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REVIEW

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## Indwelling pleural catheters for the treatment of malignant pleural effusions; where are we now?

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### ABSTRACT

**Introduction:** Malignant pleural effusions (MPE) affect many patients with advanced malignant disease and lead to significant symptomatic burden. Management is primarily focused on controlling symptoms. IPCs are considered an alternative treatment strategy to chemical pleurodesis and in randomized clinical trials, are shown to have comparable outcomes with regards to symptom management such as dyspnea score and quality of life, and are associated with shorter length of hospital stay. Additional studies have examined the optimal drainage strategy for IPCs and the combination of IPC and pleurodesis. The most common complication is infection, and management differs based on the specific infection type. For many patients, IPCs are likely a cost-effective option for management of MPE compared to alternative approaches.

**Areas covered:** This review article details the role of the indwelling pleural catheter (IPC) for symptom control, strategies for management, removal, complications, cost-effectiveness, and future directions.

**Expert opinion:** There are various management options for MPE, each with their own advantages and disadvantages. Management should be personalized, with full knowledge of the patient's life expectancy, pleural space physiology, risks and benefits of each approach, and most importantly patient preferences.

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### KEYWORDS

Indwelling pleural catheter; malignant pleural effusion; pleurodesis; Thoracoscopy; Pleural effusion

## 1. Introduction

Malignant pleural effusions (MPE) are common affecting 200,000 individuals in the United States annually [1]. MPE is associated with significant symptomatic burden, primarily presenting as dyspnea and chest discomfort. In the US alone, MPEs result in up to 125,000 hospital admissions and \$5 billion in healthcare costs annually [2]. While most cancers can metastasize to the pleural space, the most common primary malignancies leading to MPE are lung, breast, and hematologic malignancies [2]. While advancements in cancer therapeutics have led to an improved life expectancy, the global prevalence of cancer is rising, leading to an expected rise in the prevalence of MPE [3].

Except for primary pleural malignancies, a diagnosis of MPE represents advanced malignant disease. Survival varies based on the histologic type of the primary malignancy as well as patient-specific factors. In one study, survival ranged from one month to eight years with a median survival of 5 months [4]. Given the short life expectancy and often terminal diagnosis that accompanies an MPE, management is primarily palliative in nature, focusing on symptom control to maximize quality of life.

After initial histologic diagnosis of an MPE is made, recurrence is common. Fifty-five percent of patients will require another pleural procedure, with 58% of those occurring within two weeks, considered to be 'rapid reaccumulation' [5]. Most (80%) of patients with MPE present with moderate to large effusions, and 77% are

symptomatic, most commonly with dyspnea (57%) [6,7]. For patients with recurrent and symptomatic MPE, management options include serial thoracenteses, pleurodesis, indwelling pleural catheter (IPC) placement, decortication by video-assisted thoracoscopic surgery or open thoracotomy, or a combination of these procedures. Pleurodesis may be performed chemically through a chest tube (most commonly with talc) or via thoracoscopy by either chemical or mechanical means. For patients with a longer life expectancy, a definitive treatment option may offer fewer hospitalization days, fewer exposure to invasive procedures, and more consistent symptom management compared to serial thoracenteses.

Prior to the popularization of the IPC, pleurodesis was the mainstay for definitive treatment for recurrent symptomatic MPEs and a grade A recommendation by the 2010 British Thoracic Disease Guidelines [8]. Because pleurodesis requires apposition of the visceral and parietal pleura, it cannot be performed in those with non-expandable lung – which occurs in roughly 20% of patients – and thus another modality, such as IPC is used [9]. One of the earliest predecessors to the indwelling pleural catheter was a Tenckhoff catheter placed by Robinson et al in 1994, allowing nine patients with MPE the ability to drain at home, avoiding further hospitalizations and interventions [10]. Other early advances in safe, repeated drainage of the pleural space included placing a pleural port and pleural catheter placement [11,12].

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**Article highlights**

- Malignant pleural effusions are becoming increasingly prevalent and management is primarily directed at palliating the patient's symptoms.
- The indwelling pleural catheter has emerged as an alternative to chemical pleurodesis for control of MPE associated symptoms, with several trials noting similar symptomatic benefits, including dyspnea score, as well as quality of life between the two therapies.
- Compared to those with pleurodesis, patients with indwelling pleural catheters have fewer hospitalization days.
- Indwelling pleural catheter management can be individualized to meet each patient's needs through customization of drainage frequency and combination therapies.
- Although complications occur, many are manageable without hospitalization or removal of the indwelling pleural catheter.
- Indwelling pleural catheters are cost-effective treatment strategies for malignant pleural effusion management, especially in patients with limited life expectancy and high rates of fluid recurrence.

Following these initial successes, the IPC was developed. A fenestrated, smaller bore (15.5 French) silicone catheter, the IPC contains a valve on the distal end to prevent drainage unless the proper access equipment is connected. When drainage is desired, patients can easily connect the vacuum-sealed chamber to their catheter, allowing for control of their symptoms at home. The FDA approved the first catheter for use in 1997 [13]. Since that time, additional catheters have been introduced to the market.

This review is focused on IPC, and below we will discuss the role of the IPC in symptom control, provide specifics in managing catheters and their complications, discuss cost effectiveness, and postulate what the future of pleural effusion management with IPCs holds. A comprehensive search was conducted in major biomedical databases including MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials, using a combination of keywords such as 'indwelling pleural catheter,' 'pleural effusion,' 'malignant,' 'cost effectiveness,' and 'management.' Studies involving adult human subjects and articles published in English were included. Both randomized controlled trials and observational studies (retrospective and prospective cohorts, case series, and case reports) were considered for inclusion, depending on the scope. After the initial search, titles and abstracts are screened for relevance, followed by full-text review of potentially eligible articles which were included and referenced in the manuscript text.

## 2. Role of IPC in symptom control

The role of the IPC as a definitive management strategy for recurrent symptomatic MPE is established in prospective and retrospective studies. Early studies of IPC in MPE demonstrated significant improvement in dyspnea scores [14,15]. These studies established IPCs as an important alternative management strategy. Subsequent studies focused on the role of IPCs in patient-centric outcomes such as dyspnea, quality of life (QOL), and hospital length of stay, replacing spontaneous pleurodesis as the main outcomes. The two landmark trials that cemented its role in symptom

management in comparison to talc pleurodesis are the TIME2 and AMPLE trials.

The TIME2 trial was a multicenter randomized controlled trial (RCT) conducted in the United Kingdom that included 106 patients with proven or highly suspected MPE who were randomized to either IPC or chest tube with talc pleurodesis (TP). At 42 days following IPC placement, patients had improved on average 37.00 mm on the validated visual analog scale (VAS) of dyspnea, a clinically significant difference [16,17]. Additionally, 86% of patients had a statistically significant improvement in their dyspnea score. However, when compared to TP, there was no significant difference at 42 days or 3 months. In this study, QOL was measured by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-30). As with dyspnea, there was improvement at 42 days in those who received an IPC, but no significant difference when compared to TP [16].

Similarly, the AMPLE trial was a multicenter, multinational RCT that included 146 patients with histologically proven or suspected MPE. Following IPC placement, dyspnea measured by VAS was improved at day one and was sustained for 12 months, but was no different when compared to TP [18]. The AMPLE trial studied QOL as a secondary outcome as well, using a VAS for QOL as well as a modified EuroQol 5 Dimensions (EQ5D). Quality of life increased after IPC placement by both tools, and was maintained throughout the period, similar to TP [18].

For many patients, a key component to QOL is time spent at home. IPC placement is mainly performed as an outpatient procedure while pleurodesis often necessitates inpatient stay. In both the TIME2 and AMPLE trials, the IPC group had fewer initial procedure-related hospitalization days and less time readmitted to the hospital in the 12 months following the procedure [16,18]. In the AMPLE trial, repeat pleural procedures were more common in the TP group. Both trials demonstrated a higher number of adverse events in the IPC group. Older RCTs, such as the study by Putnam et al, NVALT-14, and CALGB-30102 comparing IPC and TP have shown similar findings to the TIME2 and AMPLE trials (see Table 1) [19–21].

TP (slurry or poudrage) failure rates increase over time, from 10%–28% at one month, to ~30% at three months, and 28%–50% at six months [22–24]. The TIME2 trial showed a difference in dyspnea at 6 months that favored IPC. The AMPLE study reported a slight, nonsignificant trend toward favoring IPC over TP for dyspnea at 12 months. These factors may make IPC placement a more attractive option for patients with a longer life expectancy. Ultimately, any MPE study of this time frame is limited by attrition due to death; in the AMPLE study, only approximately one third of original patients were alive at 12 months.

Given the limited survival in patients with MPE, a more suitable approach to understanding how IPC placement impacts symptoms and QOL may be the quality-adjusted life years measurement. Ost et al studied quality-adjusted life days using the Short Form Six Dimension (SF-6D) in patients with MPE who received IPCs. Following IPC placement, although dyspnea improved, there were only moderate improvements in utility. Patients who were most dyspneic

**Table 1.** Randomized controlled trials evaluating IPC placement vs chemical pleurodesis.

Trial	Comparator Group	IPC Drainage Strategy	Primary Outcome	Notable Secondary Outcomes
Putnam et al. [20]	Doxycycline Pleurodesis (DP) via Chest Tube	Every other day or as required for relief	Fewer initial hospital days in IPC group vs DP group (1.0 vs 6.5, $p < 0.001$ )	At 30, 60, and 90 days, similar improvements in Guyatt CRQ, Borg score at rest and with exercise – except for dyspnea at 30 days (Borg, exercise) for which IPC was favored ( $p = 0.05$ ).
CALGB-30102 Demmy et al. [21]	Talc Slurry Pleurodesis via Chest Tube	Daily drainage	No significant difference in composite outcome: 1) patient alive, 2) no effusion recurrence 3) lung expansion $\geq 90\%$ 4) intervention complete by 2 weeks	IPC group: improved activity without dyspnea and survival with effusion control at 30 days, both driven by subgroup of patients with incomplete lung expansion
TIME2 Davies et al. [16]	Talc Slurry Pleurodesis via Chest Tube	3x weekly or as required for relief	No significant difference in dyspnea (VAS score) at 42 days	IPC group: improved dyspnea at 6 months ( $p = .01$ ); fewer hospital days initially at one year (both $p < 0.001$ ). No difference in mortality, QOL, or adverse events
AMPLE Thomas et al. [18]	Talc Slurry Pleurodesis via Chest Tube	Guided by symptoms	Fewer hospital days in IPC group over 12 months or until death (median 10 days vs 12 days, $p = 0.03$ )	IPC group: needed fewer repeat pleural interventions ( $p = 0.001$ ). No difference in dyspnea, QOL, mortality.
NVALT-14 Boshuizen et al. [19]	Talc Pleurodesis via Chest Tube	Guided by symptoms	No statistically significant difference in improvement in dyspnea (MBS)	No statistically significant difference in hospital days, re-interventions, or number of adverse events.

and those who received chemotherapy following IPC placement had the greatest increases in utility, suggesting that dyspnea may only be one component of overall QOL for patients with MPE, and studies should focus on more comprehensive approaches [25].

While potential benefits of IPCs in symptom control, hospitalization time, and QOL were noted above, several studies have highlighted drawbacks. A consideration for patients with an IPC is the time spent draining at home. A multicenter survey of 105 patients published by Mitchell et al highlighted other relevant and less frequently studied aspects of living with an IPC. Two weeks following IPC placement, 36% reported discomfort with home drainage and 63% reported that the catheter reminded them of their disease. However, avoiding hospitalization was an important benefit to IPC for 95% of patients [26]. Shared decision-making including education on post-IPC placement care and potential drawbacks will help patients and providers determine the best course of action for their specific situation.

### 3. Drainage frequency

One method that has been studied to expedite spontaneous pleurodesis is drainage frequency. Depending on the degree of lung expansion and volume of fluid present, drainage of the pleural fluid can create pleural apposition. Maintaining pleural apposition combined with inflammation from the catheter or underlying malignancy is thought to lead to pleurodesis [27]. This has been examined in two RCTs, AMPEL2 and ASAP. In the ASAP trial, patients were randomized to daily or every other day drainage (standard management). At 12 weeks, complete and partial pleurodesis (indicating some fluid still present on chest X-Ray) were achieved in 30% and 16% of the patients, respectively. This was significantly higher than the standard arm, with 24% and 16% of patients achieving complete and partial pleurodesis, respectively [28]. No difference in performance status was noted between groups. The AMPEL2 trial compared daily drainage to symptom-guided drainage. Both at 60 days and at 6

months, daily drainage was the superior strategy in terms of rate of spontaneous pleurodesis (for daily and symptom-guided: 37.7% and 11.4% at 60 days; 44.2% and 15.9% at 6 months, respectively) [29]. Notably, dyspnea measured by VAS was not significantly different between groups. In both the ASAP and AMPEL2 trials, there was no difference in complications, especially catheter-related infections between the drainage strategies [28,29]. Providers should consider the patient's expected lifespan and goals of treatment when deciding a drainage strategy.

### 4. IPCs and combination therapies

Another approach currently being evaluated is the combination of an IPC with chemical pleurodesis. The goal of combination therapies is to maximize time at home and minimize the time to pleurodesis following outpatient IPC placement and pleurodesis. In the IPC-Plus study, following IPC placement and daily drainage for 10 days, patients were randomized to 4 grams of talc or placebo instilled in the IPC, assuming they had evidence of expandable lung. The talc arm had increased rates of pleurodesis at 35 days (43% vs 23%) compared to the placebo arm. Patients in the talc arm additionally experienced either equal or significantly improved QOL, dyspnea, and chest pain scores. No differences in adverse events or hospitalization were noted, including rate of catheter blockage [30]. Notably, the IPC plus talc arm had a much lower pleurodesis success rate compared to historical talc pleurodesis rates [21].

In another combination therapy study, the Optimum trial, patients were randomized to outpatient IPC placement followed by outpatient talc pleurodesis via IPC and aggressive drainage on day 4 if non-expandable lung was ruled out. The comparator arm was pleurodesis by talc slurry via chest drain. In the IPC group, roughly half the patients received talc pleurodesis. No change in the primary outcome, global health status measured by EORTC QLQ-C30, was noted. There was a higher pleurodesis failure rate and higher adverse intervention-associated events in the IPC arm [31].

The SWIFT trial was a comparison of standard IPC treatment with a novel silver nitrate coated indwelling pleural catheter (SNCIPC). Silver nitrate on its own is an effective pleurodesis agent and the SNCIPC had shown success in animal models [32]. However, when compared to a standard IPC, the SNCIPC was less effective at inducing pleurodesis. A post-hoc analysis suggested that the SNCIPC may have induced more loculations that led to its inability to produce pleurodesis [32]. These newer methods of treating MPE, along with further studies such as the currently ongoing AMPLE-3 and TACTIC, will add to the ever-expanding array of treatment options available to patients.

## 5. IPC removal

For many patients, despite limited life expectancy, catheter removal is a common occurrence. Spontaneous pleurodesis, although not always the primary goal, occurs often with IPCs. When cessation of drainage occurs (i.e. less than 50–150 ml removed on three consecutive drainage attempts [14]) and patients are found to have no residual fluid on imaging, spontaneous pleurodesis is deemed to have occurred and the catheter can be removed. The frequency at which pleurodesis occurs and the time to pleurodesis varies. Older observational and retrospective studies noted a rate ranging from 42% to 51%, with one study citing median time of 59 days [14,16]. More recent RCTs examining drainage frequency found longer times to and lower rate of pleurodesis in patients with standard drainage strategies [27]. Predictors of increased rate of spontaneous pleurodesis include cancer type (lymphoma, ovarian cancer) and higher functional status (Eastern Cooperative Oncology Group [ECOG] performance status score < 2) [33]. Following pleural infection, spontaneous pleurodesis often occurs [34]. In addition to pleurodesis, indwelling pleural catheters can be removed due to patient discomfort or pain that is not controllable with analgesics, which is uncommon [35].

Removal of the IPC is typically done in the outpatient setting. Catheter fractures with retained portions of the catheter have been reported [36]. In some cases, during IPC removal, pleural catheters have been reported to fracture, leading to retained parts of the catheter. In a retrospective review by Fysh et al fracture reported in nearly 10% of

removals [37]. In four of the six cases, no adverse events including infection were noted [37]. Given the palliative intent of IPCs, shared decision-making whether to undergo invasive procedures for removal of retained catheters is warranted.

## 6. Complications

Given the large number of repeated, sterile drainages performed by patients and their caregivers, the potential for IPC-related infections can cause distress for patients. According to a meta-analysis of 41 pooled studies (Table 2), the complication rate following IPC placement is 20.3%, the most common of which is infection (5.7%) [38]. The most common types of infection following IPC placement are pleural infection and empyema (combined, 1.9%), cellulitis (0.9%) and wound infection (0.4%). For cellulitis and exit-site infections, a short course of antibiotics can be given as long as the tunnel site is not involved, which may require catheter removal [39].

In general, other than noting frank pus via the pleural catheter, the diagnosis of IPC-related pleural infection can be challenging. Often, pleural fluid studies in patients with MPE will have similar laboratory markers including elevated LDH and decreased glucose and pH that are typically used to diagnose non-IPC related pleural infections. The laboratory markers may be changed from the patient's prior studies, suggesting pleural infection. Positive cultures are not always indicative of infection, as many catheters become colonized, although the true prevalence of colonization is unknown [40]. On the other hand, an infected pleural space may be culture negative as is the case with pleural infections, in general. Additionally, pleural space septations on bedside ultrasound imaging can be present in the setting of MPE which may look like a complicated parapneumonic effusion. As with all pleural infections, providers often must use a combination of imaging, laboratory, and clinical judgment to determine if the pleural space is infected. A pooled analysis of two studies found the most common bacteria isolated from suspected pleural infections with IPCs is *Staphylococcus aureus* (37.9%). The second most common organism was Coagulase-negative Staphylococci (14.5%), a frequent colonizer, although these studies are limited by the poor diagnostic sensitivity of pleural fluid culture in identifying microorganisms [40]. Obtaining pleural fluid via thoracentesis may provide more accurate

Table 2. IPC complications (rates based on meta-analysis) [38].

Complication	Rate	Suggested Management	Additional Notes
All infection types	5.7%	Varies based on infection type	
Cellulitis	0.9%	Antibiotics are appropriate unless tunnel site is infected [39]	Involvement of tunnel site may require catheter removal [34,45]
Pleural Space Infection	1.9%	Antibiotics to cover <i>Staph aureus</i> , gram negative, and anaerobic organisms or as directed by culture data [39]	Complete drainage of pleural space is recommended. Catheter removal is only necessary if conservative management fails [34–46]
Symptomatic Loculations	0.8%	Instillation of fibrinolytics [49]	Many have recurrence of loculations despite appropriate treatment
Catheter Blockage	1.5%	Instillation of fibrinolytics [52]	
Catheter Tract Metastases	26% (in MPM)	Radiation and symptom control	Most seen in MPM Prophylactic radiation prior to development of CTM is not recommended
Pain	1.2%	Supportive care	IPC removal due to pain is rare [35]

CTM: Catheter tract metastases, MPM: malignant pleural mesothelioma.



culture data so as to avoid culturing a colonized organism from the IPC [39]. Risk factors for developing pleural infection are poorly understood, but length of time since catheter placement is thought to play a role, emphasizing the importance of sterile technique for home drainage [40,41]. Multiple retrospective studies indicate that patients who are immunosuppressed from chemotherapy do not have increased risk of infection [42–44].

Treatment of the infected pleural space should focus on covering the potential infectious organism(s), including *Staphylococcus*, gram negative, and anaerobic organisms and adjusting as appropriate. The appropriate antibiotic duration has not been evaluated, but therapy should be tailored to clinical improvement [39]. As with normal pleural space infections, complete drainage is key to controlling the infection. This is often done by connecting the patient's IPC to a continuous chest drain, though this has not been directly compared to intermittent drainage. In recent cohorts of patients with IPC-associated pleural space infection, the catheter has been left in place through the duration of treatment with high rates of infection control with antibiotics and drainage alone [34,45]. This management is supported by overall low mortality (2.2%-6%) [46,47]. The AABIP and ATS do not recommend removal of IPC as standard therapy but suggest tailoring to a patient's specific scenario and clinical course [39,48,49]. Sterile saline can also be used to flush the catheter to ensure pleural space drainage [39]. If necessary, intrapleural fibrinolytics have been used in a prospective observational study successfully, avoiding surgery in the majority of patients (36/39) and without any significant pleural bleeding [50]. As discussed above, post-infectious pleurodesis rates are high (62%), especially in patients found to have *S. aureus* [47].

Pain is also a notable complication and one of special concern to patients undergoing a procedure for palliative intent. IPC-associated pain may be related to local pain from the procedure, due to negative pressure of the suction bottle, or less commonly, from intercostal nerve injury [41]. The incidence of pain found in pooled analysis by Wang et al was low, at 1.2% [38]. This number may be falsely low given inconsistent reporting and timing of symptom surveys in various studies. For example, Efthymiou et al reported pain in 35% of patients receiving IPCs. Fortunately, they also reported that pain resolved in less than three days [51]. Severe pain that is unresponsive to analgesics is rare and requires removal of the catheter which occurs in only 0.6% of cases [35].

Another frequently encountered complication is the development of symptoms due to poor drainage secondary to fibrous septations forming in the pleural space, known as symptomatic loculations. In a pooled analysis, the rate of symptomatic loculations was 0.8% [38]. They are most commonly identified approximately two months after IPC placement and may be the result of increased fibrin production from the underlying malignancy and repeated drainage attempts [49]. In a retrospective multicenter study, Thomas et al identified 66 patients with symptomatic loculations who were treated with various fibrinolytics instilled in their IPC (mainly tissue-plasminogen activator). IPC drainage improved in 93% of patients and symptoms were improved in 83% while

3% experienced pleural hemorrhage requiring transfusions [49]. Although most patients only required one dose of fibrinolytics to treat their loculation, 40% eventually had a recurrence.

Similarly, fibrin accumulation can occur within the catheter and lead to catheter blockage. This is reported to occur in 1.5% of patients by a meta-analysis [38]. In a study by Wilshire et al, 37 catheter obstructions were treated with 2–5 mg of alteplase for 1–2 h, relieving the obstruction and restoring drainage in 100% of cases. No complications were noted [52].

Catheter tract metastases (CTM) are rare but are most commonly seen in patients with malignant pleural mesothelioma (MPM) [38]. One cohort of patients with MPM identified CTM in 26% of patients at a median time post-procedure of 408 days [53]. Following disruption of the parietal pleura, malignant spread may occur along the catheter tract, leading to catheter tract metastases. These may cause pain and, in some cases, have ulcerated through the skin [54]. A randomized trial evaluated the efficacy of prophylactic radiation in patients with MPM prior to receiving pleural interventions compared to radiation in response to a procedure-tract metastasis. No difference in the incidence of tract metastases was noted among all pleural procedures, including similar rates in those receiving IPCs [55]. Analgesia or radiotherapy only after developing CTM are usually sufficient strategies for management [56].

Nutrition loss after IPC placement, especially in patients with MPE who are frequently cachectic, is a potential concern. This may be more relevant in patients with chylothoraces given the additional fat content in the pleural fluid. Jiminez et al performed a retrospective review examining the utility of IPC placement for malignant chylothoraces and found patients with and without IPCs experienced comparable decrease in their albumin levels [57].

## 7. Cost effectiveness

As stated above, MPEs represent a large financial burden to the healthcare system, accounting for greater than \$5 billion in related hospital costs each year in the United States [2]. IPCs are increasingly recognized as a cost-effective treatment option for patients suffering from MPE.

By allowing outpatient drainage of fluid, IPCs help reduce the need for recurrent hospital admissions, making them a potentially more cost-effective long-term solution [58]. In contrast, pleurodesis often requires hospital stays, both initially and afterward, and carries the risk of partial or no response. The shift from inpatient to outpatient care reduces the demand for hospital resources and minimizes healthcare expenses related to bed occupancy, nursing care, and procedural costs. One of the first studies assessing cost-effectiveness of IPCs compared to inpatient talc administration showed that there was no significant difference in the mean cost of managing patients with IPCs. Additionally, in patients with limited survival (less than 14 weeks), IPC may be less costly [59]. A subsequent study similarly showed that IPCs were cost-effective when compared with talc pleurodesis and most cost-effective in patients with limited survival. However, if patients

require significant nursing time for catheter drainage, IPC is less likely to be cost-effective [60].

For healthcare providers and insurers, the reduction in hospital readmissions and emergency visits associated with IPCs can lead to substantial cost savings. While the initial cost of IPC insertion is higher than a single thoracentesis, the long-term benefits – fewer hospitalizations, lower procedural rates, and reduced need for inpatient care – make IPCs a more cost-effective choice than serial thoracentesis for managing MPE among patients with longer expected survival.

The IPC drainage strategy utilized may also impact the cost-effectiveness of the procedure given the need for additional healthcare consumables (ex. bottles, dressings, etc.). Using a decision tree model-based analysis, the cost-effectiveness of IPC with the addition of talc was compared to symptom-guided drainage and daily drainage. The standard willingness to pay (WTP) threshold of \$100,000 per quality-adjusted life year (QALY) was used. The authors found the combination of IPC and talc was a cost-effective alternative to symptom-guided drainage (incremental cost-effectiveness ratio of \$59,729 per QALY). However, symptom-guided drainage was cost-effective for pleurodesis rates > 20% and for life expectancy < 4 months. Daily drainage was not cost effective in any scenario [58]. While the cost-effectiveness of IPCs from the healthcare system perspective is important, it is also equally imperative to consider the financial burden on patients and their families. In a cross-sectional survey of patients with an IPC in place for two months and who had insurance, the median copay for private insurers was \$238.45 (every 2–4 weeks, depending on drainage frequency) with more than half the patients reporting additional costs related to the IPC [61].

In conclusion, IPCs represent a cost-effective treatment strategy for MPEs, especially in patients with limited life expectancy and high rates of fluid recurrence. The ability to manage pleural effusions in the outpatient setting, along with reductions in hospital admissions and invasive procedures, make IPCs not only a patient-friendly option but also a financially reasonable option for healthcare systems.

## 8. Conclusion

MPEs are burdensome to patients, both reducing their quality of life and increasing healthcare costs. IPCs are an important management strategy that provide symptom relief and avoid hospitalizations and repeated procedures. While complications are possible, most can be managed in a noninvasive manner. For many patients, the IPC is a cost-effective method to manage their symptoms. In summary, IPCs provide clinicians and patients an excellent tool to help alleviate symptoms of MPEs. The best way to utilize this tool is still a question being answered.

## 9. Expert opinion

There are various definitive management options for MPE, each with their own advantages and disadvantages. Selecting the best individualized management strategy is ideally done with full knowledge of the patient's life expectancy,

lung elastance, likelihood of pleurodesis success and potential complications, and most importantly patient preferences. Involving the patient's support system in these discussions is essential to fully appreciate each patient's unique situation. The patient's decision to pursue a specific therapy should be based on an informed discussion that takes into account the benefits of each modality, potential complications, and understanding of what care will look like at home.

When a patient elects to undergo IPC placement, choosing a drainage frequency should be done with respect to patient and caregivers' ability to manage drainage at home and the associated costs. Clinicians and their healthcare team should educate patients and their support system of routine care, monitoring drainage output, and how to recognize complications. Frequent follow up and provider availability is key to address any problems that may arise.

The management of MPE is an evolving field with future directions focused on precision medicine, tailored toward improving both patient-relevant outcomes and the efficiency of care. As the understanding of pleural disease advances, new approaches and technologies are emerging to optimize treatment strategies. One of the primary goals for future management is to enhance symptom control and improve quality of life, while minimizing invasiveness and hospital resource use. IPCs and TP are well-established, but ongoing research aims to refine these treatments and develop alternatives that may improve effectiveness, reduce complications, and increase patient comfort.

A key area of investigation that we feel will be a part of pleural disease management in the next five years is personalized or targeted therapy for MPE, leveraging advances in molecular biology and cancer genomics. Research is focusing on identifying biomarkers that can predict response to specific treatment strategies, such as IPC or pleurodesis, for individual patients. This personalized approach could help optimize treatment selection and improve outcomes by tailoring therapy to the individual characteristics of the tumor and pleural space [62]. Ongoing trials are also exploring novel agents that can be delivered intrapleurally to inhibit tumor growth, slow fluid accumulation, or enhance the effectiveness of pleurodesis, including agents that target specific molecular pathways involved in effusion formation [63].

Minimally invasive techniques are another promising direction in MPE management. Advances in imaging and interventional techniques may lead to more precise and less invasive ways to manage pleural fluid accumulation. For example, image-guided pleural interventions and robot-assisted thoracoscopic procedures are being explored to improve the accuracy of pleural biopsies, drainage, and pleurodesis while reducing patient recovery times. In addition, bioengineering innovations may result in the development of next-generation IPCs with features such as drug-eluting properties to help reduce infection risks or catheters that facilitate spontaneous pleurodesis over time.

Several clinical trials are currently investigating innovative approaches to MPE management. The PROSPECT study is a multicenter study that is exploring complications related to pleural procedures as well as identifying characteristics (and thus predictors) of patients who will benefit the most

after a pleural intervention [64]. AMPLE-3 compares long-term outcomes between patients treated with IPCs and surgical pleurodesis, focusing on quality of life, complication rates, and healthcare utilization [65]. Another study currently underway compares the use of IPCs versus IPCs plus doxycycline looking at IPC time in situ to treat symptomatic pleural effusion [66]. Research into catheter-associated complications is also being investigated, such as the study from MD Anderson Cancer Center in the U.S., assessing the use of alteplase through an IPC for management of non-draining MPEs [67]. Future directions in research will include assessing the burden of drainage on patient and families as it relates to their health-related and overall quality of life, comparison of home pleurodesis through IPC vs in-hospital pleurodesis, among other interesting research questions to be addressed.

The future of MPE management lies in personalization, minimally invasive approaches, and the incorporation of new technologies and agents. With ongoing clinical research, it is likely that management strategies will continue to evolve in the next five years, focusing not only on prolonging survival but enhancing the quality of life for patients with this challenging condition. As these innovations come to fruition, they have the potential to revolutionize the standard of care for MPE, making treatment more effective, patient-friendly, and cost-efficient.

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