Rapid Pleurodesis in Patients With Chronic Noninfectious Pleural Effusion

Twenty Years of Real-world Performance Data

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Background: Small cohort studies have shown rapid pleurodesis protocol's (RPP) effectiveness and capacity to expedite pleurodesis for malignant pleural effusion (MPE). This study intends to evaluate the effectiveness of the RPP in inducing pleurodesis in patients with pleural effusions from either malignant or benign etiologies.

Methods: In this single-center, retrospective cohort study spanning 2 decades, we assessed patients with recurrent symptomatic chronic noninfectious pleural effusion, both benign and malignant. Post-RPP, chest tubes were removed when fluid output dropped below 150 mL/d, and patients were discharged with daily indwelling pleural catheter (IPC) drainage. Exclusion criteria included non-expandable lung and active pleural infection. Treatment success was defined as IPC removal on reduced output (<50 mL) on 3 consecutive drainages and radiologic effusion resolution. Recurrence was defined as the occurrence of pleural effusion requiring additional pleural procedures postsuccess. Duration outcome was expressed as median with IPC placement as time zero.

Results: Of the 210 patients studied, 72% had MPE, and 28% had benign effusions. The median hospital stay was 4 days post-RPP. Treatment was successful in 177 (84%) patients within a median of 12 days, with no significant differences between MPE and benign cases. Nine patients (5%) experienced recurrence within a median of 152 days. Complications included hemothorax in 4 (1.9%) and empyema in 2 (1%). The thirty-day mortality rate was 9%, with a median survival time of 245 days postprocedure.

Conclusion: The RPP combines the benefit of chemical pleurodesis and IPC and appears to be a reasonable option for patients with recurrent and symptomatic pleural effusion.

Key Words: benign pleural effusion, indwelling pleural catheters, malignant pleural effusion, thoracoscopic talc pleurodesis

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Chronic noninfectious pleural effusion can result from malignant or benign causes. Malignant pleural effusion (MPE) occurs in about 15%[1] of cancer patients, representing advanced disease, and has a survival of about 3 to 12 months.[2] Definitive treatment strategies for patients with recurrent, symptomatic MPE (manifested as dyspnea) include either obliteration of the pleural space via pleurodesis or periodic effusion drainage using an indwelling pleural catheter (IPC).[3] On the other hand, chronic benign pleural effusions (BPE) typically result from congestive heart failure (CHF), hepatic hydrothorax, renal failure, or nonspecific pleuritis. BPE treatment primarily targets the root cause, typically employing diuresis. When medical management fails to address a persistent and symptomatic pleural effusion, the management aligns with that of MPE.[4,5]

Chemical pleurodesis involves the instillation of a sclerosant agent either via a chest tube (slurry) or thoracoscopically (poudrage). Postprocedure, patients typically require a 3- to 7-day hospital stay to ensure effective chemical pleurodesis through chest tube drainage and pleural apposition.[6–8] Conversely, IPC is often placed in an ambulatory setting and does not require hospital admission. The rate of pleurodesis for IPC is 24% to 47%, which occurs in an average duration of 52 to 90 days.[6,9,10] IPC and chemical pleurodesis have been shown to be equally effective at relieving dyspnea.[6] Drawbacks of chemical pleurodesis include the need for hospital stay and a high failure rate (20% to 30% at 3 mo).[7,11,12] Patients with IPC still have the burden of chronic pleural effusion requiring regular drainage of the IPC, and face limitations of having the IPC in place.

The ideal treatment modality in this patient population is one that quickly and effectively relieves dyspnea, achieves

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pleurodesis, and minimizes health care system interactions. The rapid pleurodesis protocol (RPP) was first described by Reddy and colleagues; this protocol integrates chemical pleurodesis during medical thoracoscopy with IPC plus with a large-bore chest tube placement.[13] Under this protocol, patients typically remain hospitalized for a median duration of 1.79 days until the initial drainage chest tube is removed, a process usually completed within one day. This method aims to harness the benefits of both earlier described techniques while mitigating their shortcomings. In this small single-center study, the RPP demonstrated a 92% pleurodesis success rate, with a median time of 7.5 days, facilitating IPC removal.[13] In contrast to the RPP, the IPC-Plus study avoids hospitalization by performing the administration of talc pleurodesis via IPC in the outpatient setting.[14] The ongoing randomized controlled trial comparing thoracoscopic talc poudrage + indwelling IPC versus thoracoscopic talc poudrage only (TACTIC) employs a similar strategy as the RPP.[15]

We believe that the RPP adds to the armamentarium for the management of BPE and MPE, and our 20-year real-world performance data will guide physicians and patients in their choice of intervention. Our primary goal was to determine the rate of and time to pleurodesis success. Secondary goals included health care utilization, predictor of pleurodesis success, and patient survival rate.

METHODS

This was a retrospective cohort study of patients who underwent the rapid pleurodesis protocol in a single institution between April 2003 and October 2022. This study consisted of patients referred for management of recurrent symptomatic pleural effusion who had previously undergone thoracentesis with relief of dyspnea, lung re-expansion, and absence of infection. Inclusion criteria included recurrent and symptomatic pleural effusion due to MPE or benign etiology. Recurrent pleural effusion was defined as the need for a repeat procedure within 3 months from prior therapeutic thoracentesis, at which point RPP was offered to the patient. Exclusion criteria: patients with an inability or unwillingness to maintain regular IPC drainage, infected pleural effusion, or nonexpandable lung (NEL). NEL was determined based on a visual estimate of lung expansion $<90\%$ based on chest x-ray or chest computed tomography and/or pleural elastance >15 cmH20/L. Our Institutional Review Board (2020P000058) approved this study with a waiver of informed consent.

Procedure

Each RPP started with a medical thoracoscopy performed under moderate sedation and local anesthesia.[13] Complete drainage of pleural effusion was performed, and the pleural fluid was sent for analysis. In some patients, at the discretion of the performing interventional pulmonologist, a pleural biopsy was performed to determine the etiology of the chronic pleural effusion. This was followed by placing a 15.5 French (Fr) IPC (PleurX)[16] under direct visualization. The main sclerosing agent used was talc, and the amount was insufflated into the pleural cavity as per the proceduralist's choice. Concluding the intervention, a 24 Fr chest tube was placed through the thoracoscopy port. Postprocedure chest x-rays were obtained. The chest tube and the IPC were kept on a −20 cmH2O suction regimen, and their output was assessed daily. The chest tube was removed upon achieving 2 conditions: resolution of procedurally induced pneumothorax and a 24-hour drainage output below 150 mL. For patients with high pleural fluid output at 48hrs in the postoperative setting (>250 mL/d), we administered 4 g of talc through the 24 Fr chest tube. Patients were discharged home when clinically stable with daily drainage of IPC.

Outcome

In the outpatient setting, the IPC was removed once the drainage was <50 mL on 3 consecutive drainages, and chest imaging showed complete or near-complete (estimate <300 mL) resolution of the pleural effusion. On ultrasound, volume was estimated based on this formula volume (mL) = [15 × D (mm)] where the maximum distance between mid-height of the diaphragm and visceral pleura (D).[17] Estimation on chest computed tomography was based on the formula volume (mL) = [D^2 (cm) ι (cm)] where D represents the maximum depth of effusion, and ι represents the maximum length of the effusion.[18] The removal of IPC under such circumstances defined successful pleurodesis. Patients were categorized as a treatment failure if they died with IPC in place, were lost to follow-up before successful pleurodesis was achieved, required removal of the IPC due to complications, or needed an alternate method of pleurodesis. Recurrence was defined as the occurrence of a pleural effusion requiring additional pleural procedures such as therapeutic thoracentesis, chest tube placement, IPC placement, chemical pleurodesis, or RPP after initial pleurodesis success.

Pleural Effusion Characteristics

The etiology of pleural effusion was established either through a prior diagnosis before undergoing RPP or via an analysis of the pleural fluid and pleural biopsy samples obtained during the RPP procedure. To classify pleural effusion as exudative, the 3-test rule was employed, which comprises: (1) a pleural fluid protein level exceeding 2.9 g/dL, (2) pleural fluid cholesterol levels >45 mm/dL, or (3) pleural lactate dehydrogenase (LDH) levels above 0.45 of serum upper limit of normal. The LENT score was calculated to estimate survival in patients with malignant pleural effusion and the Karnofsky performance score (≥ 70) was used to determine the patients with a BPE that were appropriate candidates for a RPP procedure. The pleural effusion size at baseline was assessed through a chest x-ray, categorizing fluid accumulation as occupying $<25\%$, between 25% and 50%, between 50% and 75%, or $>75\%$ of the affected hemithorax.

Statistical Analysis

The statistical analysis was conducted using IBM SPSS Version 22. For numerical data, the mean accompanied by the SD was reported when the data were normally distributed. In instances of non-normal distribution, the median and interquartile range were utilized instead. The threshold for statistical significance was set at a *P*-value of <0.05. Kaplan-Meier survival curves were employed to evaluate the time to recurrence. One minus the Kaplan-Meier estimate of the survival function was used to estimate the cumulative incidence rate of pleurodesis success over time. Patients were censored if they died before pleurodesis success occurred. Comparison between patients with MPE and BPE was performed using the log-rank test.

RESULTS

In a span of 20 years, a total of 210 patients underwent the rapid pleurodesis protocol. Their mean age was 68.9 years; 51% were male, and the majority were white (84.5%) (Table 1). Almost two thirds (69.5%) had an Eastern Cooperative Oncology Group (ECOG) score of ≤1. The etiology of the pleural effusion when undergoing the RPP was MPE and BPE in 72% and 28% of patients, respectively. Among those with MPE, 77.5% had a moderate LENT score, corresponding to a median survival rate of 130 days.[19] Lung cancer was the predominant cause of MPE, accounting for 39% of cases, followed by breast cancer and hematological malignancy at 11% each. Active chemotherapy was ongoing in 13% of patients with MPE during the RPP.

Regarding pleural effusion size before intervention, 49% of the pleural effusions occupied <25% of the ipsilateral hemithorax, 39% occupied between 25% and 50%, and 12% occupied over 50% based on chest x-rays. Pleural effusion biochemical analysis showed 84% exudative effusions, with median levels of protein, lactate dehydrogenase, and cholesterol of 4.1 g/dL, 206 IU/L, and 76 mg/dL, respectively.

TABLE 1. Demographic Profile and Characteristics of the Chronic Pleural Effusion

Characteristics	Data, n = 210
Mean age, y ± SD	68.9 ± 0.7
Male sex, n (%)	107 (51)
Race, n (%)	
White	120 (84.5)
African American	9 (6.3)
Hispanic	4 (2.8)
Unknown/others	9 (6.3)
ECOG score, n (%)	
0	22 (10.5)
1	124 (59)
2	28 (13.3)
3	10 (4.8)
4	3 (1.4)
Etiology of pleural effusion, n (%)	
Benign	59 (28)
CHF	15 (26)
Nonspecific pleuritis	33 (56)
Others	11 (18)
Malignant	151 (72)
LENT score (median survival) (d)	
0-1 (319)	17 (14.1)
2-4 (130)	93 (77.5)
5-7 (44)	10 (8.3)
Tumor type	
Lung cancer	56 (39)
Breast cancer	17 (11)
Hematological malignancy	17 (11)
Renal cell carcinoma	14 (9)
Mesothelioma	11 (7)
Active chemotherapy	21 (13)
Pleural effusion size preintervention, n (%)	
<25	104 (49)
25-50	81 (39)
50-75	15 (7)
>75	10 (5)
Pleural effusion biochemistry	
Exudative, n (%)	177 (84)
Protein, g/dL*	4.10 (3.55-4.65)
LDH, IU/L*	206 (131.5-320.0)
Cholesterol, mg/dL*	76 (56.5-93.5)
pH*	7.44 (7.40-7.49)

*Presented in median (25th quartile, 75th quartile).
CHF indicates congestive heart failure; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase.

TABLE 2. Procedure Specifics and Outcome

Characteristics	Data, n = 210
Rapid pleurodesis procedure details	
Sclerosant agent, n (%)	
Talc	208 (99)
Doxycycline	1 (0.5)
Iodine	1 (0.5)
Sclerosant agent amount, g ± SD	6.5 ± 1.8
Pleural biopsy, n (%)	157 (75)
Length of hospital stay after IPC placement, d	4 (3-6)
Duration of chest tube in place, d	2 (2-4)
IPC outcome	
Remove due to successful pleurodesis, n (%)	177 (84)
Within 30 d	160 (76)
Within 90 d	173 (82)
Median time placement to removal, d*	12 (7.75-17)
Recurrence of pleural effusion, n (%)	9 (5)
Median time to recurrence, d*	152 (42-534)
Median duration of follow-up from index procedure, d*	272 (56-898)
Remove due to complication or failure of pleurodesis, n (%)	7 (3)
Patient died with IPC still in place, n (%)	15 (7)
Patient still had IPC in place on the last follow-up, n (%)	11 (5)
Repeat instillation of sclerosant agent, n (%)	25 (12)
Complications, n (%)	
Hemothorax <30 d	4 (2)
Empyema	2 (1)
Fever	9 (4)
Mortality, n (%)	97 (46)
30 d, n (%)	9(9.3)
Time between index procedure to death, d*	245 (65-579)

*Presented in median (25th quartile, 75th quartile).
IPC indicates indwelling pleural catheter.

Talc poudrage was the primary sclerosing agent, in 99% of cases (Table 2), with an average amount of 6.5 ± 1.8 g per procedure. Other agents, such as doxycycline and iodine, were each used once. Concurrent pleural biopsy was carried out in 75% of the cases. Postintervention, the median duration for chest tube placement and hospital stay were 2 and 4 days, respectively.

The RPP was successful in 84% of patients (177 out of 210), leading to IPC removal within a median of 12 days. At 30 days, 76% of IPCs were removed due to treatment success. Complications or failures resulted in removal in 7 (3%) cases, and 15 (7%) patients died with the IPC in place. The remaining 11 (5%) patients still had the IPC in place at their last follow-up. Repeat agent instillation was required for 25 (12%) patients. Supplemental Material Figure 1, Supplemental Digital Content 1, http://links.lww.com/LBR/A334 illustrates the recurrence event in relation to the number at risk based on the duration of follow-up data available. Pleural effusion recurred in 9 (5%) patients within a median of 152 days; 4 recurrences happened after 1 year. Complications included 4 (2%) cases of hemothorax and 2 (1%) of empyema. There were 97 (46%) deaths, with 9 (9.3%) occurring within 30 days postprocedure; the median time to death was 245 days.

Table 3 identifies factors associated with successful pleurodesis within 12 days. Exudative effusions showed a trend toward shorter time to pleurodesis than transudative effusions, although the difference was not statistically significant. This observation was primarily influenced by pleural fluid cholesterol levels (>45 mg/dL), which were significantly higher in the faster pleurodesis group (59 vs. 40 mg/dL, $P<0.01$). Conversely, MPE due to hematological malignancy tended to require a longer time to pleurodesis. When comparing the pleurodesis rates and time to pleurodesis between BPE and MPE it could be seen that there were no significant differences (Fig. 1).

DISCUSSION

In this study, we present the largest cohort to date showing the performance of the RPP outside of clinical trials, highlighting its effectiveness and unique capabilities in managing recurrent and symptomatic pleural effusion. This is the first study to encompass BPE as well as MPE, broadening the applicability and relevance of the RPP. Prior smaller studies focusing on the RPP in MPE demonstrated its remarkable efficacy in achieving pleurodesis (92% to 93%) within an abbreviated timeframe (7.5 to 10 d).[13,20] Building upon these, the current study confirms this efficacious result with an 84% pleurodesis success rate achieved within a median of 12 days, while also expanding its applicability to BPE. This figure is conservative, as the denominator for the success rate encompasses all patients in our cohort, including those who either died with an IPC in situ or still had an IPC at the last follow-up. Excluding these cases would likely yield an even higher success rate.

TABLE 3. Predictor of Median Time to Removal of IPC Due to Successful Pleurodesis

	Median time to removal of IPC		
Predictor	**<12 d (%), n=95**	**≥12 d (%), n=82**	***P***
Etiology of pleural effusion			
Benign	25 (26)	25 (30)	0.5
Malignant	70 (74)	57 (70)	0.1
Tumor type			
Lung cancer	29 (48)	19 (42)	0.8
Breast	10 (17)	7 (16)	—
Renal cell cancer	7 (12)	2 (4)	—
Gynecology	3 (5)	1 (2)	—
Hematological malignancy	5 (8)	12 (27)	—
Mesothelioma	6 (10)	4 (9)	—
Active chemotherapy			—
Yes	9 (13)	8 (14)	—
No	61 (87)	49 (86)	—
Pleural effusion size preintervention			
<25%	39 (51)	37 (49)	0.4
≥25	49 (58)	39 (44)	—
Pleural effusion biochemistry			
Transudative	11 (44)	14 (56)	0.2
Exudative	84 (55)	68 (45)	—
Cholesterol >45 mg/dL	59 (60)	40 (40)	<0.01
LDH >166 IU/L	61 (56)	47 (44)	0.2
Protein >2.9 g/dL	79 (57)	60 (43)	0.09

N=177.
LDH indicates lactate dehydrogenase; IPC, indwelling pleural catheter.

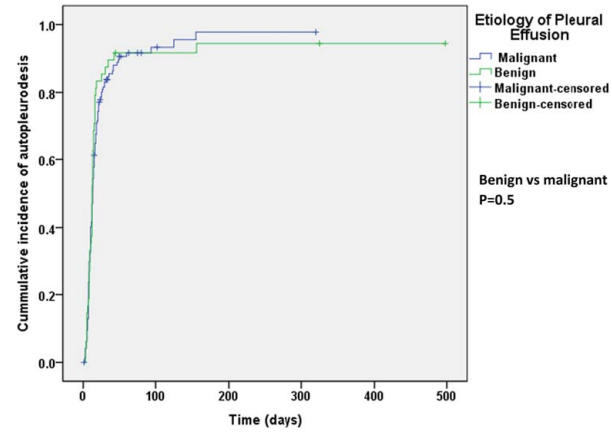

FIGURE 1. Cumulative incident curve of pleurodesis success between benign and malignant pleural effusion.

One of the key strengths of the RPP lies in its integration of the proven efficacy of chemical pleurodesis with the reliability of IPC in relieving dyspnea. Talc has been shown to be the most effective sclerosant agent for pleurodesis,[21–23] which is the main agent used for RPP in our institution. Our "real-world" cohort of patients had a median length of stay of 4 days, similar to the 3 to 8 days length of stay achieved in talc pleurodesis trials.[6,7,11] This may be partly due to our internal protocol of pulling the chest tube once output is <150 mL and repeating second pleurodesis if output is >250 mL per day to maximize treatment success. This was a deviation from the original protocol described by Reddy et al whereby the chest tube was removed in 24 hours upon resolution of the pneumothorax and allowed the patient to be discharged[13] with drainage of the pleural effusion via the IPC. In addition, we had a significant amount of patients with social issues that required an additional day in the hospital as the median time to chest tube removal was 3 days compared with the median hospital stay of 4 days. Our real-world pleurodesis failure rate of 16% (84% success rate) appears better than the 20% to 30% failure rate of chemical pleurodesis in a research trial setting.[7,11,12] And in the 16% of patients who did not achieve pleurodesis success, the presence of IPC for regular drainage allows for effective symptomatic relief. IPC has been demonstrated to alleviate dyspnea and improve quality of life.[24] Nonetheless, the patient is still faced with the burden of having chronic pleural effusion, requiring regular drainage of the IPC, and facing the limitation of having an IPC in place. Although the length of stay with the use of IPC alone for MPE is superior at 0 to 1 day,[6,25] the rate of pleurodesis is 24% to 47% in an average duration of 52 to 90 days, at which point the IPC can only be removed.[6,9,10] In this regard, RPP is the most effective treatment option for patients who want to be completely free from the burden of having a recurrent pleural effusion in the shortest possible time.

The use of MT in RPP could potentiate the pleurodesis process by inducing inflammation as a consequence of the thoracoscopic incision and the pleural biopsy performed.[26] Moreover, the capacity of thoracoscopy to disrupt loculations enhances the rate of pleurodesis in cases of loculated effusions.[27] Beyond the therapeutic goal, the RPP also serves a diagnostic purpose, as concurrent pleural biopsy was performed in three quarters of our cases. After

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discharge, the IPCs in the RPP were drained daily, which has been shown to be the optimal frequency for achieving pleurodesis, as shown by the AMPLE 2 trial.[24]

A simplified variant of the RPP is talc administration via IPC in the outpatient setting. This was explored in the IPC-Plus trial, which showed that the pleurodesis rate was improved in IPC plus Talc versus IPC alone (43% vs. 23% at 35 d).[14] One variant of the RPP described by Foo and colleagues combined ambulatory thoracoscopic pleurodesis with IPC placement, where the nontunneled chest tube was removed on the same day upon resolution of procedure-induced pneumothorax and absence of air leak. The patient was discharged home on the same day of thoracoscopy. The patient did not stay in the hospital for the pleural effusion drainage but depended solely on IPC drainage. IPC was removed at a median of 20 days, and pleurodesis was deemed successful in 71% of patients at 3 months.[28] In another variant of RPP performed without chest tube drainage, but with inpatient IPC drainage, the success rate was 79% (23/29) at 1 month.[29] The above shows an increasing performance gap when specific components of the standard RPP are omitted. This underscores the importance of performing the chemical pleurodesis via MT followed by aggressive inpatient pleural effusion drainage to allow for pleural apposition for the chemical pleurodesis to be effective. The ongoing TACTIC trial employs the same post-thoracoscopic talc poudrage effusion drainage strategy as Foo and colleagues described above.[15]

A meta-analysis evaluating the predictor of successful chemical pleurodesis showed that MPE due to mesothelioma had the lowest success rate at 72%. In comparison, lymphoma and breast cancer had the highest success rates (89% and 87%, respectively).[30] Our data showed no difference in success rates between mesothelioma and breast cancer. However, hematological malignancies tended to take a longer time to achieve pleurodesis. Interestingly, our study did not corroborate several factors considered predictive of pleurodesis success, such as higher pleural effusion pH and smaller prepleurodesis effusion size.[30] The RPP was found to be more effective in pleural effusion with cholesterol >45 mg/dL, a finding consistent with previous literature that showed that higher pleural effusion cholesterol could be used to predict chemical pleurodesis success.[31]

In contrast to MPE, there is limited evidence of the long-term relief of recurrent BPE. A meta-analysis on the use of IPC for BPE found an overall pleurodesis rate of 51% within a timeframe of 56 to 176 days.[32] In our study, RPP for BPE was predominantly for nonspecific pleuritis followed by CHF. A small study of thoracoscopic talc pleurodesis in CHF showed a recurrence rate of 5%.[4] This was higher than our findings, which showed only a 2% recurrence rate among 50 patients with BPE. In CHF, the vast performance gap between RPP and IPC alone is still evident, with the RPP group achieving an 80% IPC removal in the median of 11.5 days, compared with a 25% success rate in the median of 66 days with IPC alone.[33] A direct comparison between MPE and BPE indicated that MPE achieved pleurodesis in a shorter time with IPC, taking only 36 days compared with 110 days.[5] The RPP performed equally well in BPE as in MPE and can be used for the goal of rapidly achieving pleurodesis and independence from IPC.

While the RPP offers numerous benefits, its efficacy comes at a cost. Shafiq and colleagues performed a cost-utility analysis of the various treatment modalities for MPE. For an estimated survival of 6 months, IPC ($7314) was found to be the most cost-effective modality, and unfortunately, RPP ($7650 to $11,439) was deemed cost-ineffective even with an estimated 85% lasting pleurodesis.[34] On the other hand, bedside chemical pleurodesis is the most cost-effective treatment for patients, with an expected survival of 12 months.[35] The assumptions made by these studies were that the MPE was already diagnosed, but we performed a pleural biopsy as part of the RPP (75%), making it a one-stop diagnostic and treatment modality. The RPP is more cost-effective in patients with BPE, given their longer life expectancy.

Since the RPP consists of chemical pleurodesis and IPC, contraindication to either intervention applies to the RPP. In cases of NEL, this restriction is grounded in the inefficacy of chemical pleurodesis under the circumstances of lacking parietal and visceral pleural apposition. This led to the exclusion of patients with recurrent pleural effusion and NEL from our study. The significance of this limitation is underscored by the prevalence of NEL in 30% of MPE cases.[36] Contraindications to IPC placement include bleeding diathesis, infection at the potential site of placement, and inability or unwillingness of the patient to maintain regular IPC drainage. Active pleural infection is a contraindication to both chemical pleurodesis and IPC placement. One limitation of this study is its retrospective nature, which lacks complete data on patient's symptoms, such as dyspnea, pain, and quality of life. Our study also lacks a non-RPP comparative group and is vulnerable to selection bias. This constraint acknowledges the potential influence of factors related to the choice of treatment and their impact on study outcomes. The ongoing randomized controlled TACTIC trial will be able to assess these concerns.[15]

CONCLUSIONS

Our study substantiates the potent efficacy of the rapid pleurodesis protocol. By merging medical thoracoscopy, talc pleurodesis, and IPC placement, the RPP appears to be a reasonable option for patients with both malignant and benign pleural effusions that are recurrent and symptomatic in the absence of an NEL.

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REFERENCES

1. Rodriguez-Panadero F, Naranjo FB, Mejias JL. Pleural metastatic tumours and effusions. Frequency and pathogenic mechanisms in a post-mortem series. *Eur Respir J*. 1989;2:366–369.
2. Roberts ME, Neville E, Berrisford RG, et al. Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010. *Thorax*. 2010;65(suppl 2):ii32–ii40.
3. 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;198:839–849.
4. Freeman RK, Ascioti AJ, Mahidhara RS. A Propensity-matched comparison of pleurodesis or tunneled pleural catheter in patients undergoing diagnostic thoracoscopy for malignancy. *Ann Thorac Surg*. 2013;96:259–264.
5. Chalhoub M, Harris K, Castellano M, et al. The use of the PleurX catheter in the management of non-malignant pleural effusions. *Chron Respir Dis*. 2011;8:185–191.
6. Davies HE, Mishra EK, Kahan BC, et al. Effect of an indwelling pleural catheter vs vhest tube and talc pleurodesis for

relieving dyspnea in patients with malignant leural effusion: the TIME2 randomized controlled trial. *JAMA*. 2012;307:2383.
7. Thomas R, Fysh ETH, Smith NA, et al. Effect of an indwelling pleural catheter as talc oleurodesis on hospitalization days in patients with malignant pleural effusion: the AMPLE randomized clinical trial. *JAMA*. 2017;318:1903–1912.
8. Putnam JB, Walsh GL, Swisher SG, et al. Outpatient management of malignant pleural effusion by a chronic indwelling pleural catheter. *Ann Thorac Surg*. 2000;69:369–375.
9. 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; 26:70–76.
10. Wahidi MM, Reddy C, Yarmus L, et al. Randomized trial of pleural fluid grainage frequency in patients with malignant pleural effusions. The ASAP trial. *Am J Respir Crit Care Med*. 2017;195:1050–1057.
11. 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 wffusion: the TIME1 randomized clinical trial. *JAMA*. 2015; 314:2641–2653.
12. 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. *JAMA*. 2020;323:60–69.
13. Reddy C, Ernst A, Lamb C, et al. Rapid pleurodesis for malignant pleural effusions. *Chest*. 2011;139:1419–1423.
14. Bhatnagar R, Keenan EK, Morley AJ, et al. Outpatient talc administration by indwelling pleural catheter for malignant effusion. *N Engl J Med*. 2018;378:1313–1322.
15. Dipper A, Sundaralingam A, Hedley E, et al. The randomised thoracoscopic talc poudrage+indwelling pleural catheters versus thoracoscopic talc poudrage only in malignant pleural effusion trial (TACTIC): study protocol for a randomised controlled trial. *BMJ Open Respir Res*. 2023;10:e001682.
16. PleurX™ Pleural Catheter Kit Cat. 50-7000B/50-7700. Accessed April 8, 2023. https://www.bd.com/documents/guides/directions-for-use/IS_PleurX-pleural-kit_DF_EN.pdf
17. Usta E, Mustafi M, Ziemer G. Ultrasound estimation of volume of postoperative pleural effusion in cardiac surgery patients. *Interact Cardiovasc Thorac Surg*. 2010;10:204–207.
18. Mergo PJ, Helmberger T, Didovic J, et al. New formula for quantification of pleural effusions from computed tomography. *J Thorac Imaging*. 1999;14:122.
19. Clive AO, Kahan BC, Hooper CE, et al. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. *Thorax*. 2014;69:1098–1104.
20. Krochmal R, Reddy C, Yarmus L, et al. Patient evaluation for rapid pleurodesis of malignant pleural effusions. *J Thorac Dis*. 2016;8:2538–2543.
21. Xia H, Wang XJ, Zhou Q, et al. Efficacy and safety of talc pleurodesis for malignant pleural effusion: a meta-analysis. *PLoS One*. 2014;9:e87060.
22. Clive AO, Jones HE, Bhatnagar R, et al. Interventions for the management of malignant pleural effusions: a network meta-analysis. *Cochrane Database Syst Rev*. 2016;2016: CD010529.
23. 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: CD010529.
24. Muruganandan S, Azzopardi M, Fitzgerald DB, 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;6:671–680.
25. Putnam JB Jr, Light RW, Rodriguez RM, et al. A randomized comparison of indwelling pleural catheter and doxycycline pleurodesis in the management of malignant pleural effusions. *Cancer*. 1999;86:1992–1999.
26. Agrawal A, Murgu S. Multimodal approach to the management of malignant pleural effusions: role of thoracoscopy with pleurodesis and tunneled indwelling pleural catheters. *J Thorac Dis*. 2020;12:2803–2811.
27. Suzuki K, Servais EL, Rizk NP, et al. Palliation and pleurodesis in malignant pleural effusion: the role for tunneled pleural catheters. *J Thorac Oncol*. 2011;6:762–767.
28. Foo CT, Pulimood T, Knolle M, et al. Ambulatory thoracoscopic pleurodesis combined with indwelling pleural catheter in malignant pleural effusion. *Front Surg [Internet]*. 2021;8: 738719.
29. Boujaoude Z, Bartter T, Abboud M, et al. Pleuroscopic pleurodesis combined with tunneled pleural catheter for management of malignant pleural effusion: a prospective observational study. *J Bronchol Interv Pulmonol*. 2015;22:237.
30. 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;14:645–654.
31. Yildirim H, Metintas M, Ak G, et al. Predictors of talc pleurodesis outcome in patients with malignant pleural effusions. *Lung Cancer*. 2008 Oct;62:139–144.
32. Patil M, Dhillon SS, Attwood K, et al. Management of benign pleural effusions using indwelling pleural catheters: a systematic review and meta-analysis. *Chest*. 2017;151:626–635.
33. Majid A, Kheir F, Fashjian M, et al. Tunneled pleural catheter placement with and without talc poudrage for treatment of pleural effusions due to congestive heart failure. *Ann Am Thorac Soc*. 2016;13:212–216.
34. Shafiq M, Frick KD, Lee H, et al. Management of malignant pleural effusion: a cost-utility analysis. *J Bronchol Interv Pulmonol*. 2015;22:215.
35. Puri V, Pyrdeck TL, Crabtree TD, et al. Treatment of malignant pleural effusion: a cost-effectiveness analysis. *Ann Thorac Surg*. 2012;94:374–380.
36. Dresler CM, Olak J, Herndon JE, et al. Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. *Chest*. 2005;127:909–915.