-1-4614-4292-9_59.
13. Rodriguez-Panadero F, Janssen JP, Astoul P. Thoracoscopy: general overview and place in the diagnosis and management of pleural effusion. Eur Respir J. 2006;28:409–22.
14. Munavvar M, Khan MAI, Edwards J, Waqaruddin Z, Mills J. The autoclavable semirigid thoracoscope: the way forward in pleural disease? Eur Respir J. 2007;29:571–4.
15. Yap KH, Phillips MJ, Lee YCG. Medical thoracoscopy: rigid thoracoscopy or flexi-rigid pleuroscopy? Curr Opin Pulm Med. 2014;20:358–65.
16. Thomas R, Karunarathne S, Jennings B, Morey S, Chai SM, Lee YCG, et al. Pleuroscopic cryoprobe biopsies of the pleura: a feasibility and safety study. Respirology. 2015;20:327–32.
17. Sasada S, Kawahara K, Kusunoki Y, Okamoto N, Iwasaki T, Suzuki H, et al. A new electrocautery pleural biopsy technique using an insulated-tip diathermic knife during semirigid pleuroscopy. Surg Endosc. 2009;23:1901–7.
18. Loddenkemper R. Thoracoscopy--state of the art. Eur Respir J. 1998;11(1):213–21.
19. Khan MAI, Ambalavanan S, Thomson D, Miles J, Munavvar M. A comparison of the diagnostic yield of rigid and semirigid thoracoscopes. J Bronchology Interv Pulmonol. 2012;19(2):98–101. DOI: 10.1097/LBR.0b013e31824ee45b.
20. Rozman A, Camlek L, Marc-Malovrh M, Triller N, Kern I. Rigid versus semi-rigid thoracoscopy for the diagnosis of pleural disease: a randomized pilot study. Respirology. 2013;18:704–10.
21. Rodriguez-Panadero F, Montes-Worboys A. Mechanisms of pleurodesis. Resp. 2012;83(2):91–8.
22. Mierzejewski M, Korczynski P, Krenke R, Janssen JP. Chemical pleurodesis - a review of mechanisms involved in pleural space obliteration. Respir Res. 2019;20:247.
23. Agrenius V, Chmielewska J, Widström O, Blombäck M. Increased coagulation activity of the pleura after tube drainage and quinacrine instillation in malignant pleural effusion. Eur Respir J. 1991;4:1135–9.
24. Rodriguez-Panadero F, Segado A, Martin Juan J, Ayerbe R, Torres Garcia I, Castillo J. Failure of talc pleurodesis is associated with increased pleural fibrinolysis. Am J Respir Crit Care Med. 1995;151:785–90.
25. Montes-Worboys A, Rodriguez-Portal JA, Arellano-Orden E, Digón-Pereiras J, Rodriguez-Panadero F. Interleukin-8 activates coagulation and correlates with survival after talc pleurodesis. Eur Respir J. 2010;35:160–6.
26. Feller-Kopman DJ, Reddy CB, DeCamp MM, Diekemper RL, Gould MK, Henry T, et al. Management of malignant pleural effusions. an official ATS/STS/STR clinical practice guideline. Am J Respir Crit Care Med. 2018;198:839–49.
27. Ferreiro L, San José E, Gude F, Valdés L. Pleural fluid analysis and pleural elastance as predictors of response to pleurodesis in patients with malignant pleural effusion. Arch Bronconeumol (Engl Ed). 2018;54:163–5.
28. Pardessus Otero A, Rafecas-Codern A, Porcel JM, Serra-Mitjà P, Ferreiro L, Botana-Rial M, et al. Malignant pleural effusion: A multidisciplinary approach. Open Respir Arch. 2024;6(4):100349.
29. Lester M, Maldonado F, Rickman OB, Roller LJ, Avasarala SK, Katsis JM, et al. Association between terminal pleural elastance and radiographic lung re-expansion after therapeutic thoracentesis in patients with symptomatic pleural effusion: a post-hoc analysis of a randomised trial. BMJ Open. 2022;12:e053606.
30. Botana Rial M, Perez Pallarés J, Cases Viedma E, et al. Diagnosis and treatment of pleural effusion. Rec Span Soc Pulm Thorac Surg Update. 2023;59:27–35.
31. Janssen JP, Collier G, Astoul P, Tassi GF, Noppen M, Rodriguez-Panadero F, et al. Safety of pleurodesis with talc poudrage in malignant pleural effusion: a prospective cohort study. Lancet. 2007;369(9572):1535–9.
32. Arellano-Orden E, Romero-Falcon A, Martín JuanJ, Ocaña Jurado M, Rodriguez-Panadero F, Montes-Worboys A. Small particle-size talc is associated with poor outcome and increased inflammation in thoracoscopic pleurodesis. Respir. 2013;86:201–9.
33. Zhang W, Zhao YL, Li SJ, Zhao YN, Guo NN, Liu B. Complications of thoracoscopic talc insufflation for the treatment of malignant pleural effusions: a meta-analysis. J Cardiothorac Surg. 2021;16:125.
34. Bhatnagar R, Luengo-Fernandez R, Kahan BC, Rahman NM, Miller RF, Maskell NA. Thoracoscopy and talc poudrage compared with intercostal drainage and talc slurry infusion to manage malignant pleural effusion: the TAPPS RCT. Health Technol Assess. 2020;24:1–90.
35. Bielsa S, Hernández P, Rodriguez-Panadero F, Taberner T, Salud A, Porcel JM. Tumor type influences the effectiveness of pleurodesis in malignant effusions. Lung. 2011;189(2):151–5.
36. Mager HJ, Maesen B, Verzijlbergen F, Schramel F. Distribution of talc suspension during treatment of malignant pleural effusion with talc pleurodesis. Lung Cancer. 2002;36:77–81.
37. Van Meter MEM, McKee KY, Kohlwes RJ. Efficacy and safety of tunneled pleural catheters in adults with malignant pleural effusions: a systematic review. J Gen Intern Med. 2011;26:70–6.
38. Davies HE, Mishra EK, Kahan BC, Wrightson JM, Stanton AE, Guhan A, et al. Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. JAMA. 2012;307:2383–9.
39. Thomas R, Fysh ETH, Smith NA, Lee P, Kwan BCH, Yap E, et al. Effect of an indwelling pleural catheter vs talc pleurodesis on hospitalization days in patients with malignant pleural effusion: the AMPLE randomized clinical trial. JAMA. 2017;318:1903–12.
40. Wahidi MM, Reddy C, Yarmus L, Feller-Kopman D, Musani A, Shepherd RW, et al. Randomized trial of pleural fluid drainage frequency in patients with malignant pleural effusions. the asap trial. Am J Respir Crit Care Med. 2017;195:1050–7.
41. Muruganandan S, Azzopardi M, Fitzgerald DB, Shrestha R, Kwan BCH, Lam DCL, et al. Aggressive versus symptom-guided drainage of malignant pleural effusion via indwelling pleural catheters (AMPLE-2): an open-label randomised trial. Lancet Respir Med. 2018;6:671–80.
42. Suzuki K, Servais EL, Rizk NP, Solomon SB, Sima CS, Park BJ, et al. Palliation and pleurodesis in malignant pleural effusion: the role for tunneled pleural catheters. J Thorac Oncol. 2011;6:762–7.