Review Article

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Effusion recurrence and patient outcomes in malignant pleural effusion: a systematic review of pleurodesis and indwelling pleural catheters

Recidiva de derrame pleural e desfechos clínicos nos derrames pleurais malignos: uma revisão sistemática de pleurodese e cateteres pleurais de longa permanência

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ABSTRACT

Objective: This review aimed to compare the efficacy and safety of these approaches. **Methods:** A systematic review was conducted in accordance with PRISMA 2020 guidelines. Studies published from 2014 to May 2025 were searched in PubMed, LILACS, and SciELO. After filtering and applying the inclusion criterias, 38 studies were selected for analysis. **Results:** A total of 3088 patients were analyzed. Pleurodesis showed significantly lower recurrence rates compared to IPC (RR = 1.548; 95% CI: 1.31–1.80; $p < 0.05$). Among pleurodesis agents, iodopovidone 5%, doxycycline, and 0.3% silver nitrate were associated with the lowest effusion recurrence rates. However, silver nitrate had the highest incidence of severe adverse events. Talc poudrage and slurry are the most commonly used, but had higher recurrence rates than the aforementioned alternatives. Daily or periodic drainage showed better outcomes than mixed-drainage strategies for IPC. Pleurodesis, especially with talc or iodopovidone, yielded superior results in dyspnea relief and quality-of-life scores compared to IPC. On the other hand, IPC was associated with shorter hospitalization durations and fewer immediate procedural complications, although it required prolonged catheter use and maintenance. Adverse events were more frequent in pleurodesis, particularly with talc and silver nitrate. **Conclusions:** Pleurodesis is more effective in reducing MPE recurrence and improving symptoms. IPC remains useful for select patients, especially those unsuitable for hospitalization or with non-expandable lungs.

Keywords: "Pleural Effusion, Malignant"; "Pleurodesis"; "Catheters, Indwelling"; "Pleura"

RESUMO

Objetivo: Esta revisão tem como objetivo comparar a eficácia e a segurança dessas abordagens. **Métodos:** Foi realizada uma revisão sistemática de acordo com as diretrizes PRISMA 2020. Estudos publicados entre 2014 e maio de 2025 foram pesquisados nas bases PubMed, LILACS e SciELO. Após a triagem e aplicação dos critérios de inclusão, 38 estudos foram selecionados para análise. **Resultados:** Um total de 3088 pacientes foram analisados. A pleurodese apresentou taxas de recorrência significativamente menores em comparação ao cateter pleural de demora (CPD) (RR = 1,548; IC 95%: 1,31–1,80; p < 0,05). Entre os agentes de pleurodese, iodopovidona a 5%, doxiciclina e nitrato de prata a 0,3% estiveram associados às menores taxas de recorrência do derrame pleural. Entretanto, o nitrato de prata apresentou a maior incidência de eventos adversos graves. O talco em pó ou em pasta são os métodos mais comumente utilizados, porém apresentaram maiores taxas de recorrência em comparação às alternativas supracitadas. A drenagem diária ou periódica apresentaram melhores desfechos do que as estratégias de drenagem mista para CPD. A pleurodese, especialmente com talco ou iodopovidona, demonstrou melhores resultados no alívio da dispneia e nos escores de qualidade de vida em comparação ao IPC. Por outro lado, o IPC esteve associado a menores tempos de hospitalização e menos complicações imediatas relacionadas ao procedimento, embora exija uso prolongado do cateter e manutenção contínua. Eventos adversos foram mais frequentes na pleurodese, particularmente com talco e nitrato de prata. **Conclusões:** A pleurodese é mais eficaz na redução da recorrência do derrame pleural maligno e na melhora dos sintomas. O IPC permanece útil para pacientes selecionados, especialmente aqueles sem condições para hospitalização ou com pulmão não expansível.

Palavras-chave: "Derrame Pleural Maligno"; "Pleurodese"; "Cateteres de Demora"; "Pleura"

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INTRODUCTION

Malignant pleural effusion (MPE) consists in the accumulation of fluid and cancer cells at the pleural space. It's a common complication of cancer, with incidence nearly at 15%, and most cases being secondary to metastatic lung and breast cancer, however MPE can also occur due to primary pleural cancer, such as mesotheliomas. Diagnosis generally means advanced staged disease and poor prognosis, with median overall survival of up to 12 months, so most patients have indication of palliative management.[1-3]

In 2022, the 2 utmost typical MPE sites were among the 5 most prevalent cancers in Brazil, with breast cancer as the second most prevalent and lung cancer the fourth. Worldwide, breast is the first most prevalent and lung is the third, meanwhile in India breast is the first and lung is the fifth most prevalent cancers. A pattern of increased incidence can be observed in both neoplasms during the period of 2020-2022.[4,5]

Most MPE cases present symptoms, such as coughing, progressive dyspnea and thoracic pleuritic pain. Small effusions can be asymptomatic and diagnosed incidentally through imaging exams, like chest radiography (XR), chest ultrasound (USG) and computed tomography (CT). Even though CXR is the initial imaging exam on MPE, CT is a better exam to visualize small effusions, subpulmonary effusions and solid pleural disease, and thoracic USG is the most sensitive imaging exam to detect the effusion and is critical when drainage is needed.[1,6,7]

Pleurodesis consists in the obliteration of the visceral and parietal pleura, impeding fluid from accumulating in the pleural space, through an inflammatory process caused by different chemical agents. On the other hand, the insertion of an indwelling pleural catheter (IPC), a silicone tube, into the pleural space provides the capacity of drainage of all pleural fluid to a vacuum compartment.[1-3,6,7]

Therefore, given the global rising incidence in malignant neoplasms that cause MPE over the last few years, more studies should be conducted approaching its management and which therapy is better for each cluster of patients.

The main objective of the study is to analyze effectiveness of MPE treatment through recurrence rate after treatment.

MATERIAL AND METHODS

This systematic review was conducted in accordance with the PRISMA 2020 checklist, and included studies published up to May 23rd 2025, in the following databases: PubMed, LILACS, and SciELO. The descriptors and Boolean operators "Pleurodesis" OR "Indwelling Pleural Catheter" AND "Pleural Effusion, Malignant" were used, resulting in a total of 1,020 publications. 943 studies were automatically excluded using the following filters: randomized clinical trials (RCTs) conducted in humans through 2014–2024, additionally, 16 duplicate studies were excluded. The remaining 61 studies were individually and manually assessed by two independent authors, resulting in the exclusion of 16 literature reviews and meta-analyses, 2 studies that did not meet the review's objective and 5 studies that were not available in full text, furthermore, non-randomized clinical trials that passed the platform filters were included. A total of 38 studies were ultimately included: 29 from the PubMed database, 7 from LILACS, and 2 from SciELO.

The inclusion and exclusion criteria for RCTs in this systematic review were defined using the PICO strategy. The population of interest consisted exclusively of patients with pleural effusion secondary to neoplasms or malignant pleural implants. The intervention evaluated was either chemical pleurodesis or indwelling pleural catheter, both aiming the resolution of the effusion. Therefore, the comparison necessarily had to involve chemical pleurodesis agents and/or indwelling pleural catheters. The outcome of this study is to assess the effectiveness of these therapeutic modalities in the treatment of malignant pleural effusions, enabling a comparative analysis between these approaches. Every study that did not meet these criteria were excluded (Figure 1).

Additional research has been conducted in the databases for relevant articles, textbooks and guidelines that did not meet the inclusion criteria. Those studies have not been used for data extraction, therefore have not been assessed for risk of bias, outcomes and statistical analysis, but were included in the introduction and discussion sections. Those articles are mentioned in bibliographic references at numbers: Scott and Phil[1], Cho et al.[3], IARC[4], DATASUS[5], Haddaway et al.[8], Feller-Kopman and Light[9], Kwok et al.[10], Penz et al.[11] and Olfert et al.[12].

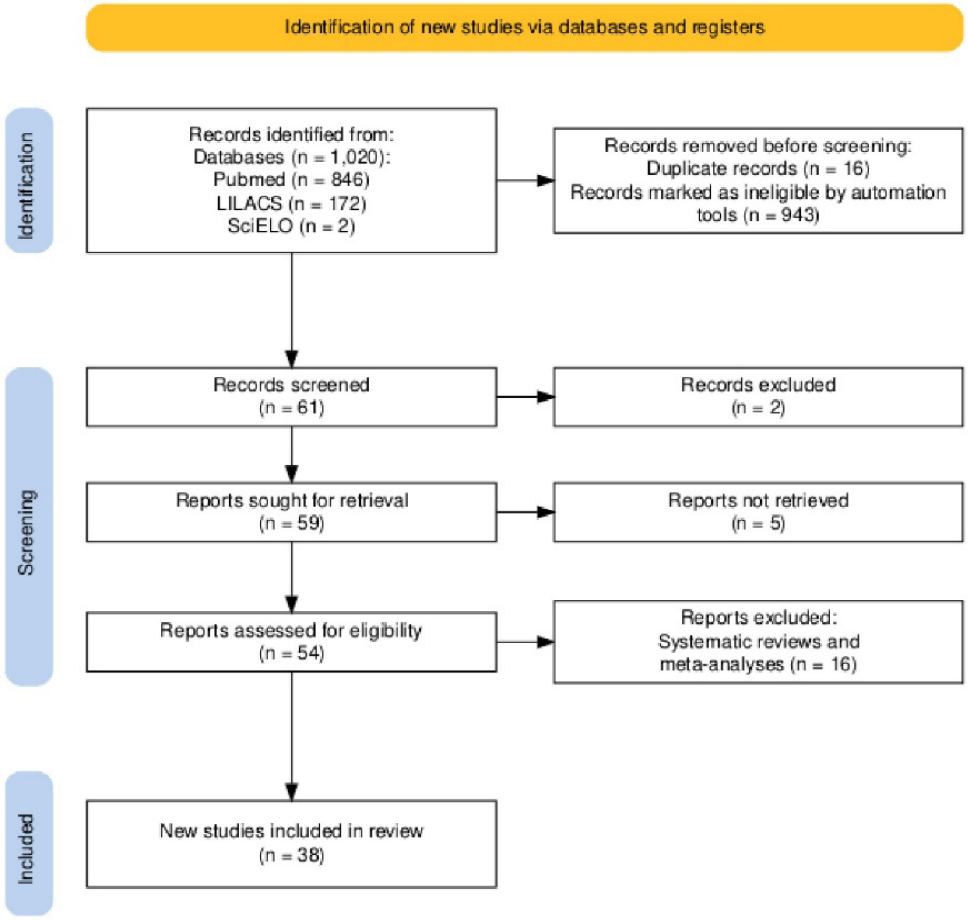

Figure 1. Flowchart of the studies selected for review.
Source: Adapted from the PRISMA2020 package.[8]

Data Collection and Statistical Analysis:

Data collection was carried out independently by the authors and compiled in an Excel spreadsheet, RCT protocols and economic focused publications were not included in analysis.

The primary outcome for data retrieval is to quantify the recurrence rate of MPE after chemical pleurodesis or IPC, as well as to evaluate differences between the chemical agents used for pleurodesis and the drainage intensity of the effusion through the catheter. Secondary outcomes include patient characteristics, improvement in dyspnea and patient quality of life, time between procedures and achievement of pleurodesis, presence of adverse effects, and duration of hospital stay.

After data collection, variables were moved to Graphpad Prism software and accessed for statistical analysis and also graphs and tables generation. The primary objective data was analyzed using Chi-square test and Fisher's exact test, assessing relative risk (RR) and 95% confidence intervals (95% CI), they were presented in charts and tables. Variables related to the secondary objectives were subjected to descriptive analysis and calculation of means and medians with 95% CI, and were also presented in charts and tables.

Risk of Bias:

All publications were assessed for risk of bias using the Jadad scale. Three studies were not classified for risk of bias due to their purely economic focus. Due to the nature of the topic, double blinding was rarely feasible, because the therapeutics involved are invasive, thus, oftentimes, both the patient and the physician are aware of the procedure performed (Table 1).

Table 1. Description of the Jadad Scale and classification of all selected studies.

JADAD Scale	Studies included classified by Jadad Scale (n)
Is the article described as randomized? (0 or 1)	Jadad 1= 4
Is randomization done appropriately? (0 or 1)	Jadad 2= 0
Is the article described as double-blind? (0 or 1)	Jadad 3= 16
Is the blinding method appropriately (0 or 1)	Jadad 4= 10
Does the study describe losses and exclusions? (0 or 1)	Jadad 5= 5

Source: Elaborated by the authors.

RESULTS

3088 patients were evaluated, 1537 were males (49.8%) and 1551 females (50.2%). Mean patients per study were 118.8 (IC95%: 68.39-169.20; n=26) with a mean age of 64.22 years (IC95%: 61.56-66.87; n=24). Most described diagnoses were lung cancer (946), breast cancer (571) and mesothelioma (383). Mean diagnoses per study were 39.42 patients with lung cancer (IC95%: 22.40-56.43; n=24), 27.19 with breast cancer (IC95%: 16.63-37.75; n=21) and 34.82 with mesotelioma (IC95%: 6.18-63.46; n=11) (Figure 2).

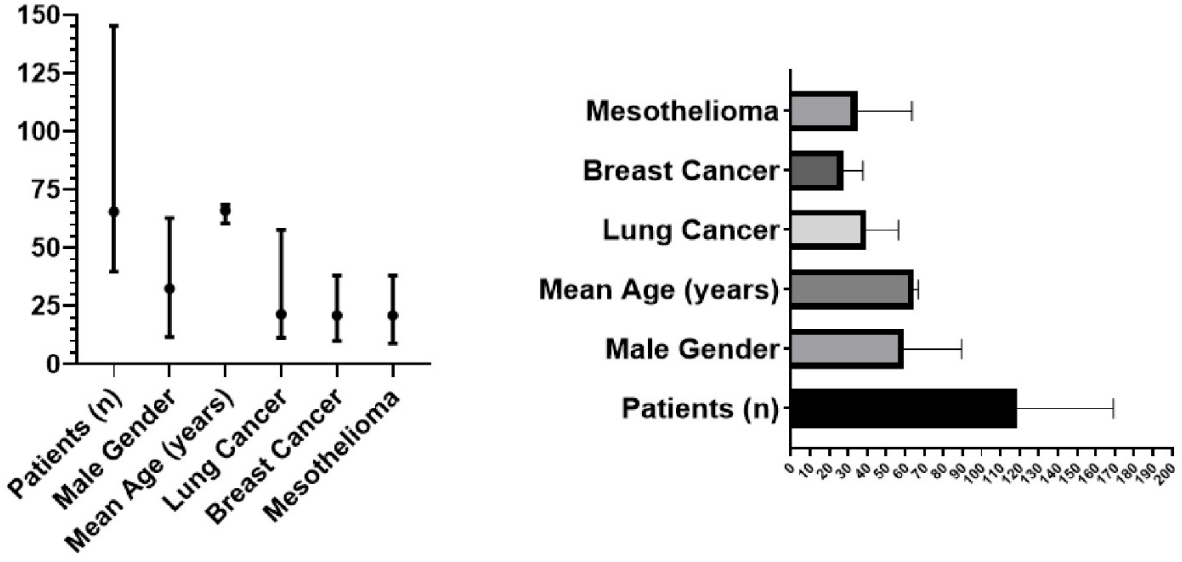

Figure 2. The left graph shows the median and interquartile range of the variables described for the studies population, while the right graph shows the mean and 95% confidence interval for the same variables.
Source: Elaborated by the authors.

Talc slurry and talc poudrage were the most utilized pleurodesis induction agents. Periodic IPC, especially symptom-guided, was the most frequent drainage protocol. 2 studies did not describe the pleurodesis agent (n=2) (Figure 3).

After exclusion of the placebo group, IPC and pleurodesis effusion recurrence were compared, obtaining a chi-square test value of 27.03 ($p<0.05$) and RR of 1.548 (IC95%: 1.31-1.80). Thus, effusion recurrence rate (ERR) is 54% higher in patients undergoing IPC compared to pleurodesis.

Individual analysis of IPC patients compared daily, periodic and mixed-drainage protocols (part of the trial time daily and part of the trial time periodic). Chi-square test valued 160, with both daily and periodic drainages being superior than mixed-drainage, with RRs of 4.683 (IC95%: 2.86-8.03) and 8.520 (IC95%: 5.29-13.98), respectively and both presenting p-value<0.05. There is no statistically significant difference between daily and periodic protocols (p=0.12) or between silver coated and normal catheters, utilized in the mixed-drainage protocol (p=0.82) (Table 2).

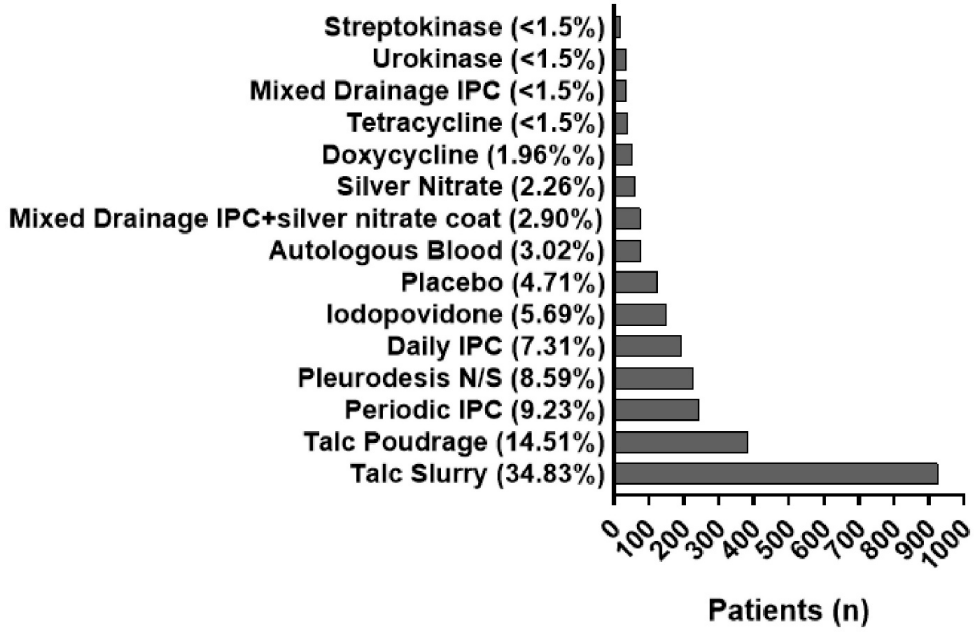

Figure 3. Different chemical agents and drainage protocols applied for patients undergoing chemical pleurodesis and/or IPC drainage.
Legend: IPC= indwelling pleural catheter; N/S= not specified.
Source: Elaborated by the authors.

Table 2. Drainage protocol used for IPC, indicating absolute recurrence and non-recurrence values for MPE, and also their respective ERR.

Drainage Protocol	Recurrence	Non-Recurrence	Patients (n)	ERR (%)
Periodic	15	151	166	9,03
Daily	12	61	73	16,43
Mixed (normal catheter)	37	12	49	75,51
Mixed (silver coated catheter)	60	17	77	77,92
Total	**124**	**241**	**365**	**51,45**

Legend: MPE= malignant pleural effusion; ERR= effusion recurrence rate.
Source: Elaborated by the authors.

Regarding pleurodesis, the chemical age0nts utilized have been compared resulting in a chi-square value of 143.5 ($p<0.05$). Most utilized agents were talc slurry and talc poudrage, meanwhile agents with the smallest ERR were doxycycline, iodopovidone 5% and 0.3% silver nitrate. There is no statistically significant difference between talc slurry and talc poudrage ($p=0.30$), nor between iodopovidone 5%, 2% and 1%, doxycycline and 0.3% silver nitrate ($p=0.98$).

Iodopovidone 5% presented the lowest ERR among iodine composts. Risk of recurrence was 6 times bigger in iodopovidone 10% then 5% (RR= 6.759, 95% CI: 1.90–23.48; $p<0.05$), while iodopovidone 5%, 2% and 1% had similar rates (RR= 0.8111, 95% CI: 0.11–5.36, $p>0.99$). When compared to talc poudrage and slurry, iodopovidone 5% ERR was around 6 to 7 times smaller (RR= 6.077, 95% CI: 2.60–14.54, $p<0.0001$; RR= 7.106, 95% CI: 3.09–16.74, $p<0.0001$) and iodopovidones 1% and 2% were around 6 to 8 times smaller (RR= 6.853, 95% CI: 1.96–25.27, $p=0.0002$; RR= 8.014, 95% CI: 2.32–29.29, $p<0.0001$).

When compared to doxycycline, talc poudrage ERR presented a RR of 5.940 (95% CI: 1.72–21.88, $p=0.0008$) and talc slurry of 6.946 (95% CI: 2.03–25.36, $p<0.0001$). Similarly, when compared to 0.3% silver nitrate, talc poudrage presented a RR of 4.569 (95% CI: 1.35–16.80, $p=0.0092$) and talc slurry of 5.343 (95% CI: 1.60–19.47, $p=0.001$) (Table 3, Figure 4).

Table 3. Agents used for chemical pleurodesis, indicating absolute recurrence and non-recurrence values for MPE, and also their respective ERR.

Pleurodesis Agent	Recurrence	Non-Recurrence	Patients (n)	ERR (%)
Iodopovidone 1%	1	29	30	3,33
Iodopovidone 2%	1	29	30	3,33
Doxycycline	2	50	52	3,84
Iodopovidone 5%	3	70	73	4,1
0.3% Silver Nitrate	2	38	40	5
Streptokinase	2	16	18	11,11
Autologous Blood	14	66	80	17,5
Talc Poudrage	53	179	232	22,84
Talco Slurry	113	310	423	26,71
Iodopovidone 10%	5	13	18	27,77
Tetracycline	14	25	39	35,89
Urokinase	13	22	35	37,14
Placebo	70	45	115	60,86
Total	**293**	**892**	**1185**	**24,72**

Legend: MPE= malignant pleural effusion; ERR= effusion recurrence rate.
Source: Elaborated by the authors.

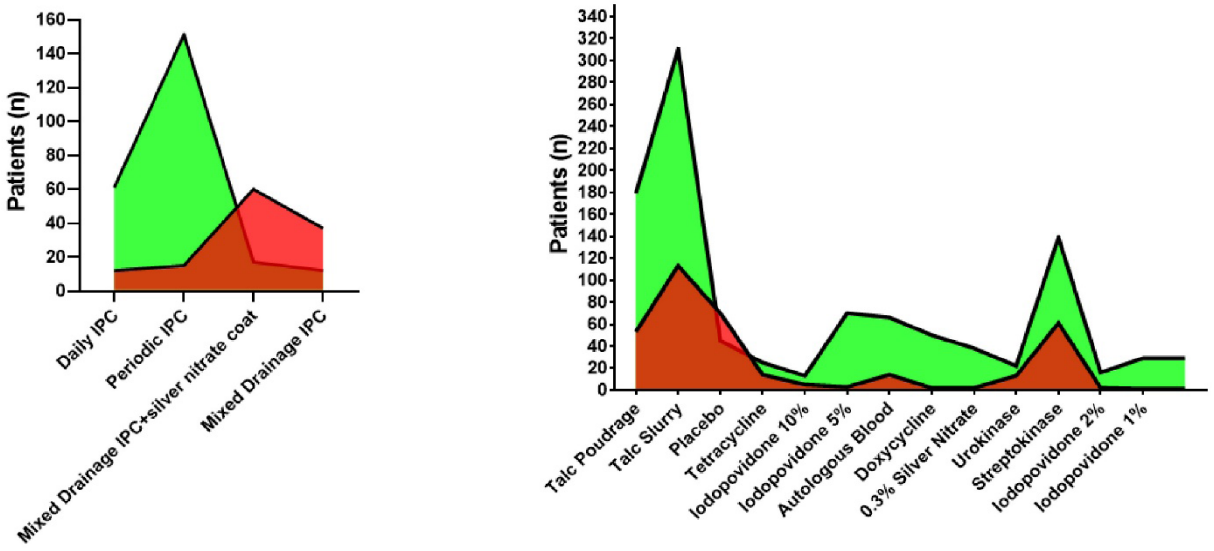

Figure 4. Number of patients with recurrence (red) and non-recurrence (green) of MPE. The graph on the left refers to IPC and the one on the right to pleurodesis.
Legend: MPE= malignant pleural effusion; IPC= indwelling pleural catheter.
Source: Elaborated by the authors.

VAS scale was utilized to assess dyspnea in 11 different studies, including pleurodesis and IPC procedures. 9 variables evaluated dyspnea with temporal progression, whereas 2 only evaluated mean reduction of the scale after the conclusion of the RCT.

Pleurodesis with talc slurry and periodic drainage IPC obtained a reduction of 11.85 mm and 2.06mm, respectively. In absolute numbers, talc poudrage presented the biggest reduction with 30mm, while one periodic drainage IPC RCT increased 19.40 mm in 1 year (Figure 5).

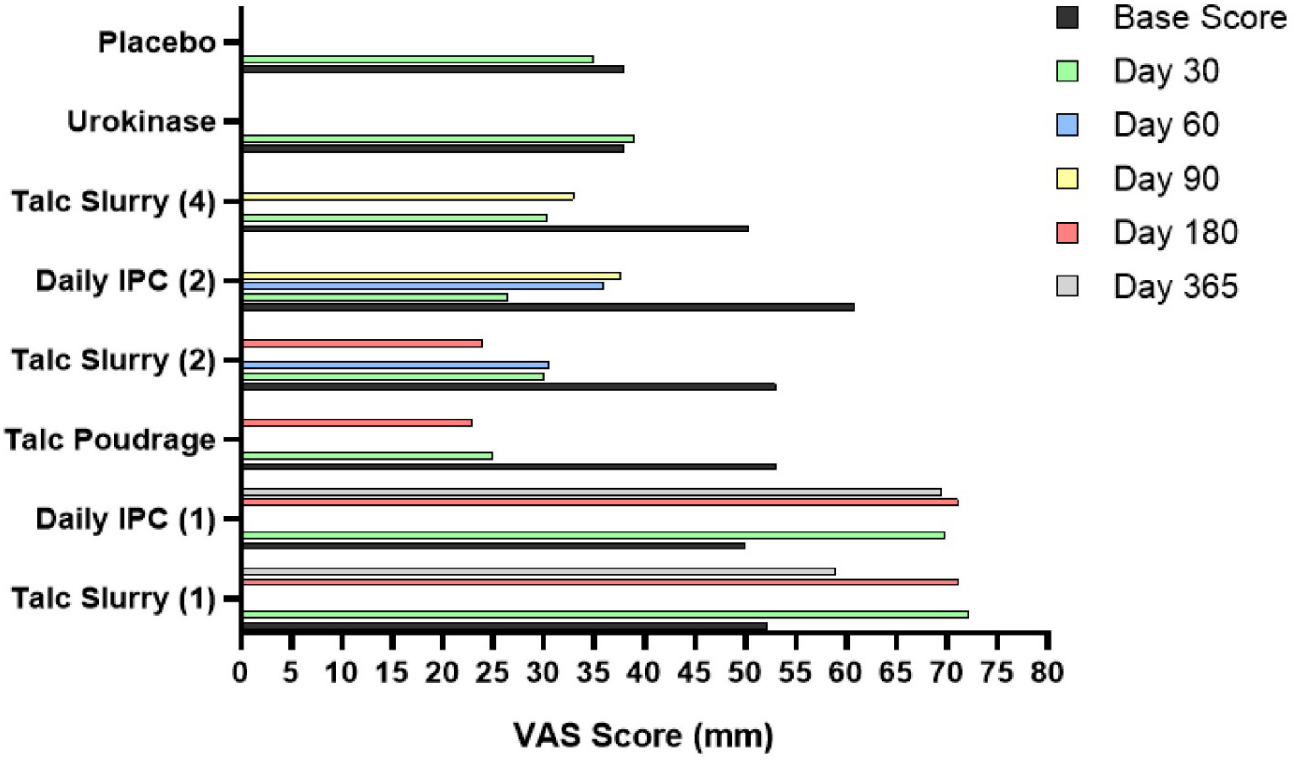

Figure 5. Bar graph of the pleural procedures performed correlated to the assessment of dyspnea perceived by the patients over time.
Legend: IPC= indwelling pleural catheter.
Source: Elaborated by the authors.

Quality of life (QoL) has been assessed through different questionnaires, making associations between interventions challenging and imprecise. Most used questionnaires were: QLQ-C30 (4), EQ-5D-5L (2), WHOQoL-bref (1) and VAS (1).

Patients who underwent talc slurry pleurodesis had a better QoL than those who underwent periodic drainage IPC, represented by 6 points in the EORTC QLQ-C30 questionnaire. QoL in patients from the talc slurry and talc poudrage groups had similar scores in the EQ-5D-5L. VAS scale showed better QoL improvement after talc slurry pleurodesis than periodic drainage IPC, with a difference of 9.7 mm (Table 4).

Mean hospitalization stay was 8.10 days (IC95%: 5.85-10.35). Pleural procedures with the longest hospital stay were periodic IPC (12.7; n=1), tetracycline (9.8; n=1), talc slurry (9.74; n=5), autologous blood (9.2; n=2), urokinase (6.2; n=2), talc poudrage (5.99; n=3), placebo (5.85; n=2) and iodopovidone 10% (4.2; n=1).

Average time to pleurodesis was 45.16 days, the lowest time was obtained in mixed-drainage IPC (7.5 days) and the highest time in periodic IPC (90 days).

Average time for catheter removal was 15.91 days (IC95%: -1.15-32.97), doxycycline had a removal time of 1.5 days, tetracycline of 2.1 days, iodopovidone 5% of 2.38 days (n=2), talc poudrage of 25 days and periodic IPC of 39 days (n=2).

A total of 40 severe adverse events (AEs) and 1450 non severe AEs have been reported (n=32). Silver nitrate was the most associated pleurodesis agent that caused severe AEs, being responsible for 57.5% of the total severe cases, while a group of patients that underwent periodic drainage IPC developed less severe AEs (2.5%). Talc slurry had the most AEs with a total of 340 cases (n=6), followed by: iodopovidones 1% and 2% (247, n=1), silver nitrate (199, n=1), talc poudrage (198, n=2), mixed-drainage IPC (174, n=1) and periodic drainage IPC (157, n=4). In opposite ways, iodopovidone 10% had the least AEs reported, totalling 18 cases (n=1), and iodopovidone 5% had only 5 AEs (n=1), other agents associated with a small amount of AEs were: autologous blood (7, n=2), tetracycline (7, n=1), doxycycline (2, n=1) and urokinase (2 severe, n=1) (Table 5).

Table 4. Different patients' quality of life questionnaires after pleural procedure, and during periodic follow-up.

Procedure	QLQ-C30	EQ-5D-5L	EQ-5D	WHOQoL-bref	EVA	Main Results
Periodic IPC (2)	Base= 62.98 Day 30= 76.33 Day 60= 73.34 Day 90= 69.17	-	-	-	-	Diference after 3 months= 6.19 Quality of life increased in the first 60 days and decreased in the final 30
Talc Slurry (1)	Base= 62.73 Day 30= 76.13 Day 60= 74.33 Day 90= 74.92	-	-	-	-	Diference after 3 months= 12.19 Quality of life increased through 90 days
Talc Slurry (2)	NI	-	-	-	-	Difference from final day acessed to day 0= 11.95
Talc Poudrage (1)	NI	-	-	-	-	Difference from final day acessed to day 0= 5.3
Talc Poudrage (2)	-	Base= 0,57 Day 30= 0,60 Day 180= 0,71	-	-	-	Diference after 6 months= 0.14 Better quality of life from 30-180 days than from procedure to day 30
Talc Slurry (3)	-	Base= 0,55 Day 30= 0,60 Day 180= 0,68	-	-	-	Diference after 6 months= 0.13 Better quality of life from 30-180 days than from procedure to day 30
Mixed-Drainage IPC	-	-	NI	-	-	Difference from final day acessed to day 0= 8.2
0.3% Silver Nitrate	-	-	-	NI	-	Difference from final day acessed to day 0= 10.72
Talc Slurry (4)	-	-	-	-	Base= 56,7 Day 30= 67,3 Day 180= 66,1 Day 365= 56,3	Diference after 1 year= -0.4 After the 1st semester, quality of life decreases significantly
Periodic IPC (3)	-	-	-	-	Base= 52,4 Day 30= 61,5 Day 180= 67,4 Day 365= 61,7	Diference after 1 year= 9.3 After the 1st semester, quality of life decreases significantly

Legend: IPC= indwelling pleural catheter; QLQ-C30= Quality of Life Questionnaire-Core 30; EQ-5D-5L= EuroQol 5 Dimension and 5 Level Quality of Life Questionnaire; EQ-5D= EuroQol 5 Dimension Quality of Life Questionnaire; WHOQoL-bref= World Health Organization Quality of Life Questionnaire- Brief version; VAS= Visual Analog Scale.

Source: Elaborated by the authors.

Table 5. Main adverse events reported after pleurodesis and IPC.

Adverse Events	Pleurodesis	IPC
Non Severe	1081	369
Severe	30	10

Source: Elaborated by the authors.

DISCUSSION

Low pleural fluid pH, especially lower than 7.2, effusions larger than 50% of the hemithorax, diagnosis of mesothelioma and increasing age are all associated with definitive MPE therapy. Definitive management of MPE is oftentimes difficult and its main objective is to give the patient comfort and minimize symptoms. Actually, pleurodesis and IPC are both considered great options in long term management of MPE.[13]

To ensure treatment effectiveness in pleurodesis, it is essential to diagnose non-expandable lung (NEL), using either USG or pleural manometer. Pleurodesis usually is the first line of treatment, with talc being the most used agent, on the other hand, IPC is a great outpatient setting that can also manage the effusion effectively.[1,9,10,14]

Pleurodesis has a success rate of effusion control from 75 to 80%, while IPC is associated with lower rates, of around 50%. This review indicates that MPE is 50% more likely to recur in patients undergoing IPC. Even though pleurodesis is more effective in reducing ERR, other factors should be considered when deciding between IPC and pleurodesis, like clinical factors (e,g, presence of expandable lung following fluid drainage) and patient and clinician preference.[15]

Talc pleurodesis is preconized over other agents, and talc delivery to the pleural space is not well established. Other agents, such as iodopovidone, are still utilized nowadays, especially in services that do not dispose of sterile talc.[16]

Over the past 10 years, RCTs did not have optimal ERRs for either talc poudrage or slurry. Iodopovidone has managed to achieve a much smaller ERR than talc, as well as less AEs. This does not mean talc should not be considered the most adequate pleurodesis agent anymore, especially because its sample size is much bigger than any other agent. Either way, pleurodesis agents with low ERR, like iodopovidone and doxycycline, should have more RCTs conducted analysing bigger population samples, reconsidering them as possible high standard pleurodesis agents.

Adjunctive therapy with octreotide has been investigated in cases of excessive effusion. Even though it was conducted in a small population, octreotide managed to decrease fluid output and hospital stay, without causing any additional AE. Another great question surrounding pleurodesis regards chest tube size and pain medications. TIME1 RCT stated that smaller tubes (12 frenchs) cause less pain than bigger tubes (24 frenchs), and non steroidal anti-inflammatories (NSAID) and opiates have no difference on pain scores after the procedure.[17,18]

As stated before, iodopovidone is considered a great sclerosing agent and more research on its use should be conducted, a topic of study should be its effect on thyroid function. Subclinical hypothyroidism has been detected in a few patients right after pleurodesis, with thyroid function returning to normal after 1 month.[19]

There has been a recent trend towards increasing use of IPCs in MPE. The PRE-EDIT trial assessed pleural elastance to define whether a patient should be allocated to IPC or pleurodesis, with the pleural pressure cut value being 14.5 cm H2O/L, and effectively diagnosing NEL with 100% sensitivity and 67% specificity.[15,20]

Accelerometers can be used to correlate patient activity and QoL in IPC, suggesting that the patient's perception of symptoms may not directly reflect their capacity of movement. Still, objective evaluation of the effusion and catheter positioning is vital for clinical decision-making, as to when to remove the IPC, and CT is the gold standard exam to determine catheter removal.[21,22]

In 2014, no statistical differences in cost between IPC and talc pleurodesis was established, even though IPC had a U$ 401 higher cost. Later, in 2017, IPC was considered cost effective when compared to talc pleurodesis, especially in patients with shorter life expectancy. Finally, in 2020, daily drainage IPC associated with talc pleurodesis was considered more costly, yet more effective, than symptom-guided drainage in the absence of NEL, offering a new answer to the debate.[11,12,23]

Currently, several studies and protocols are being developed to provide more discoveries in MPE area, searching for positive impacts that culminate in success when it comes to the treatment of MPE. New RCTs guidelines have been proposed and are already ongoing, such as OPTIMUM, IPC-PLUS and AMPLEs 3 and 4.[24-29]

CONCLUSION

Primary results demonstrate that pleurodesis is significantly more effective in reducing effusion recurrence compared to IPC. Among pleurodesis agents, alternatives to talc, such as doxycycline, iodopovidone 5%, and silver nitrate, showed promising results in terms of lower ERR, though further studies with larger populations are needed to validate their efficacy and safety.

Secondary outcomes support pleurodesis as to improvements in dyspnea and quality of life, despite having a longer hospital stay and an incidence of AEs in some cases. IPC, on the other hand, remains a valuable option for patients with poor performance status, non-expandable lung, or when outpatient management is prioritized.

Ultimately, the choice between pleurodesis and IPC should be individualized, taking into account clinical factors such as lung expandability, prognosis, patient preferences, and resource availability.

Future research should focus on optimizing pleurodesis protocols to minimize hospital stay and AEs, as well as on evaluating underused agents like iodopovidone and doxycycline in larger, well-designed trials. Expanding knowledge in this field is essential to refine therapeutic strategies and improve patient care.

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