Review

Juan David Botero[1], Javier Iván Lasso[2]
[1]Clínica Cardiovid, Medellín, Colombia
[2]Hospital Universitario San Ignacio, Bogotá, Colombia

Pleurodesis

Abstract

Pleurodesis is a definitive management strategy in malignant pleural effusion, its history is briefly described, and a narrative review is made about its indication, patient selection, response predictors and benefits.

Palliat Med Pract 2023; 17, 1: 48–58

Key words: pleurodesis, malignant pleural effusion, cancer, palliative care

Introduction

The pleura is a serous lining derived from the mesoderm whose function is related to allowing the coupling of the movement of the thoracic cage with the lung during respiratory movements, the pleural fluid being the lubricant for such movement [1]. The accumulation of pleural fluid is attributed to 3 possible factors: alteration of transpleural pressures, alteration of lymphatic drainage, or increased permeability of mesothelial and endothelial capillaries; of these, the former is the only one that does not alter protein concentrations [2]. This chapter discusses pleurodesis, especially in the setting of malignant pleural effusion, its history, indications, complications, and benefits, giving general guidelines and indicating some particularities when relevant.

Pleurodesis

It comes from the Greek roots *pleurá* (pleura) and *desmos* (union), referring to the obliteration of the pleural space by the adherence of the visceral pleura with the parietal pleura, through a stimulus that generates inflammation and fibrosis. It's indicated for the management and prevention of pleural effusions and pneumothorax [3].

History

The first description of this procedure is attributed to Luios Spengler in 1906 when he administered glucose solutions and silver nitrate in the pleural cavity to favour the adhesions as management of pneumothorax [4]; Noman Bethune in 1935 proposed the use of iodized talc after lobectomy for bronchiectasis [5]; pleurodesis by abrasion was described by Dr Edward Delos in 1941 [6], and only in 1958 was described the use of talc in malignant disease by Dr J. Chambers [7]. Multiple substances or interventions on the pleura have been used to achieve pleurodesis, all with the purpose of generating fibrosis and adhesion between pleurae, starting with talc [8–10], iodized talc [7, 11], silver nitrate [12], iodine [13], extending to the use of antimicrobials such as tetracycline [14, 15], doxycycline [16–20], minocycline [18, 21] tigecycline [22,

Address for correspondence:
Juan David Botero
Clinica Cardiovid, Cl. 78b #75–21, 050036 Medellin, Colombia
e-mail: juanb89@gmail.com

Palliative Medicine in Practice 2023; 17, 1, 48–58

DOI: 10.5603/PMPI.a2022.0028

Received: 10.10.2022 Accepted: 29.10.2022 Early publication date: 31.10.2022

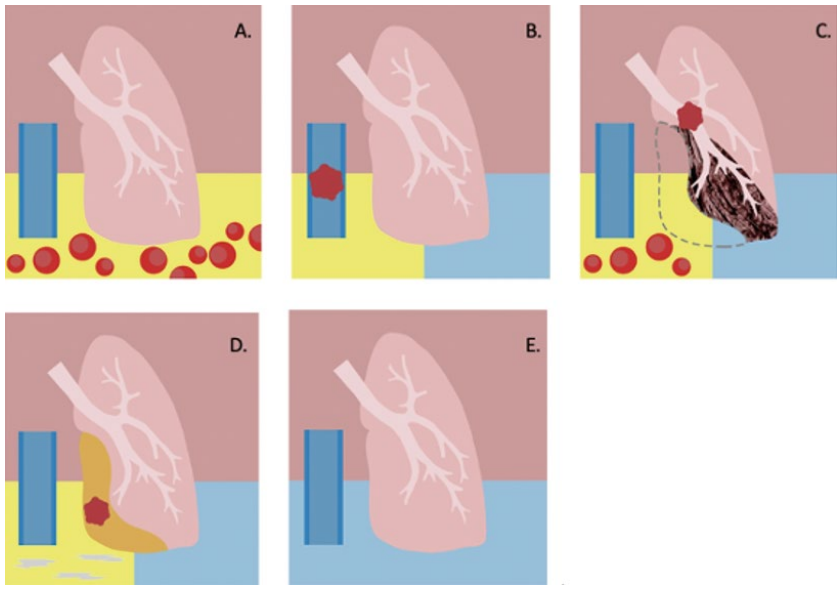

Figure 1. Pleural effusion associated with cancer; (**A**) Direct pleural involvement with malignant cells and yellow pleural colouration representing exudation; (**B**) Venous occlusion with exudation or transudation; (**C**) Tumour causing atelectasis with exudation with malignant cells or transudation; (**D**) Post-obstructive pneumonia, were yellow and blue represent complicated and uncomplicated parapneumonic effusion; (**E**) Effusion cause by oncotic pressure decrease

23], quinacrine [24], mepacrine [25], cytotoxics such as bleomycin [18, 19], mitomycin [26, 27], mitoxantrone [28, 29], platinum derivatives [30, 31], bacterial agents such as *Corynebacterium parvum* [32], OK-432 (a derivative of *Streptococcus*) [26, 33], *Staphylococcus superantigens* [26, 34, 35], lipoteichoic acid [36], reaching haematic patches [37–39], hypertonic glucose [40–42], mistletoe-derived substances such as *Viscum album* [43–45] and thermal ablation [46]; with new tools in the future such as the use of natural glues such as sericin [47] and the use of transforming factor β [48]. Emerging closed variations by thoracotomy, thoracoscopy, pleuroscopy, and even hybrid techniques of permanent pleural catheters with talc with and without thoracoscopy [49].

Pleural involvement due to cancer

The diagnosis of malignant pleural effusion is based on documentation of malignant cells in the fluid or on pleural biopsy. Closed biopsy achieves a yield of about 45%, cytology of the liquid about 60%, biopsy guided by computed axial tomography (CT) 87%, biopsy guided by ultrasound 90%, and reaching values of 95% thoracoscopy and pleuroscopy [50].

Chronic pleural effusion, absence of fever, haemorrhagic features of the fluid, and some findings on CT scans predict malignant aetiology [51]. Pleural involvement by cancer is attributed to a local invasion by contiguity or haematogenous or lymphatic dissemination [52], most of them being metastatic [53].

Situations in which pleural effusion associated with cancer can be found are (1) direct involvement of the pleura, (2) lymphatic or venous obstruction, (3) bronchial obstruction with atelectasis, (4) post-obstructive pneumonia with parapneumonic effusion, (5) hypoalbuminemia (Fig. 1) [54]. Most malignant pleural effusions are attributed to adenocarcinomas, especially of the lung [55–58].

According to necropsy reports, 28% of patients with cancer present pleural metastases and 15% pleural effusion [3]. Malignant pleural effusion is characterized by a lymphocytic exudate [59, 60]. However, a non-negligible percentage, between 5% to 10% of malignant pleural effusions, are transudates considered as a superposition of both or false transudates [61]. They can also occur as histiocytic [62] or neutrophilic exudates [63], the latter being a marker of poor prognosis [64]; therefore, it is important to keep this possibility in mind when performing thoracentesis [54, 65, 66].

Patient selection

Dyspnoea is the main marker of pleural involvement due to malignant effusion; its presence impairs patient survival [67], and the basis of its management is the systemic treatment of the disease [68]. However, some chemosensitive tumours, despite having a good

response to systemic management, may persist with pleural effusion [69]. Therefore, early pleurodesis is advised to avoid recurrences [70].

In patients with epidermal growth factor receptor (EGFR) driver mutations, pleurodesis may be deferred according to reports, of similar recurrence when early pleurodesis was performed [71–73].

The management choice depends on the clinical scenario, where the type of tumour, the functionality and characteristics of the pleural fluid, and some other parameters stratify survival [64, 74]. The LENT (Tab. 1) [55] and PROMISE (Tab. 2) [75] scores are used to evaluate survival. Once the patient's probability of survival has been stratified, the possibility of expectant management, pleurodesis, permanent pleural catheter, or thoracentesis can be considered if necessary [76, 77]. A decision that should be based on multidisciplinary monitoring and management, seeking to improve the quality of care according to the guidelines and, probably, improving outcomes [78–80].

Table 1. LENT score

Variable	Points
Lactate dehydrogenase (pleural fluid)	
< 1,500 IU/L	0
>/= 1,500 IU/L	1
ECOG score	
0	0
1	1
2	2
3–4	3
Neutrophil to lymphocyte ratio (serum)	
< 9	0
≥ 9	1
Tumour type	
Lowest risk: mesothelioma, haematologic	0
Moderate risk: breast, gynaecologic, renal cell carcinoma	1
Highest risk: lung, other types	2
Risk category (median survival in days)	**Total score**
Low (319 days)	0–1
Moderate (130 days)	2–4
High (44 days)	5–7

ECOG — Eastern Cooperative Oncology Group

Pathophysiology of pleurodesis

Pleurodesis is achieved through two types of interventions, the first of them is the direct injury of the pleura with mechanical or physical interventions or through the administration of different substances that favour the development of pleural adhesions [81].

Four primary factors are required: adequate apposition and contact between the pleurae, development of inflammation, activation of coagulation with limitation of fibrinolysis, and involvement of the mesothelium [82].

Such is the response to the foreign body phenomenon generated by some substances such as talc, that pseudomasses or thalcomas can subsequently develop, an element that can generate recurrence concerns in patients undergoing lobectomy for malignant causes [83], with the particularity of showing glucose consumption almost 20 years after the intervention [84].

Respiratory alterations due to pleural involvement

The main symptom attributed to pleural involvement with effusion is dyspnoea, explained by multiple mechanisms such as atelectasis and loss of thoracic distensibility, which generate an increase in respiratory drive and alter ventilatory mechanics [85]. The development of hypoxemia is supported by the appearance of a shunt [86]. In patients with pleural effusion, oxygen consumption (VO_2) is low, reaching only 37% of the predicted value; this limitation pattern shows an alteration of ventilatory efficiency with elevated respiratory equivalents for oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2) and high heart rates with a decrease in oxygen beats (VO_2/HR) [87]. This limitation in exercise performance seems to be related to a restrictive component with a drop in forced vital capacity (FVC) [88–90].

Pleural effusion is associated with an increased percentage of N1 stage sleep and decreased REM sleep, which decreases sleep efficiency and impairs sleep quality; management of pleural effusion restores sleep architecture, increases REM sleep, and therefore sleep efficiency and rest [90, 91].

Pleurodesis indications

The indications for pleurodesis are aimed at treating: the recurrence of pneumothorax [92], malignant pleural effusion [76], and exceptionally benign pleural effusion pathologies [93, 94].

The outcomes after pleurodesis in malignant pleural effusion can be classified as follows [95]:

— Complete success: when there is long-term relief of effusion-related symptoms, with an absence of

Table 2. PROMISE score

Previous chemotherapy	
No	0
Yes	4
Previous radiotherapy	
No	0
Yes	2
Haemoglobin (g/dL)	
16	0
14–16	1
14–12	2
12–10	3
< 10	4
White blood cells (10 ^ 9 cells/uL)	
< 4	0
4–6.3	2
6.3–10	4
10–15.8	7
> 15.8	10
C-reactive protein IU/L	
< 3	0
3–10	3
10–32	5
32–100	8
> 100	11
ECOG score	
0–1	0
2–4	7
Cancer type	
Mesothelioma	0
All other cancers	4
Lung cancer	5
Risk category	
Category A (< 25%)	0–20
Category B (25% to 50%)	21–27
Category C (50 to 75%)	28–35
Category D (> 75%)	> 35

ECOG — Eastern Cooperative Oncology Group

fluid reaccumulation on chest radiographs until death.

— Partial success: decrease in dyspnoea related to the effusion with only partial fluid reaccumulation (less than 50% of the amount of fluid seen on the initial radiograph), without requiring thoracentesis for the rest of the patient's life.

— Failed pleurodesis: when the definitions previously described are not met.

Selection of the intervention

Particularly for malignant pleural effusion, surgical interventions by thoracoscopy are not superior to drainage and administration of substances by catheter [96, 97]. Bonding agent selections are based on specialist experience who perform the procedure, substance efficacy, whether it can be used for benign and malignant causes, and whether it is widely available, economical, and easy to use; these characteristics have traditionally been achieved by talc and iodine [94, 98, 99].

Adjuvant conditions for pleurodesis

Considering the physiopathogenesis of the procedure (which generates pain), the need to leave a thoracostomy tube to evacuate the air and liquid that enters during the different pleurodesis manoeuvres is imperative to keep in mind to provide measures to reduce the pain burden of the procedure. As an initial measure, administering lidocaine into the cavity is an option [100], and some systemic absorption may occur [101].

The use of smaller calibre drainage tubes improves comfort and pain and is not inferior to larger calibre tubes [102]. Contrary to what occurs with corticosteroids [103], the provision of analgesia with NSAIDs or opioids does not correlate with recurrence or failure of the procedure, but with symptomatic control [104], especially when talc slurry is used, which is particularly painful [105]. Another practice that has been re-evaluated in the procedure is the need to rotate the patient after the administration of the substance, since it has not been associated with any benefit and, on the contrary, it can perpetuate discomfort during pleurodesis [106, 107]. Strikingly, haematic patches have better pain control than the other strategies [37].

After administration of the substance, it is suggested to occlude the drainage for one to four hours and then open it with controlled negative pressure of −10 to −20 cm of water, to allow adequate interaction of the substance with the pleura, favours apposition between the pleurae, and prevent oedema by reexpansion [108]. In addition, the patient should be followed daily with ultrasound guidance to review the evolution of the pleurodesis and define the removal of the tube when the drainage is less than 100 to 150 cc [109], thus impacting hospitalization times [110].

Predictors of response and additional strategies

Traditionally, the importance of nutritional status in the performance of pleurodesis has been emphasized, based on the need to mount a good inflammatory response, for which there are not many studies that support patient nutrition as a marker of response. However, having decreased albumin values does correlate with lower survival rates [111].

The following factors are predictors of successful pleurodesis, some of which are specific to the aetiology of the effusion, such as those secondary to lymphoma, primary ovarian, primary breast, mesothelioma; having an ECOG (Eastern Cooperative Oncology Group) score less than or equal to 2; having performed the procedure by medical thoracoscopy; and having high levels of protein, albumin, and eosinophils in the pleural fluid [112, 113].

Recently, a meta-analysis found that high pH fluid, low amount of fluid at the time of pleurodesis, and complete re-expansion after drainage are the strongest predictors of successful pleurodesis. There are other weaker markers or contradictory reports such as short duration of tube drainage, use of thoracostomy tube, high glucose levels in the fluid, low pleural LDH, and low tumour burden during thoracoscopic evaluation [95, 114]. Achieving a marked elevation of C--reactive protein is related to achieving a good response to pleurodesis, explained by mounting an adequate inflammatory response [115].

Among the different substances used to perform pleurodesis, the performance of all of them is variable. Talc is used as a comparator in many scenarios [116] due to its availability and cost could become one of the substances that achieve greater success in pleurodesis [117]. However, there is retrospective evidence of greater effectiveness with silver nitrate [118], making it a proven rescue option for those who have failed with talc [119]. Atypically, pleurodesis with *Corynebacterium parvum* is not affected by the pH of the fluid to induce pleurodesis, this being another option in patients with no predictors of response [120, 121].

Another strategy that can be useful to ensure adequate pleurodesis is to use combinations of different substances to increase effectiveness and limit toxicity, such as combining doxycycline and talc [15, 122], bleomycin and doxycycline [123], or even mechanical and chemical strategies [124], with the possibility of repeated infusions in the case of iodine [125].

Recently, a pilot study evaluated the possibility of adding low doses of tissue plasminogen activator together or after talc to avoid mini-loculations and pleurodesis failure, significantly reducing the need for a second intervention [126].

When pleurodesis is attempted using indwelling catheters, the catheter can be combined with talc [49] with daily drainage [127]. At the moment, the strategy with silver nitrate-coated catheters has not been shown to achieve an adequate pleurodesis rate compared to the usual indwelling catheter [128].

Older age, male gender, using a pigtail catheter, haemorrhagic fluid or having a very low pH seem to be related to pleurodesis failure [95, 129]. Having received chemotherapy and radiotherapy or having an ECOG score greater than 2 are predictors of poor post-procedure survival [55, 75, 130].

Exposure to antibiotics before the procedure is a risk factor for developing empyema after pleurodesis [131].

Complications

Considering the mechanism by which pleurodesis is produced, once the process is initiated, an elevation of different inflammatory mediators is expected, which have variable behaviour depending on the substance used, with nitrate and talc being the substances that generate the greatest inflammatory response with respect to iodine [132].

Several complications have been described with pleurodesis, most of them mild to moderate, the most frequent being hypoxemia [133], an event dependent on the inflammatory response, size, and dose when talking about talc [104, 134]. Complications usually tend to be mild to moderate, although anecdotally there have been reports of pneumonitis [135], respiratory failure and ARDS [136, 137], and death from this cause [138]. This phenomenon can occur regardless of the substance used [139, 140]. Risk factors described in this setting are older age and underlying interstitial disease [141].

Recently, a meta-analysis has evaluated the safety and frequency of complications after talc pleurodesis. The complications described are pain associated with the procedure, fever, dyspnoea, pneumothorax, pneumonia, emphysema, persistent leak, persistent drainage, pulmonary embolism, lung injury, respiratory failure, pulmonary oedema due to re-expansion, and ARDS, which tends to be 0% in the cohorts [142]. Chronic pain has also been reported [143].

The possibility of tumour disease has often been highlighted with the use of talc in benign diseases due to possible asbestos contamination, but current medical talc is free of this contaminant and the risk of a second malignancy has been re-evaluated in different series of benign diseases, in which favourable short and long term effects have been found, without

clearly documenting a relationship with secondary malignancies [9, 11, 144, 145].

In addition, there is a possibility of developing an interstitial disease, especially in those patients who receive pleurodesis with OK-432, who receive EGFR ITK at the time of pleurodesis, or who initiate it within 30 days after pleurodesis [146]. Failure of pleurodesis with an initial strategy could be resolved by enhancing a new approach with another substance [119].

The infectious complications described after the procedure include pleural involvement and pneumonia, empyema, cellulitis, and seeding in the intervened sites. There are other complications such as pulmonary embolism, infarction, bleeding, and pulmonary oedema. Additionally, episodes of air embolism have been described [147].

Particularly with iodine, loss of vision due to retinopathy has been reported, leaving significant scotomas when large volumes of 10% iodine are used [148], being necessary to clarify that, despite this, greater toxicity due to systemic absorption has not been documented attributed to a diseased pleura that limits its absorption [125, 149].

Regarding the use of doxycycline, when used in high doses it can cause pleural burns [150] and renal failure due to systemic absorption of the drug [151].

Special care is required for patients who present communication of the airway with the pleura, as they may present complications derived from pleural instillation and subsequent passage to the airway, which poses a risk of death [152].

Benefit of pleurodesis

Pleurodesis is the standard for the control of dyspnoea generated by the recurrence of effusions as a definitive strategy, surpassing in this sense the pleural catheter [117], being more cost-effective in those patients with prolonged expected survival [153, 154].

It has been established that changes greater than 10 on the visual analogue scale of dyspnoea are clinically significant for patients submitted to pleurodesis [155, 156]. This change occurs in approximately 74% of patients, showing in some opportunities a lower tendency to adverse effects than with the use of the pleural catheter [157].

Finally, it is important to mention that the main benefit of pleurodesis lies in improving the survival of well-selected patients in whom the procedure is successful [157–160].

Declaration of conflict of interests

The authors declare that there is no conflict of interest.

Funding

None declared.

References

1. Charalampidis C, Youroukou A, Lazaridis G, et al. Physiology of the pleural space. J Thorac Dis. 2015; 7(Suppl 1): S33–S37, doi: 10.3978/j.issn.2072-1439.2014.12.48, indexed in Pubmed: 25774305.
2. Zocchi L. Physiology and pathophysiology of pleural fluid turnover. Eur Respir J. 2002; 20(6): 1545–1558, doi: 10.1183/09031936.02.00062102, indexed in Pubmed: 12503717.
3. Rodriguez-Panadero F, Antony VB. Pleurodesis: state of the art. Eur Respir J. 1997; 10(7): 1648–1654, doi: 10.1183/09031936.97.10071648, indexed in Pubmed: 9230261.
4. Spengler L. Zur chirurgie des pneumothorax. Beitr Klin Chir. 1906(49): 80.
5. Bethune N. Pleural poudrage. J Thorac Surg. 1935; 4(3): 251–261, doi: 10.1016/s0096-5588(20)32384-9.
6. Tyson M, Crandall W. The surgical treatment of recurrent idiopathic spontaneous pneumothorax. J Thorac Surg. 1941; 10(5): 566–571, doi: 10.1016/s0096-5588(20)32206-6.
7. Chambers JS. Palliative treatment of neoplastic pleural effusion with intercostal intubation and talc instillation. West J Surg Obstet Gynecol. 1958; 66(1): 26–28, indexed in Pubmed: 13507360.
8. Nandi P. Recurrent spontaneous pneumothorax; an effective method of talc poudrage. Chest. 1980; 77(4): 493–495, doi: 10.1378/chest.77.4.493, indexed in Pubmed: 7357969.
9. A survey of the long-term effects of talc and kaolin pleurodesis. Research Committee of the British Thoracic Association and the Medical Research Council Pneumoconiosis Unit. Br J Dis Chest. 1979; 73(3): 285–288, indexed in Pubmed: 553661.
10. Adler RH, Levinsky L. Persistent chylothorax. Treatment by talc pleurodesis. J Thorac Cardiovasc Surg. 1978; 76(6): 859–864, indexed in Pubmed: 713591.
11. Viskum K, Lange P, Mortensen J. Long term sequelae after talc pleurodesis for spontaneous pneumothorax. Pneumologie. 1989; 43(2): 105–106, indexed in Pubmed: 2717548.
12. Andersen I, Nissen H. Results of silver nitrate pleurodesis in spontaneous pneumothorax. Dis Chest. 1968; 54(3): 230–233, doi: 10.1378/chest.54.3.230, indexed in Pubmed: 5676468.
13. Echavarría A, Pinzón V, Barés JP, et al. [Intracavitary treatment of malignant pleural effusion with iodine-povidone]. Rev Med Panama. 1991; 16(1): 69–74, indexed in Pubmed: 2024059.
14. Wied U, Halkier E, Hoeier-Madsen K, et al. Tetracycline versus silver nitrate pleurodesis in spontaneous pneumothorax. J Thorac Cardiovasc Surg. 1983; 86(4): 591–593, indexed in Pubmed: 6353077.
15. Dikensoy O, Zhu Z, Donnelly E, et al. Combination therapy with intrapleural doxycycline and talc in reduced doses is effective in producing pleurodesis in rabbits. Chest. 2005; 128(5): 3735–3742, doi: 10.1378/chest.128.5.3735, indexed in Pubmed: 16304341.
16. Salomaa ER, Pulkki K, Helenius H. Pleurodesis with doxycycline or Corynebacterium parvum in malignant pleural effusion. Acta Oncol. 1995; 34(1): 117–121, doi: 10.3109/02841869509093649, indexed in Pubmed: 7865226.
17. Prevost A, Nazeyrollas P, Milosevic D, et al. Malignant pleural effusions treated with high dose intrapleural

doxycycline: clinical efficacy and tolerance. Oncol Rep. 1998; 5(2): 363–366, doi: 10.3892/or.5.2.363, indexed in Pubmed: 9468558.
18. Walker-Renard PB, Vaughan LM, Sahn SA. Chemical pleurodesis for malignant pleural effusions. Ann Intern Med. 1994; 120(1): 56–64, doi: 10.7326/0003-4819-120-1-199401010-00010, indexed in Pubmed: 8250457.
19. Patz EF, McAdams HP, Erasmus JJ, et al. Sclerotherapy for malignant pleural effusions: a prospective randomized trial of bleomycin vs doxycycline with small-bore catheter drainage. Chest. 1998; 113(5): 1305–1311, doi: 10.1378/chest.113.5.1305, indexed in Pubmed: 9596311.
20. Dikensoy O, Light RW. Alternative widely available, inexpensive agents for pleurodesis. Curr Opin Pulm Med. 2005; 11(4): 340–344, doi: 10.1097/01.mcp.0000166587.24127.91, indexed in Pubmed: 15928503.
21. Hsu LH, Feng AC, Soong TC, et al. Clinical outcomes of chemical pleurodesis using a minocycline. Ther Adv Respir Dis. 2019; 13: 1753466619841231, doi: 10.1177/1753466619841231, indexed in Pubmed: 30945619.
22. Daddi N, Vannucci J, Maggio C, et al. Efficacy of tigecycline pleurodesis: a comparative experimental study. J Surg Res. 2011; 169(2): e109–e118, doi: 10.1016/j.jss.2010.07.001, indexed in Pubmed: 20934718.
23. Yilmaz N, Zeybek A, Tharian B, et al. Efficacy of nonsurgical tigecycline pleurodesis for the management of hepatic hydrothorax in patients with liver cirrhosis. Surg Case Rep. 2015; 1(1): 62, doi: 10.1186/s40792-015-0049-x, indexed in Pubmed: 26366359.
24. Stiksa G, Korsgaard R, Simonsson BG. Treatment of recurrent pleural effusion by pleurodesis with quinacrine. Comparison between instillation by repeated thoracenteses and by tube drainage. Scand J Respir Dis. 1979; 60(4): 197–205, indexed in Pubmed: 531540.
25. Boe J, Florvaag E. [Chemical pleurodesis induced by mepacrine chloride. An alternative in the treatment of malignant pleural effusions]. Tidsskr Nor Laegeforen. 1976; 96(23): 1203–1206, indexed in Pubmed: 968841.
26. Luh KT, Yang PC, Kuo SH, et al. Comparison of OK-432 and mitomycin C pleurodesis for malignant pleural effusion caused by lung cancer. A randomized trial. Cancer. 1992; 69(3): 674–679, doi: 10.1002/1097-0142(19920201)69:3<674::aid-cncr2820690313>3.0.co;2-5, indexed in Pubmed: 1309678.
27. Cheng D, Chan YM, Ng TY, et al. Mitomycin chemotherapeutic pleurodesis to palliate malignant pleural effusions secondary to gynecological cancer. Acta Obstet Gynecol Scand. 1999; 78(5): 443–446, indexed in Pubmed: 10326892.
28. Sreter KB, Jakopovic M, Janevski Z, et al. A pilot study — is there a role for mitoxantrone pleurodesis in the management of pleural effusion due to lung cancer? Ann Transl Med. 2016; 4(9): 162, doi: 10.21037/atm.2016.04.15, indexed in Pubmed: 27275475.
29. van Belle AF, ten Velde GP, Wouters EF. Chemical pleurodesis with mitoxantrone in the management of malignant effusions. Eur J Cancer. 1998; 34(1): 205–206, doi: 10.1016/s0959-8049(97)00355-9, indexed in Pubmed: 9624262.
30. Wang CQ, Huang XR, He M, et al. Intrapleural administration with rh-endostatin and chemical irritants in the control of malignant pleural effusion: a systematic review and meta-analysis. Front Oncol. 2021; 11: 649999, doi: 10.3389/fonc.2021.649999, indexed in Pubmed: 34414103.
31. Sasaki T, Yasuda H, Nakayama K, et al. Pleurodesis with carboplatin in elderly patients with malignant pleural effusion and lung adenocarcinoma. J Am Geriatr Soc. 2006; 54(4): 722–723, doi: 10.1111/j.1532-5415.2006.00668_9.x, indexed in Pubmed: 16686896.
32. Foresti V. Intrapleural Corynebacterium parvum for recurrent malignant pleural effusions. Respiration. 1995; 62(1): 21–26, doi: 10.1159/000196384, indexed in Pubmed: 7716350.
33. Ishihara K, Hasegawa T, Okazaki M, et al. [OK432 chemical pleurodesis as a standard therapy of spontaneous pneumothorax]. Nihon Kyobu Shikkan Gakkai Zasshi. 1988; 26(1): 10–15, indexed in Pubmed: 3373914.
34. Jiang H, Yang XM, Wang CQ, et al. Intrapleural perfusion with staphylococcal enterotoxin c for malignant pleural effusion: a clustered systematic review and meta-analysis. Front Med (Lausanne). 2022; 9: 816973, doi: 10.3389/fmed.2022.816973, indexed in Pubmed: 35547209.
35. Ren S, Terman DS, Bohach G, et al. Intrapleural staphylococcal superantigen induces resolution of malignant pleural effusions and a survival benefit in non-small cell lung cancer. Chest. 2004; 126(5): 1529–1539, doi: 10.1378/chest.126.5.1529, indexed in Pubmed: 15539723.
36. Rahman NM, Davies HE, Salzberg M, et al. Use of lipoteichoic acid-T for pleurodesis in malignant pleural effusion: a phase I toxicity and dose-escalation study. Lancet Oncol. 2008; 9(10): 946–952, doi: 10.1016/S1470-2045(08)70205-5, indexed in Pubmed: 18775668.
37. Keeratichananont W, Kaewdech A, Keeratichananont S. Efficacy and safety profile of autologous blood versus talc pleurodesis for malignant pleural effusion: a randomized controlled trial. Ther Adv Respir Dis. 2018; 12: 1753466618816625, doi: 10.1177/1753466618816625, indexed in Pubmed: 30526440.
38. Martínez-Escobar S, Ruiz-Bailén M, Lorente-Acosta MJ, et al. Pleurodesis using autologous blood: a new concept in the management of persistent air leak in acute respiratory distress syndrome. J Crit Care. 2006; 21(2): 209–216, doi: 10.1016/j.jcrc.2005.10.003, indexed in Pubmed: 16769470.
39. Narenchandra V, Vishnukanth G, Dwivedi DP, et al. Comparison of efficacy of autologous blood patch pleurodesis versus doxycycline pleurodesis in the management of persistent air leak in patients with secondary spontaneous pneumothorax. A randomized control trial. Monaldi Arch Chest Dis. 2022 [Epub ahead of print], doi: 10.4081/monaldi.2022.2036, indexed in Pubmed: 35698824.
40. Hamada S, Okamoto N, Watanabe I, et al. Is pleurodesis with 50% glucose solution in patients with spontaneous pneumothorax safe?: A case series. Arch Bronconeumol. 2017; 53(4): 210–211, doi: 10.1016/j.arbres.2016.08.018, indexed in Pubmed: 27890463.
41. Chen Y, Li C, Xu L, et al. Novel treatment for chylothorax after esophagectomy with 50% glucose pleurodesis. Ann Vasc Surg. 2010; 24(5): 694.e9–694.13, doi: 10.1016/j.avsg.2009.10.021, indexed in Pubmed: 20579587.
42. Tsukioka T, Inoue K, Oka H, et al. Intraoperative mechanical and chemical pleurodesis with 50 % glucose solution for secondary spontaneous pneumothorax in patients with pulmonary emphysema. Surg Today. 2013; 43(8): 889–893, doi: 10.1007/s00595-013-0497-5, indexed in Pubmed: 23361597.
43. Song KS, Keum D, Kim JB. Chemical pleurodesis using doxycycline and extract. Korean J Thorac Cardiovasc Surg. 2017; 50(4): 281–286, doi: 10.5090/kjtcs.2017.50.4.281, indexed in Pubmed: 28795034.
44. Kim JD, Choi JW, Park HOh, et al. Chemical pleurodesis with L. extract for secondary spontaneous pneumothorax in elderly patients. J Thorac Dis. 2020; 12(10): 5440–5445, doi: 10.21037/jtd-20-708, indexed in Pubmed: 33209377.

45. Park JB, Lee SAm, Lee WS, et al. The management of chemical pleurodesis with viscum album in patients with persistent air leakage. J Thorac Dis. 2018; 10(1): 371–376, doi: 10.21037/jtd.2017.12.67, indexed in Pubmed: 29600069.
46. Mai Z, Feng B, He Q, et al. Medical thoracoscopic thermal ablation therapy for metastatic pleural tumors with malignant effusion: an exploratory retrospective study. Int J Gen Med. 2021; 14: 9349–9360, doi: 10.2147/IJGM.S339596, indexed in Pubmed: 34898999.
47. Yazicioglu A, Uysal S, Sahinoglu T, et al. Does sericin, as a novel pleurodesis agent, have higher effectiveness compared to talcum powder, doxycycline, and silver nitrate pleurodesis? Arch Bronconeumol (Engl Ed). 2019; 55(7): 357–367, doi: 10.1016/j.arbres.2018.10.003, indexed in Pubmed: 30473265.
48. Lee YCG, Teixeira LR, Devin CJ, et al. Transforming growth factor-beta2 induces pleurodesis significantly faster than talc. Am J Respir Crit Care Med. 2001; 163(3): 640–644, doi: 10.1164/ajrccm.163.3.2002091, indexed in Pubmed: 11254517.
49. Bhatnagar R, Keenan EK, Morley AJ, et al. Outpatient talc administration by indwelling pleural catheter for malignant effusion. N Engl J Med. 2018; 378(14): 1313–1322, doi: 10.1056/NEJMoa1716883, indexed in Pubmed: 29617585.
50. Kaul V, McCracken DJ, Rahman NM, et al. Contemporary approach to the diagnosis of malignant pleural effusion. Ann Am Thorac Soc. 2019; 16(9): 1099–1106, doi: 10.1513/AnnalsATS.201902-189CME, indexed in Pubmed: 31216176.
51. Ferrer J, Roldán J, Teixidor J, et al. Predictors of pleural malignancy in patients with pleural effusion undergoing thoracoscopy. Chest. 2005; 127(3): 1017–1022, doi: 10.1378/chest.127.3.1017, indexed in Pubmed: 15764788.
52. Karpathiou G, Mobarki M, Stachowicz ML, et al. Pericardial and pleural metastases: clinical, histologic, and molecular differences. Ann Thorac Surg. 2018; 106(3): 872–879, doi: 10.1016/j.athoracsur.2018.04.073, indexed in Pubmed: 29852147.
53. Sahn SA. Pleural diseases related to metastatic malignancies. Eur Respir J. 1997; 10(8): 1907–1913, doi: 10.1183/09031936.97.10081907, indexed in Pubmed: 9272937.
54. Chernow B, Sahn S. Carcinomatous involvement of the pleura. Am J Med. 1977; 63(5): 695–702, doi: 10.1016/0002-9343(77)90154-1.
55. Clive AO, Kahan BC, Hooper CE, et al. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. Thorax. 2014; 69(12): 1098–1104, doi: 10.1136/thoraxjnl-2014-205285, indexed in Pubmed: 25100651.
56. Jovanovic D. Etiopathogenesis of malignant pleural effusion. AME Medical Journal. 2021; 6: 28–28, doi: 10.21037/amj-2019-mpe-05.
57. Awadallah SF, Bowling MR, Sharma N, et al. Malignant pleural effusion and cancer of unknown primary site: a review of literature. Ann Transl Med. 2019; 7(15): 353, doi: 10.21037/atm.2019.06.33, indexed in Pubmed: 31516899.
58. Awasthi A, Gupta N, Srinivasan R, et al. Cytopathological spectrum of unusual malignant pleural effusions at a tertiary care centre in north India. Cytopathology. 2007; 18(1): 28–32, doi: 10.1111/j.1365-2303.2007.00382.x, indexed in Pubmed: 17250600.
59. Puchalski JT, Argento AC, Murphy TE, et al. Etiologies of bilateral pleural effusions. Respir Med. 2013; 107(2): 284–291, doi: 10.1016/j.rmed.2012.10.004, indexed in Pubmed: 23219348.
60. Tian P, Qiu R, Wang M, et al. Prevalence, causes, and health care burden of pleural effusions among hospitalized adults in China. JAMA Netw Open. 2021; 4(8): e2120306, doi: 10.1001/jamanetworkopen.2021.20306, indexed in Pubmed: 34374774.
61. Kellie S, Pfister G, Mann J, et al. A novel approach to classifying pleural effusions using a new reagent. Chest. 2012; 142(4), doi: 10.1378/chest.1382068.
62. Chae G, Jun JB, Jung HS, et al. Histiocytic pleural effusion: the strong clue to malignancy. World J Surg Oncol. 2021; 19(1): 180, doi: 10.1186/s12957-021-02296-1, indexed in Pubmed: 34134706.
63. Lee J, Lee YH, Seo H, et al. Laboratory discrimination between neutrophilic malignant and parapneumonic pleural effusions. Am J Med Sci. 2019; 358(2): 115–120, doi: 10.1016/j.amjms.2019.04.009, indexed in Pubmed: 31331448.
64. Popowicz N, Cheah HM, Gregory C, et al. Neutrophil-to-lymphocyte ratio in malignant pleural fluid: Prognostic significance. PLoS One. 2021; 16(4): e0250628, doi: 10.1371/journal.pone.0250628, indexed in Pubmed: 33901252.
65. Johnson L, Fakih HA, Daouk S, et al. Transudative pleural effusion of malignant etiology: Rare but real. Respir Med Case Rep. 2017; 20: 188–191, doi: 10.1016/j.rmcr.2017.02.015, indexed in Pubmed: 28316930.
66. Ryu JS, Ryu ST, Kim YS, et al. What is the clinical significance of transudative malignant pleural effusion? Korean J Intern Med. 2003; 18(4): 230–233, doi: 10.3904/kjim.2003.18.4.230, indexed in Pubmed: 14717231.
67. Yang J, Lee OJ, Son SM, et al. EGFR mutation status in lung adenocarcinoma-associated malignant pleural effusion and efficacy of EGFR tyrosine kinase inhibitors. Cancer Res Treat. 2018; 50(3): 908–916, doi: 10.4143/crt.2017.378, indexed in Pubmed: 28934846.
68. Stathopoulos GT. Translational advances in pleural malignancies. Respirology. 2011; 16(1): 53–63, doi: 10.1111/j.1440-1843.2010.01890.x, indexed in Pubmed: 21044230.
69. Holling N, Patole S, Medford ARL, et al. Is systemic anticancer therapy associated with higher rates of malignant pleural effusion control in people with pharmacologically sensitive tumors?: A retrospective analysis of prospectively collected data. Chest. 2021; 160(5): 1915–1924, doi: 10.1016/j.chest.2021.05.027, indexed in Pubmed: 34023321.
70. Verma A, Chopra A, Lee YW, et al. Can EGFR-tyrosine kinase inhibitors (TKI) alone without talc pleurodesis prevent recurrence of malignant pleural effusion (MPE) in lung adenocarcinoma. Curr Drug Discov Technol. 2016; 13(2): 68–76, doi: 10.2174/1570163813666160524142846, indexed in Pubmed: 27216707.
71. Kashiwabara K, Fuji S, Tsumura S, et al. Prognosis of -mutant lung adenocarcinoma patients with malignant pleural effusion receiving first-line EGFR-TKI therapy without pleurodesis: a single-institute retrospective study. Anticancer Res. 2020; 40(2): 1117–1121, doi: 10.21873/anticanres.14051, indexed in Pubmed: 32014962.
72. Yin W, Zhang H, Gu Y, et al. [Clinical characteristics and prognosis of 76 lung adenocarcinoma patients harboring EGFR mutations with pleural effusion at initial diagnosis: a single-center retrospective study]. Zhongguo Fei Ai Za Zhi. 2022; 25(3): 156–166, doi: 10.3779/j.issn.1009-3419.2022.101.13, indexed in Pubmed: 35340158.
73. Anevlavis S, Kouliatsis G, Sotiriou I, et al. Prognostic factors in patients presenting with pleural effusion revealing malignancy. Respiration. 2014; 87(4): 311–316, doi: 10.1159/000356764, indexed in Pubmed: 24457947.
74. Chiang KY, Ho JCM, Chong P, et al. Role of early definitive management for newly diagnosed malignant pleural effusion related to lung cancer. Respirology. 2020; 25(11):

1167–1173, doi: 10.1111/resp.13812, indexed in Pubmed: 32249488.
75. Psallidas I, Kanellakis NI, Gerry S, et al. Development and validation of response markers to predict survival and pleurodesis success in patients with malignant pleural effusion (PROMISE): a multicohort analysis. Lancet Oncol. 2018; 19(7): 930–939, doi: 10.1016/S1470-2045(18)30294-8, indexed in Pubmed: 29908990.
76. Feller-Kopman DJ, Reddy CB, DeCamp MM, et al. Management of malignant pleural effusions. An official ATS/STS/STR clinical practice guideline. Am J Respir Crit Care Med. 2018; 198(7): 839–849, doi: 10.1164/rccm.201807-1415ST, indexed in Pubmed: 30272503.
77. N Maskell, N Rahman, M Roberts, A Bibby, K Blyth, J Corcoran, et al. BTS Guideline for Pleural Disease. 2022.
78. Heinke MY, Vinod SK. A review on the impact of lung cancer multidisciplinary care on patient outcomes. Transl Lung Cancer Res. 2020; 9(4): 1639–1653, doi: 10.21037/tlcr.2019.11.03, indexed in Pubmed: 32953538.
79. Croke JM, El-Sayed S. Multidisciplinary management of cancer patients: chasing a shadow or real value? An overview of the literature. Curr Oncol. 2012; 19(4): e232–e238, doi: 10.3747/co.19.944, indexed in Pubmed: 22876151.
80. Pillay B, Wootten AC, Crowe H, et al. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: a systematic review of the literature. Cancer Treat Rev. 2016; 42: 56–72, doi: 10.1016/j.ctrv.2015.11.007, indexed in Pubmed: 26643552.
81. Mierzejewski M, Korczynski P, Krenke R, et al. Chemical pleurodesis — a review of mechanisms involved in pleural space obliteration. Respir Res. 2019; 20(1): 247, doi: 10.1186/s12931-019-1204-x, indexed in Pubmed: 31699094.
82. Rodriguez-Panadero F, Montes-Worboys A. Mechanisms of Pleurodesis. Respiration. 2012; 83(2): 91–98, doi: 10.1159/000335419.
83. Hobbs SB, Martin JT, Walker CM, et al. Nodular pleural thickening after lobectomy for lung cancer. Insights on imaging of the pleura. Ann Am Thorac Soc. 2016; 13(8): 1424–1425, doi: 10.1513/AnnalsATS.201604-238CC, indexed in Pubmed: 27509157.
84. Bhupathy S, Huynh T. Positive 18F-fluorodeoxyglucose positron emission tomography/computed tomography 20 years after talc pleurodesis. World J Nucl Med. 2022, doi: 10.1055/s-0042-1750394.
85. Parshall MB, Schwartzstein RM, Adams L, et al. American Thoracic Society Committee on Dyspnea. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. Am J Respir Crit Care Med. 2012; 185(4): 435–452, doi: 10.1164/rccm.201111-2042ST, indexed in Pubmed: 22336677.
86. Agustí AG, Cardús J, Roca J, et al. Ventilation-perfusion mismatch in patients with pleural effusion: effects of thoracentesis. Am J Respir Crit Care Med. 1997; 156(4 Pt 1): 1205–1209, doi: 10.1164/ajrccm.156.4.9612113, indexed in Pubmed: 9351623.
87. Richard W. Light. Pleural Diseases. 6th edition. Lippincott Williams & Wilkins; 2013.
88. Cartaxo AM, Vargas FS, Salge JM, et al. Improvements in the 6-min walk test and spirometry following thoracentesis for symptomatic pleural effusions. Chest. 2011; 139(6): 1424–1429, doi: 10.1378/chest.10-1679, indexed in Pubmed: 21051387.
89. Thomas R, Jenkins S, Eastwood PR, et al. Physiology of breathlessness associated with pleural effusions. Curr Opin Pulm Med. 2015; 21(4): 338–345, doi: 10.1097/MCP.0000000000000174, indexed in Pubmed: 25978627.
90. DeBiasi EM, Feller-Kopman D. Physiologic basis of symptoms in pleural disease. Semin Respir Crit Care Med. 2019; 40(3): 305–313, doi: 10.1055/s-0039-1693648, indexed in Pubmed: 31525806.
91. Marcondes BF, Vargas F, Paschoal FH, et al. Sleep in patients with large pleural effusion: impact of thoracentesis. Sleep Breath. 2012; 16(2): 483–489, doi: 10.1007/s11325-011-0529-6, indexed in Pubmed: 21573912.
92. MacDuff A, Arnold A, Harvey J, et al. BTS Pleural Disease Guideline Group. Management of spontaneous pneumothorax: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010; 65 Suppl 2: ii18–ii31, doi: 10.1136/thx.2010.136986, indexed in Pubmed: 20696690.
93. Andres JJR, Canto A, Moya J. Pleurodesis: indicaciones, tecnicas y resultados. Archivos de Bronconeumología. 1984; 20(6): 256–263, doi: 10.1016/s0300-2896(15)32223-7.
94. Sonoda A, Jeudy J, White CS, et al. Pleurodesis: indications and radiologic appearance. Jpn J Radiol. 2015; 33(5): 241–245, doi: 10.1007/s11604-015-0412-7, indexed in Pubmed: 25791777.
95. Rafei H, Jabak S, Mina A, Tfayli A. Pleurodesis in malignant pleural effusions: Outcome and predictors of success. Integr Cancer Sci Ther [Internet]. 2015. http://oatext.com/Pleurodesis-in-malignant-pleural-effusions-Outcome-and-predictors-of-success.php (10.09.2022).
96. Bhatnagar R, Luengo-Fernandez R, Kahan BC, et al. 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(26): 1–90, doi: 10.3310/hta24260, indexed in Pubmed: 32525474.
97. Bhatnagar R, Piotrowska HEG, Laskawiec-Szkonter M, et al. Effect of thoracoscopic talc poudrage vs talc slurry via chest tube on pleurodesis failure rate among patients with malignant pleural effusions: a randomized clinical trial. JAMA. 2020; 323(1): 60–69, doi: 10.1001/jama.2019.19997, indexed in Pubmed: 31804680.
98. Lee YC, Baumann MH, Maskell NA, et al. Pleurodesis practice for malignant pleural effusions in five English-speaking countries: survey of pulmonologists. Chest. 2003; 124(6): 2229–2238, doi: 10.1378/chest.124.6.2229, indexed in Pubmed: 14665505.
99. Diacon AH, Wyser C, Bolliger CT, et al. Prospective randomized comparison of thoracoscopic talc poudrage under local anesthesia versus bleomycin instillation for pleurodesis in malignant pleural effusions. Am J Respir Crit Care Med. 2000; 162(4 Pt 1): 1445–1449, doi: 10.1164/ajrccm.162.4.2002030, indexed in Pubmed: 11029359.
100. Sherman S, Ravikrishnan KP, Patel AS, et al. Optimum anesthesia with intrapleural lidocaine during chemical pleurodesis with tetracycline. Chest. 1988; 93(3): 533––536, doi: 10.1378/chest.93.3.533, indexed in Pubmed: 3342661.
101. Wooten SA, Barbarash RA, Strange C, et al. Systemic absorption of tetracycline and lidocaine following intrapleural instillation. Chest. 1988; 94(5): 960–963, doi: 10.1378/chest.94.5.960, indexed in Pubmed: 3180899.
102. Thethi I, Ramirez S, Shen W, et al. Effect of chest tube size on pleurodesis efficacy in malignant pleural effusion: a meta-analysis of randomized controlled trials. J Thorac Dis. 2018; 10(1): 355–362, doi: 10.21037/jtd.2017.11.134, indexed in Pubmed: 29600067.
103. Xie C, Teixeira LR, McGovern JP, et al. Systemic corticosteroids decrease the effectiveness of talc pleurodesis. Am J Respir Crit Care Med. 1998; 157(5 Pt 1): 1441–1444, doi: 10.1164/ajrccm.157.5.9708032, indexed in Pubmed: 9603121.

104. Rahman NM, Pepperell J, Rehal S, et al. Effect of opioids vs nsaids and larger vs smaller chest tube size on pain control and pleurodesis efficacy among patients with malignant pleural effusion: the TIME1 randomized clinical trial. JAMA. 2015; 314(24): 2641–2653, doi: 10.1001/jama.2015.16840, indexed in Pubmed: 26720026.
105. Stefani A, Natali P, Casali C, et al. Talc poudrage versus talc slurry in the treatment of malignant pleural effusion. A prospective comparative study. Eur J Cardiothorac Surg. 2006; 30(6): 827–832, doi: 10.1016/j.ejcts.2006.10.002, indexed in Pubmed: 17113008.
106. Mager HJ, Maesen B, Verzijlbergen F, et al. Distribution of talc suspension during treatment of malignant pleural effusion with talc pleurodesis. Lung Cancer. 2002; 36(1): 77–81, doi: 10.1016/s0169-5002(01)00475-5, indexed in Pubmed: 11891037.
107. Dryzer SR, Allen ML, Strange C, et al. A comparison of rotation and nonrotation in tetracycline pleurodesis. Chest. 1993; 104(6): 1763–1766, doi: 10.1378/chest.104.6.1763, indexed in Pubmed: 8252959.
108. Lamb C, Li A, Thakkar D, et al. Pleurodesis. Semin Respir Crit Care Med. 2019; 40(3): 375–385, doi: 10.1055/s-0039-1693997, indexed in Pubmed: 31525812.
109. Villanueva AG, Gray AW, Shahian DM, et al. Efficacy of short term versus long term tube thoracostomy drainage before tetracycline pleurodesis in the treatment of malignant pleural effusions. Thorax. 1994; 49(1): 23–25, doi: 10.1136/thx.49.1.23, indexed in Pubmed: 7512285.
110. Psallidas I, Hassan M, Yousuf A, et al. Role of thoracic ultrasonography in pleurodesis pathways for malignant pleural effusions (SIMPLE): an open-label, randomised controlled trial. Lancet Respir Med. 2022; 10(2): 139–148, doi: 10.1016/S2213-2600(21)00353-2, indexed in Pubmed: 34634246.
111. Ford A, Jennings S, Tharion J. Low serum albumin as a predictor of poor outcome in pleurodesis for malignant pleural effusion. Heart, Lung and Circulation. 2015; 24: e9, doi: 10.1016/j.hlc.2014.12.022.
112. Li P, Graver A, Hosseini S, et al. Clinical predictors of successful and earlier pleurodesis with a tunnelled pleural catheter in malignant pleural effusion: a cohort study. CMAJ Open. 2018; 6(2): E235–E240, doi: 10.9778/cmajo.20170163, indexed in Pubmed: 29898894.
113. Barbetakis N, Asteriou C, Papadopoulou F, et al. Early and late morbidity and mortality and life expectancy following thoracoscopic talc insufflation for control of malignant pleural effusions: a review of 400 cases. J Cardiothorac Surg. 2010; 5: 27, doi: 10.1186/1749-8090-5-27, indexed in Pubmed: 20403196.
114. Hassan M, Gadallah M, Mercer RM, et al. Predictors of outcome of pleurodesis in patients with malignant pleural effusion: a systematic review and meta-analysis. Expert Rev Respir Med. 2020; 14(6): 645–654, doi: 10.1080/17476348.2020.1746647, indexed in Pubmed: 32213100.
115. Zablockis R, Danila E, Gruslys V, et al. Systemic inflammatory response to different sclerosing agents as a predictor of pleurodesis outcome. In Vivo. 2021; 35(4): 2391–2398, doi: 10.21873/invivo.12516, indexed in Pubmed: 34182522.
116. Thomas R, Francis R, Davies HE, et al. Interventional therapies for malignant pleural effusions: the present and the future. Respirology. 2014; 19(6): 809–822, doi: 10.1111/resp.12328, indexed in Pubmed: 24947955.
117. Dipper A, Jones HE, Bhatnagar R, et al. Interventions for the management of malignant pleural effusions: a network meta-analysis. Cochrane Database Syst Rev. 2020; 4(160): CD010529, doi: 10.1002/14651858.CD010529.pub3, indexed in Pubmed: 32315458.
118. Paschoalini Md, Vargas FS, Marchi E, et al. Prospective randomized trial of silver nitrate vs talc slurry in pleurodesis for symptomatic malignant pleural effusions. Chest. 2005; 128(2): 684–689, doi: 10.1378/chest.128.2.684, indexed in Pubmed: 16100154.
119. Menna C, Andreetti C, Ibrahim M, et al. The effect of silver nitrate pleurodesis after a failed thoracoscopic talc poudrage. Biomed Res Int. 2013; 2013: 295890, doi: 10.1155/2013/295890, indexed in Pubmed: 24073398.
120. Bilaçeroğlu S, Cağirici U, Perim K, et al. Corynebacterium parvum pleurodesis and survival is not significantly influenced by pleural pH and glucose level. Monaldi Arch Chest Dis Arch Monaldi Mal Torace. 1998; 53: 14–22.
121. Shehata S, Sileem A, El-Fakharany K. Pleural fluid CRP, LDH, and pH as predictors of successful pleurodesis in malignant pleural effusions. Egypt J Chest Dis Tuber. 2015; 64(3): 593–599, doi: 10.1016/j.ejcdt.2015.05.003.
122. Hassaan K. Combination therapy with intrapleural doxycycline and talc in reduced doses for pleurodesi. Eur Respir J. 2012; 40 (Suppl 56)(P1265).
123. Emad A, Rezaian GR. Treatment of malignant pleural effusions with a combination of bleomycin and tetracycline. A comparison of bleomycin or tetracycline alone versus a combination of bleomycin and tetracycline. Cancer. 1996; 78(12): 2498–2501, doi: 10.1002/(sici)1097-0142(19961215)78:12<2498::aid-cncr8>3.0.co;2-g, indexed in Pubmed: 8952557.
124. Kumar S, Sonkar A, Kumar D, et al. Comparative evaluation of VATS assisted combined mechanical and chemical pleurodesis with chemical pleurodesis — is it worthwhile? Indian J Thorac Cardiovasc Surg. 2013; 29(2): 106–109, doi: 10.1007/s12055-013-0211-7.
125. Mohsen TA, Zeid AA, Meshref M, et al. Local iodine pleurodesis versus thoracoscopic talc insufflation in recurrent malignant pleural effusion: a prospective randomized control trial. Eur J Cardiothorac Surg. 2011; 40(2): 282–286, doi: 10.1016/j.ejcts.2010.09.005, indexed in Pubmed: 20961772.
126. Bellini A, Tarrazzi F, Tami C, et al. Intrapleural fibrinolytic therapy improves results with talc slurry pleurodesis. Cureus. 2020; 12(8): e10122, doi: 10.7759/cureus.10122, indexed in Pubmed: 33005537.
127. Wahidi MM, Reddy C, Yarmus L, 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(8): 1050–1057, doi: 10.1164/rccm.201607-1404OC, indexed in Pubmed: 27898215.
128. Shrager JB, Bhatnagar R, Kearney CT, et al. Silver nitrate-coated versus standard indwelling pleural catheter for malignant effusions: the SWIFT randomized trial. Ann Am Thorac Soc. 2022; 19(10): 1722–1729, doi: 10.1513/AnnalsATS.202111-1301OC, indexed in Pubmed: 35363591.
129. Santos PS, Marques MA, Cruz C, et al. Predictors of talc slurry pleurodesis success in patients with malignant pleural effusions. Rev Port Pneumol (2006). 2017; 23(4): 216–220, doi: 10.1016/j.rppnen.2017.01.008, indexed in Pubmed: 28606378.
130. Yoon DW, Cho JHo, Choi YS, et al. Predictors of survival in patients who underwent video-assisted thoracic surgery talc pleurodesis for malignant pleural effusion. Thorac Cancer. 2016; 7(4): 393–398, doi: 10.1111/1759-7714.12354, indexed in Pubmed: 27385980.
131. D'Ambrosio PD, de Araújo PH, Junior ER, et al. Risk factors related to pleural empyema after talc slurry pleurodesis. Clinics (Sao Paulo). 2022; 77: 100098, doi: 10.1016/j.clinsp.2022.100098, indexed in Pubmed: 36041370.
132. Terra RM, da Costa PB, Dela Vega AJ, et al. Adverse events after pleurodesis in patients with malignant

pleural effusion. J Thorac Dis. 2020; 12(7): 3507–3513, doi: 10.21037/jtd-19-3850, indexed in Pubmed: 32802429.
133. Bridevaux PO, Tschopp JM, Cardillo G, et al. Short-term safety of thoracoscopic talc pleurodesis for recurrent primary spontaneous pneumothorax: a prospective European multicentre study. Eur Respir J. 2011; 38(4): 770–773, doi: 10.1183/09031936.00189710, indexed in Pubmed: 21436351.
134. Montes JF, Ferrer J, Villarino MA, et al. Influence of talc dose on extrapleural talc dissemination after talc pleurodesis. Am J Respir Crit Care Med. 2003; 168(3): 348–355, doi: 10.1164/rccm.200207-767OC, indexed in Pubmed: 12773332.
135. Griffo S, Musumeci A, De Luca G, et al. Talc-induced interstitial pneumonitis with respiratory failure. Anaesth Intensive Care. 2009; 37(1): 127–129, doi: 10.1177/0310057X0903700114, indexed in Pubmed: 19157360.
136. Rehse DH, Aye RW, Florence MG. Respiratory failure following talc pleurodesis. Am J Surg. 1999; 177(5): 437–440, doi: 10.1016/s0002-9610(99)00075-6, indexed in Pubmed: 10365887.
137. Evans TJ, Sivakumar P, Ahmed L. Progressive respiratory failure: a rare complication after graded talc pleurodesis. Br J Hosp Med (Lond). 2017; 78(5): 294–295, doi: 10.12968/hmed.2017.78.5.294, indexed in Pubmed: 28489449.
138. Park S, Lee H, Kim D, et al. Two cases of fatal hypoxemia after talc pleurodesis for recurrent malignant pleural effusion. Tuberc Respir Dis. 2007; 62(3): 217, doi: 10.4046/trd.2007.62.3.217.
139. Noh D, Park JS, Lee DY. Acute respiratory distress syndrome after pleurodesis for primary spontaneous pneumothorax. Korean J Thorac Cardiovasc Surg. 2017; 50(1): 64–67, doi: 10.5090/kjtcs.2017.50.1.64, indexed in Pubmed: 28180108.
140. Amundson WH, Racila E, Allen T, et al. Acute exacerbation of interstitial lung disease after procedures. Respir Med. 2019; 150: 30–37, doi: 10.1016/j.rmed.2019.02.012, indexed in Pubmed: 30961948.
141. Shinno Y, Kage H, Chino H, et al. Old age and underlying interstitial abnormalities are risk factors for development of ARDS after pleurodesis using limited amount of large particle size talc. Respirology. 2018; 23(1): 55–59, doi: 10.1111/resp.13192, indexed in Pubmed: 28980363.
142. Zhang W, Zhao YL, Li SJ, et al. Complications of thoracoscopic talc insufflation for the treatment of malignant pleural effusions: a meta-analysis. J Cardiothorac Surg. 2021; 16(1): 125, doi: 10.1186/s13019-021-01475-1, indexed in Pubmed: 33947423.
143. Milton R, Cale ARJ. Chronic pain due to talc pleurodesis for spontaneous pneumothorax. Ann Thorac Surg. 2003; 76(5): 1740–1741, doi: 10.1016/s0003-4975(03)00687-8, indexed in Pubmed: 14602332.
144. Cardillo G, Carleo F, Giunti R, et al. Videothoracoscopic talc poudrage in primary spontaneous pneumothorax: a single-institution experience in 861 cases. J Thorac Cardiovasc Surg. 2006; 131(2): 322–328, doi: 10.1016/j.jtcvs.2005.10.025, indexed in Pubmed: 16434260.
145. Noppen M. Who's (still) afraid of talc? Eur Respir J. 2007; 29(4): 619–621, doi: 10.1183/09031936.00001507, indexed in Pubmed: 17400875.
146. Yokoe N, Katsuda E, Kosaka K, et al. Interstitial lung disease after pleurodesis for malignant pleural effusion. Intern Med. 2017; 56(14): 1791–1797, doi: 10.2169/internalmedicine.56.7464, indexed in Pubmed: 28717073.
147. Togo T, Ota S, Hirose M, et al. [Air embolism at the pleurodesis for air leakage after pulmonary resection]. Kyobu Geka. 2012; 65(3): 201–204, indexed in Pubmed: 22374594.
148. Wagenfeld L, Zeitz O, Richard G. Visual loss after povidone-iodine pleurodesis. N Engl J Med. 2007; 357(12): 1264–1265, doi: 10.1056/NEJMc070128, indexed in Pubmed: 17881764.
149. Agarwal R, Khan A, Aggarwal AN, et al. Efficacy & safety of iodopovidone pleurodesis: a systematic review & meta-analysis. Indian J Med Res. 2012; 135: 297–304, indexed in Pubmed: 22561614.
150. Chaugle H, Parchment C, Keenan DJ, et al. Overdose of tetracycline for pleurodesis leading to chemical burns of the pleura. Eur J Cardiothorac Surg. 1999; 16(4): 469––470, doi: 10.1016/s1010-7940(99)00293-6, indexed in Pubmed: 10571097.
151. Smythe WR, Bavaria JE. Tetracycline pleurodesis--associated acute renal failure. Chest. 1993; 104(4): 1274–1276, doi: 10.1378/chest.104.4.1274, indexed in Pubmed: 8404207.
152. Li CY, Kuo SW, Lee JM. Life-threatening complications related to minocycline pleurodesis. Ann Thorac Surg. 2011; 92(3): 1122–1124, doi: 10.1016/j.athoracsur.2011.02.049, indexed in Pubmed: 21871317.
153. Puri V, Pyrdeck TL, Crabtree TD, et al. Treatment of malignant pleural effusion: a cost-effectiveness analysis. Ann Thorac Surg. 2012; 94(2): 374–9; discussion 379, doi: 10.1016/j.athoracsur.2012.02.100, indexed in Pubmed: 22579398.
154. Olfert JAP, Penz ED, Manns BJ, et al. Cost-effectiveness of indwelling pleural catheter compared with talc in malignant pleural effusion. Respirology. 2017; 22(4): 764–770, doi: 10.1111/resp.12962, indexed in Pubmed: 27983774.
155. Mishra EK, Corcoran JP, Hallifax RJ, et al. Defining the minimal important difference for the visual analogue scale assessing dyspnea in patients with malignant pleural effusions. PLoS One. 2015; 10(4): e0123798, doi: 10.1371/journal.pone.0123798, indexed in Pubmed: 25874452.
156. Ries AL. Minimally clinically important difference for the UCSD Shortness of Breath Questionnaire, Borg Scale, and Visual Analog Scale. COPD. 2005; 2(1): 105–110, doi: 10.1081/copd-200050655, indexed in Pubmed: 17136970.
157. Davies HE, Mishra EK, Kahan BC, 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(22): 2383–2389, doi: 10.1001/jama.2012.5535, indexed in Pubmed: 22610520.
158. Hassan M, Harriss E, Mercer RM. Survival and pleurodesis outcome in patients with malignant pleural effusion — a systematic review. Pleura and Peritoneum. 2021; 6(1): 1–5, doi: https://doi.org/10.1515/pp-2020-0147.
159. Hassan M, Mercer RM, Maskell NA, et al. Survival in patients with malignant pleural effusion undergoing talc pleurodesis. Lung Cancer. 2019; 137: 14–18, doi: 10.1016/j.lungcan.2019.09.003, indexed in Pubmed: 31521977.
160. Wajda A, Engström H, Persson HL. Medical talc pleurodesis: which patient with cancer benefits least? J Palliat Med. 2014; 17(7): 822–828, doi: 10.1089/jpm.2013.0591, indexed in Pubmed: 24885834.