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Pleural controversy: Pleurodesis versus indwelling pleural catheters for malignant effusions

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ABSTRACT

Malignant pleural effusions (MPE) are a common complication of advanced malignancy. The treatment of MPE should be focused on palliation of associated symptoms. The traditional approach to MPE has been to attempt pleurodesis by introducing a sclerosant into the pleural space. A more recent development in the treatment of MPE has been the use of indwelling pleural catheters (IPC) for ongoing drainage of the pleural space. Controversy exists as to which approach is superior. Pleurodesis approaches will have the advantage of a time-limited course of treatment and high pleurodesis rate at the cost of a more invasive procedure requiring a general anaesthetic or conscious sedation (for thoracoscopic approaches) and an inpatient hospital stay. Use of IPC will allow the patient to be treated on an outpatient basis with a minimally invasive procedure, at the cost of long-term need for catheter drainage and care. Symptom control appears similar between techniques. Complication rates between the two approaches cannot be easily compared, but studies suggest more frequent severe complications such as respiratory failure, arrhythmias and even mortality following pleurodesis, with infection rates similar between the two approaches. IPC will likely see increasing utilization in the future but patient preference and local resources and expertise will continue to play a significant part in treatment decisions. Randomized trials directly comparing the two approaches are needed and some are underway. Novel combination approaches utilizing both IPC and pleurodesis agents have the potential to further improve the care of these patients.

Key words: indwelling pleural catheters, malignant pleural effusion, pleurodesis, talc, thoracoscopy.

INTRODUCTION

Malignant pleural effusions (MPE) are a common complication of advanced malignancy. They can be seen in common tumours such as lung, breast and colon cancer but can occur with almost any metastatic malignancy as well as in mesothelioma. Estimates with regards to the prevalence of MPE suggest that approximately 150 000 such cases occur every year in the USA (5/10 000 population).[1] It has been estimated that up to 15% of lung cancer patients will initially present with a MPE and that as many as 46% will develop a pleural effusion at some point in their disease process. In those with advanced breast cancer, effusions can be seen in half of all patients.[1]

The most important symptom associated with MPE is that of dyspnoea.[2,3] This is usually subacute, progressing over days and weeks and may be associated with chest discomfort or cough. Symptoms associated with advanced malignancy such as weight loss, anorexia and fatigue can be present. In some cases, the pleural effusion is the initial presentation of an advanced malignancy while in others the effusion occurs as a sign of progression of the cancer.

Unfortunately the presence of a MPE portends a poor prognosis. Overall median survival rates are in the 4–6 month range, although patients with certain tumour cell types do better than others. For example, patients with mesothelioma and breast cancer have been noted to have median survival rates of 6–10 months[4,5] and 9–11 months,[6,7] respectively, while those with lung cancer may only survive a median of 4 months.[8] Presence of pleural effusion does not appear to affect prognosis in those with lymphoma.[9]

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GOALS OF MPE TREATMENTS

The treatment of MPE should be focused on palliation of associated symptoms. The importance of symptom control is based on the lack of a convincing effect of MPE treatments on survival[5] as well as the incurable nature of most malignancies once spread to the pleural space has occurred. For similar reasons, specific treatment of small asymptomatic pleural effusions is not warranted.[10,11]

An ideal treatment method for MPE should offer a rapid and complete relief of associated symptoms. This improvement should be long-lasting and without the need for repeat procedures for the duration of the patient's life time.[1] Minimally invasive procedures should be favoured, and discomfort or side effects of the treatment should be minimal or non-existent. If at all possible, treatment should be offered on an ambulatory basis minimizing hospitalization time for these patients who may have only a few months to live. The burden of this treatment should be minimal for both patients and their caregivers. Costs should be minimal and treatment should not interfere with other oncologic therapies. Finally, the treatment should be broadly applicable to a majority of patients suffering from MPE.

Pleurodesis, typically assessed radiologically at 30 days, has been used as the primary endpoint for most studies on MPE treatment and is assumed to correlate with symptom control. While some patients may have relief of dyspnoea despite not achieving the radiologic definition of pleurodesis, some patients who achieve pleurodesis may still experience dyspnoea. The advent of alternative treatments not specifically based on pleurodesis has led to the recognition that pleurodesis in itself is not a requirement for effective MPE symptom control.[12] We believe that future studies investigating and comparing MPE treatments should include objective measures of dyspnoea as well as overall quality of life as important outcome measures.

Therapeutic thoracentesis is usually recommended as the initial treatment for patients with suspected symptomatic MPE.[1] This allows rapid relief of symptoms[13] as well as procurement of diagnostic material to confirm MPE and exclude other causes. In patients with known metastatic disease to other sites presenting with exudative effusions and without an alternative aetiology, specific cytological or histological confirmation of malignancy in the pleural space is not mandatory to initiate treatment. Thoracentesis also allows confirmation of symptom improvement following pleural drainage, an important predictor of symptomatic response to other treatment modalities. We advocate that a treatment plan for management of the effusion be considered soon after the thoracentesis given that recurrence is highly likely in the short term.[11] Repeated thoracentesis is not recommended as an optimal method for control of MPE. This is due to the relatively rapid recurrence of effusion resulting in a need for multiple procedures, the symptom-prompted nature of the intervention that is incompatible with sustained relief and the potential for development of trapped lung over time making other treatment options more difficult. As such, this approach should be limited to patients with very short expected life expectancy and the relatively uncommon patients with long symptom-free intervals following thoracentesis.[11]

PLEURODESIS APPROACHES

The traditional approach to MPE has been to attempt obliteration of the pleural space thereby removing the potential space where fluid can accumulate and cause symptoms. This is achieved by introducing a sclerosing agent to the pleural space, stimulating inflammation and fibrosis while maintaining apposition between the visceral and parietal pleural surfaces. Several different sclerosing agents have been used, most commonly talc, tetracycline, doxycycline, bleomycin and silver nitrate with talc generally felt to be the most effective.[14]

The agents can be introduced into the pleural space through chest tubes or via thoracoscopy. While both approaches require hospitalization, thoracoscopy is usually performed under general anaesthetic or conscious sedation while chest tube approaches can be done at the bedside with oral or i.v. analgesics. Despite suggestions that thoracoscopic approaches are more effective,[14] randomized controlled trials have failed to demonstrate the superiority of one technique over the other[15,16] and the recent British Thoracic Society guidelines support the position that either approach is equally efficacious.[11]

Following the application of a sclerosing agent, a chest tube is maintained for several days to ensure apposition of the pleural surfaces. The optimal length of time for which the chest tube must remain in place is controversial, but one trial suggested that once the lung has re-expanded, awaiting a reduction in drainage prior to administering tetracycline did not alter the effectiveness of the procedure[17] and another suggesting that tube removal at 24 h versus 72 h post talc slurry also did not compromise outcomes.[18]

INDWELLING PLEURAL CATHETER APPROACH

A more recent development in the treatment of malignant pleural disease has been the use of indwelling pleural catheters (IPC) for ongoing drainage of the pleural space. Symptom relief is achieved rapidly following placement, but maintenance of lung expansion is achieved not by obliteration of the pleural space, but by repeated drainage through the catheter in the home setting. As such, symptom control is the primary goal of treatment rather than pleurodesis, even if 'spontaneous pleurodesis' does occur in a subset of patients allowing eventual catheter removal. Catheters can be inserted in an outpatient setting under local anaesthesia. The typical drainage schedule is every other day using disposable plastic bottles (550 mL to 1 L), while rare patients with rapid fluid re-accumulation require daily procedures. We favour

Table 1 Contrast between pleurodesis and IPC

	Pleurodesis	IPC
Pleurodesis rates	++++	++
Symptom control/QoL	+++	+++
Patient selection	++	++++
Invasiveness/hospitalization	++	++++
Burden of care	+++	++
Complications	++(+)	+++
Cost	++	++

+ least favourable, ++ less favourable, +++ favourable, ++++ most favourable.

IPC, indwelling pleural catheter; QoL, quality of life.

involvement of home care nursing support for catheter care and drainage as well as a specialty clinic approach[19] for initial assessment and follow-up. Nevertheless, catheter care is strait forward and patients and family members are encouraged to learn the drainage procedure as well, facilitating additional as needed drainage or out of town travel. Details of our approach to evaluation, insertion and maintenance of IPC have been published.[20,21]

When considering treatment for a MPE, physician and patient will need to choose between a pleurodesis procedure or an IPC. The best management option will depend on numerous factors including performance status, life expectancy, local expertise, resources available, as well as patient preference. Within the context of limited availability of high-quality comparative trials, the following discussion will attempt to compare and contrast important components of MPE treatment between pleurodesis procedures and IPC (Table 1).

PATIENT SELECTION/INDICATIONS/ CONTRAINDICATIONS

As stated above, patients are typically selected for treatment of MPE on the basis of dyspnoea, and confirmation that symptoms are initially improved by large volume thoracentesis.

To undergo a thoracoscopic pleurodesis procedure a patient must generally be well enough to undergo a general anaesthetic. This is reflected in the inclusion criteria of some of the larger studies examining this approach. For example, a large randomized trial of talc slurry versus talc insufflation only included patients with an ECOG status of 0–2 and a life expectancy of greater than 2 months.[15] The use of medical pleuroscopy may expand the population for which talc insufflations is feasible as this can be performed under conscious sedation or even with a local anaesthetic alone, but guidelines still suggest limiting these procedures to those with WHO status 0, 1 or 2.[22] Pleurodesis using talc slurry can also be performed at the bedside and studies have supported the use of smaller bore chest tubes for this purpose.[23]

Indwelling pleural catheters insertion is not limited by severe dyspnoea or performance status. In our experience, patients with poor performance status, or those already in hospice care who are too debilitated to undergo pleurodesis procedures can still experience substantial benefit from IPC drainage without having to undergo repeated thoracentesis. As such, IPC placement is considered the preferred option in this patient population.

A key factor associated with successful pleurodesis is the ability to achieve apposition of the pleural surfaces,[11] which means there must be good re-expansion of the underlying lung following drainage of the effusion. Most studies of pleurodesis exclude patients who did not achieve adequate re-expansion of their lung and this is considered a relative contraindication to thoracoscopy.[22] However, the frequency in which patients planned for pleurodesis do not end up receiving the sclerosant, because their lung is trapped or other reason, has been reported to be 5–12%.[15,24,25] This is not insignificant as these patients have already been exposed to the thoracoscopic or tube thoracostomy procedure but would not be expected to have any lasting benefit. The prevalence of trapped lung in MPE is unclear, but is likely higher as these patients would not be included in pleurodesis studies if suspicion of trapped lung was present pre-operatively. In one series in a centre where VATS is reportedly used liberally even if trapped lung may be present, 41% of subjects had an IPC inserted because of inadequate lung re-expansion, with favourable outcomes in this group.[26] In our series, 26% of IPC insertions were associated with >20% residual fluid at 2 weeks, suggesting a degree of trapped lung.[27] Other series have also describe the beneficial impact of IPC in this setting[28–30] and the British Thoracic Society guideline on MPE suggests that IPC may be a more attractive option in the setting of trapped lung given the usual alternative of repeated thoracentesis.[11]

The use of IPC is not limited to situations where pleurodesis attempts are not an option, and have been used as a first line treatment for all patients with MPE in some centres.[31–33] In fact the use of IPC as first line in patients who were fit for pleurodesis has been described with good results.[27] Bilateral effusions can also be approached with bilateral IPC and appear well-tolerated, accounting for 7.6% of procedures in our centre.[31]

Another situation where IPC may be used preferentially over thoracoscopic procedures is in the setting of chemotherapy treatments. In a study of 82 IPC insertions in 78 patients there was no association with infection when patients were also receiving chemotherapy[34] and our practice has been to offer IPC even if chemotherapy is planned or ongoing.

There are situations where a thoracoscopic procedure may be a better alternative to an IPC. A patient found to have malignant pleural involvement at the time of thoracoscopy for an undiagnosed exudative effusion could undergo simultaneous talc poudrage if pleural nodularity consistent with metastatic disease is visualized at the time of procedure and lung expansion can occur.

Contraindications to IPC placement for malignant effusions are uncommon and generally include

uncontrolled coagulopathy, extensive skin involvement with malignancy (inflammatory breast cancer) or infection over the planned insertion site and multiloculated pleural effusion. Chylothorax has previously been considered a contraindication to prolonged drainage with an IPC although successful use has been described in this setting.[35]

In summary, IPC appear to have a broader range of application in patients with MPE with particular usefulness in patients with trapped lung, poor performance status and shorter life expectancy although they also appear effective in patients with better performance status and well re-expanded lung. Pleurodesis procedures may be preferred if the patient requires diagnostic pleuroscopy and in cases of malignant chylothorax, but a substantial portion of all MPE patients will not qualify for these procedures.

PLEURODESIS RATES

In trials examining the benefit of talc or other sclerosants, the frequency of pleurodesis is the outcome most often reported. Successful pleurodesis is usually determined radiographically but has been variably defined and evaluated at various time points, often at 30 days. Reviews of pleurodesis outcomes have suggested success rates in MPE to be as high at 91%;[36] however, many of these studies are retrospective, lack consistent follow-up, have significant selection bias, do not use intention to treat analysis, exclude patients not surviving to day 30 or do not allow adequate follow-up to account for recurrences beyond 30 days. For example, in a large randomized trial of talc slurry versus poudrage, the overall rate of pleurodesis reported in the two groups was 71% and 78%, respectively; however, patients not alive at 30 days who did not get full re-expansion of their lung were excluded from this analysis. When including all enrolled patients on an intention to treat basis, only 53% and 60% were alive and recurrence free at 30 days.[15] These analytical biases need to be carefully considered when evaluating the results of pleurodesis procedures.

Spontaneous pleurodesis will often occur in patients treated with an IPC. Spontaneous pleurodesis is generally defined as the finding of minimal IPC drainage (50 mL or less) on three consecutive attempts without evidence of symptomatic re-accumulation of fluid. Whether or not there is actual pleural symphysis present is not known but this fact may not be clinically relevant. Frequency of spontaneous pleurodesis is reported to range from 26% to 70% in various series[27,31,32,37] and a systematic review found the mean rate to be 46%.[38] When spontaneous pleurodesis does occur it has been reported to occur at 29–59 days.[31–33] The rate of pleurodesis is likely affected by survival as some patients do not survive long enough to achieve a spontaneous pleurodesis but this does not imply they did not benefit from the IPC, as symptom relief can be substantial even in the absence of pleurodesis. Some patients will not achieve spontaneous pleurodesis and continue to drain until they die of their underlying malignancy, which can be associated with considerable use of supplies, and therefore cost, as discussed later in this manuscript. Several factors beyond survival may affect pleurodesis rates. This includes adequacy of lung re-expansion,[27] presence of breast and gynecologic malignancies, positivity of fluid cytology and lower total fluid drained in the first week.[37] Nevertheless, these findings have not been confirmed across studies, and a recent large series found no association between tumour type and spontaneous pleurodesis rates.[32]

Not surprisingly, patients with trapped lung are unlikely to achieve spontaneous pleurodesis because good pleural apposition cannot be achieved. While patients with trapped lungs are usually excluded in pleurodesis trials, they often comprise of a significant portion of those in the IPC series. This will bias the results to a lower rate of spontaneous pleurodesis with IPC and needs to be kept in mind when comparing the two approaches. When a subset of patients who had good (<20% residual fluid) re-expansion of their lung with IPC drainage, and >3 month survival were evaluated, the rate of spontaneous pleurodesis was found to be 70%,[27] approaching rates achieved with sclerosing agents.

Overall the rates of pleurodesis using sclerosing agents are higher (and achieved faster) than that associated with IPC, but studies directly comparing these two approaches in matched patient populations are not available.

SYMPTOMS

Despite the fact that the management of MPE is primarily palliative, few studies have considered objective measures of dyspnoea in their designs. As such, few data are available on the degree and frequency of symptom relief following treatments. Significant short-term improvements in dyspnoea, as assessed by a visual analogue score, was noted in 32 patients 3 days post pleurodesis with talc or bleomycin.[39] Longer-term assessments of dyspnoea are limited to two studies. A small randomized trial of pleurodesis using talc versus iodine did show that all patients in both groups had modified Medical Research Council dyspnoea scores of I or II post procedure compared with III or greater before pleurodesis although the time point was not clearly defined.[40] Another group reported that 77% of patients described an improvement in dyspnoea following thoracoscopic poudrage, up although they only had data on only 172 of 273 patients.[25]

Indwelling pleural catheters have been shown to have good rates of dyspnoea control in various studies. Clinical improvement in dyspnoea have been noted in 89–95% of patients treated with IPC[28,31] although validated scores were not used. In another series, 50% of patients reported being moderately satisfied or very satisfied with their degree of symptom control with an IPC despite the presence of trapped lung precluding pleurodesis.[30]

Only one randomized study compared the use of IPC with a pleurodesis procedure (doxycycline), with

dyspnoea assessed with the Borg scale and the Guyatt Chronic Respiratory Questionnaire. Both groups were found to have similar clinically significant improvement in both scores at 30 days, with the improvement maintained to 90 days.[41]

Overall it appears both therapeutic approaches have the ability to improve dyspnoea. A lack in objective measurements of symptoms and quality of life is noted for both techniques, and investigators are encouraged to include such measures in future studies.

REPEAT PROCEDURES AND RE-ACCUMULATION

Recurrences of pleural fluid and symptoms can occur following pleurodesis or treatment with an IPC, necessitating additional procedures. In series with IPC, once a catheter is placed, no further ipsilateral procedure is required in 90–91% of patients.[31,32] When a catheter has been removed because of spontaneous pleurodesis, fluid re-accumulation has been noted in 3.8–8.7% of patients.[31,33]

Delayed recurrence of MPE have been reported in as many as 6–38% of patients treated with talc, often occurring after the 30-day time point selected as a measure for effectiveness.[15,24,25,42,43] Recurrences have been noted to increase as further times passes from the intervention although not all of these patients require further intervention.[15]

It would appear that IPC offer a definitive treatment approach for the vast majority of patients, in a manner equivalent or superior to pleurodesis regimens.

BURDEN OF CARE AND HOSPITALIZATION

One of the potential burdens associated with IPC has been the ongoing care associated with their use. A regular draining schedule is required, and while some patients may be able to care for the IPC themselves, most will require assistance from a family member or visiting health-care worker. We encourage family members to gain comfort with the procedure, especially for the patient who wishes to travel or be drained on an as needed basis, but this may place a significant burden of responsibility on the family member or caregiver. Although associated with higher costs, we favour a model based on community nursing support. This may not always be feasible in communities where this resource is not available but has the advantage of maintaining the patient as an outpatient, an important consideration in patients whose goals of care are palliative, as well as not placing undo strain directly on the patient or family. Other issues relating to the patient's illness can also be addressed as part of the regular visits, such as pain and symptom management.

Pleurodesis procedures have the potential advantage of a finite treatment period requiring no specific management once completed. This is at the cost of an inpatient stay, with mean hospital stays after thoracoscopic pleurodesis of 5–7 days.[25,39,40,42] Patients with MPE often have limited survival so even a few additional days in hospital may be a significant portion of their remaining lifespan. In the only randomized trial comparing IPC with pleurodesis, patients in the doxycycline arm were admitted a median of 6.5 days compared with 1.0 days for the IPC arm.[41] As more comfort and experience have been gained with IPC most centres will insert them without hospital admission, with 91% of catheters in a recent series inserted on an outpatient basis.[33]

This key tradeoff of inpatient stay versus long-term catheter care may in many cases play an important role in patients' decisions regarding their treatment.

COMPLICATIONS

Complications from pleurodesis and indwelling catheters have been reported in several studies. The severity and frequency of these complications is an important factor in evaluating each procedure's place in clinical practice and should be assessed in the context of the palliative indication for such treatments.

The most commonly reported complications of tunnelled catheters include infection (cellulitis and empyema), catheter dislodgement, poor drainage (catheter blockage or loculation of fluid), pain and pneumothorax. A systematic review of several studies of tunnelled catheters suggested that 87.5% of patients will have no complication at all and that despite complications in some, 95.6% will have improvement in their symptoms.[38]

Complication rates following pleurodesis will vary according to the method of administration (thoracoscopic insufflation vs administration via a chest tube) as well as the choice of sclerosant. This discussion will focus mainly on talc given its preferred role for pleurodesis in most clinical centres.

Pain and fever are very frequently associated with talc pleurodesis, and whether these are defined as a complication or an expected part of the procedure is a matter of debate. A Cochrane review suggested the frequency of pain and fever in association with talc to be 31% and 26%, respectively,[14] with systemic opioids commonly used in this setting. Pain beyond the immediate post-procedure period has been noted in 3.2% of IPC patients.[38] Our experience is that pain due to IPC insertion can usually be managed with non-prescription analgesics such as acetaminophen.

Empyema is a serious complication, which is reported in 0–4.0% of pleurodesis procedures.[15,24,41,44] Rates of empyema are similar for IPC and have been reported to be 0.4–5.0%,[31–33,45] averaging 2.8% in a systematic review.[38]

Other severe complications have been reported with pleurodesis procedures. ARDS has been associated with talc pleurodesis in as many as 9% of cases.[46] The size of the talc particles appears to play a role as use of graded large particle talc has been shown to be safe with no cases of ARDS in a large series of 558

patients.[47] Unfortunately calibrated large particle talc is not uniformly available. ARDS has not been reported in association with IPC. Other complications such as arrhythmia, myocardial infarction and respiratory failure occasionally noted following pleurodesis[15,47] have not been associated with IPC.[38]

Peri-procedure mortality can be difficult to evaluate as patients have metastatic malignancy and limited life expectancy due to their disease. Mortality immediately after or in the following 30 days is variably reported in the literature. Several pleurodesis studies describe 30-day all-cause mortality to ranging from 2% to 20%.[15,24,41,44] A large randomized trial of talc poudrage versus talc slurry described treatment-related death in 3.7% and 2.9% as well as post-operative death in 8.4% and 6.1% respectively.[15] These deaths were in patients selected as well enough to undergo surgery and the majority of treatment-related deaths were described as due to respiratory failure. While 30-day all-cause mortality is rarely described in studies evaluating indwelling catheters (12.8% in our series[31]), a systematic review of tunnelled pleural catheters identified only one procedure/sedation-related death during insertion of a pleural Tenckoff catheter in 1370 patients described in 19 studies.[38]

Overall, IPC appear to have a better safety profile compared with talc pleurodesis performed via either talc slurry or thoracoscopy, in particular with regards to severe complications, but with similar rates of empyema.

COST

The cost of caring for patients with MPE can be significant and there is currently minimal literature comparing the IPC and pleurodesis in terms of the cost associated with each. There are significant upfront costs with a pleurodesis approach as this typically involves a hospital stay of several days and often a surgical procedure. The initial cost of an indwelling catheter is quite minimal as this can be inserted on an outpatient basis. The main expenses associated with IPC are the ongoing costs of drainage supplies as well as any associated nursing care needed to perform the drainage. These costs continue to accumulate as long as a patient continues to drain fluid, essentially until the patient has a spontaneous pleurodesis or dies. A successful pleurodesis procedure should be associated with minimal ongoing costs.

It is therefore not surprising that a short-term costs analysis has been shown to favour pleural catheters by nearly $8000 when comparing mean costs for the initial 7 days after intervention.[45] In this analysis only hospital charges were examined. When total hospital charges were compared from intervention to death or last follow-up there was no difference between the groups.

A decision analysis using 2008 Medicare data was performed to examine the cost effectiveness of IPC.[48] Relatively high estimates of success were used for the talc arm in this analysis and relatively low estimates of success were used in the catheter arm biasing the study towards pleurodesis. Additionally no further costs were assumed for patients failing talc while a percentage of those estimated to fail catheter management were crossed over to the talc arm, an unusual scenario from our point of view. When assuming a survival of approximately 6 months, they concluded that the approaches were similar and the treatment of choice may need to be individualized based on the clinical situation and patient preference. IPC appeared to be more cost-effective when survival was less than 6 weeks. Unfortunately at this time, no prospective data exist directly comparing actual costs between different methods of managing malignant effusions and more research is needed in this area.

FUTURE DEVELOPMENTS: RESEARCH GAPS

The above discussions are significantly limited by the lack of randomized comparative studies between pleurodesis procedures and IPC, with only one such trial published.[41] While this trial was well designed and conducted, pleurodesis was attempted with doxycycline, which many do not consider as the gold standard. The paucity of randomized controlled trials between these two approaches likely relate to the significant differences between the approaches and associated patient and physician preferences. We eagerly await results of a recently completed randomized trial in the UK comparing talc slurry versus IPC, with symptom control considered as a primary outcome measure. Additional studies will still be required to settle the pleurodesis versus IPC controversy as physicians may criticize the use of slurry instead of poudrage in this trial, and the use of 'as needed' drainage instead of routine drainage in the IPC arm. The optimal drainage protocol for IPC remains an area devoid of good outcome data, although an ongoing trial will attempt to determine whether a more aggressive daily draining protocol is associated with more benefits than the more commonly used every other day draining regimen (Clinical trials.gov # NCT00978939).

Until additional prospective comparative trials are available, significant caution must be used when comparing case series from different centres, different patient populations, inclusion criteria and outcome measures. We also believe that it is critical for treatment trials in MPE to include objective symptom, quality of life and treatment satisfaction assessments on an intention to treat basis as important outcome measures. Follow-up should also be adequate to assess for recurrence of symptoms or effusion.

Indwelling pleural catheters can also offer research opportunities for increasing our understanding of pleural disease by allowing easy and repeated access to the pleural space with minimal impact on subjects in a way not feasible in the past. IPC may also be ideally suited as delivery devices for new therapeutic compounds targeted to the pleural space.[49,50]

FUTURE DEVELOPMENTS: COMBINATION PROCEDURES

Moving beyond the pleurodesis versus IPC debate, several groups have described treatment algorithms, which attempt to exploit advantages of each technique sequentially or in combination rather than use one or the other in isolation. This has included insertion of an IPC at the time of attempted VATS pleurodesis when trapped lung is encountered[26,30] or following post-pleurodesis recurrence of MPE.[28] Others have used IPC in order to administer sclerosing agents. Perhaps the most integrated combined use of pleurodesis procedures and IPC made use of these catheters post thoracoscopic talc poudrage to facilitate early hospital discharge (median/mean length of stay: 1.8/3.2 days), followed by early outpatient removal of the IPC (median/mean: 7.5/16.7 days) while maintaining an 80% pleurodesis success rate.[51] We have recently published preliminary experimental data on integration of a sclerosing agent onto an IPC in an attempt to accelerate and improve the occurrence of pleurodesis associated with IPC while potentially maintaining advantages of a minimally invasive outpatient-based approach.[52,53]

CONCLUSIONS

Patients with MPE now have several different treatment options. Although some patients will be favoured to undergo one procedure over another based on clinical circumstances such as performance status and presence of trapped lung, many would potentially benefit from either a pleurodesis procedure or IPC. Pleurodesis approaches will have the advantage of a time-limited course of treatment and high pleurodesis rate at the cost of a more invasive procedure requiring a general anaesthetic or conscious sedation and an inpatient hospital stay. Use of IPC will allow the patient to be treated on an outpatient basis with a minimally invasive procedure requiring only a local anaesthetic, at the cost of long-term need for catheter drainage and care. Symptom control appears similar between techniques, but comparative data are very limited. Similarly, complication rates between the two approaches cannot be easily compared, but studies suggest more frequent severe complications such as respiratory failure, arrhythmias and even mortality following pleurodesis, with infection rates similar between the two approaches. As such, patient preference and local resources and expertise will continue to play a significant part in treatment decisions.

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