Interventions to Treat Malignant Pleural Effusions

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Malignant pleural effusions (MPEs) are common complications that occur with advanced stages of cancer. In general, they indicate a poor prognosis and greatly affect quality of life (QOL). The treatment goal of MPEs is to provide relief of symptoms. The standard treatment for MPEs is talc pleurodesis; however, indwelling pleural catheters have become more frequently used. This article focuses on current management strategies for MPEs and assesses their influence on QOL.

At a Glance
- Symptoms of malignant pleural effusions (MPEs), which involve the accumulation of fluid in the pleural space, include dyspnea, shortness of breath, chest pain, and other issues that decrease functional status.
- Treatment for MPEs should be palliative, achieving immediate symptom relief and improved quality of life.
- The optimal treatment strategy for MPEs should have minimal side effects, require minimal or no hospitalization, and have low rates of recurrence.

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Pathophysiology

Malignant pleural effusions (MPEs) are accumulations of fluid-containing cancer cells in the pleural space (Lombardi et al., 2010). MPEs are common and frequent complications that occur in advanced stages of cancer, affecting about 150,000 people in the United States each year (Hunt et al., 2012). Common malignancies associated with MPEs include lung, breast, gastrointestinal, and ovarian cancers (Thomas & Musani, 2013). Patients with MPEs often have a poor prognosis, with a life expectancy of 3–12 months (Bertolaccini, Viti, Gorla, & Terzi, 2012). MPEs greatly affect quality of life (QOL) by causing dyspnea, shortness of breath, activity intolerance, and chest pain (Lombardi et al., 2010).

The treatment goal for patients with MPEs is to provide relief of symptoms, consequently increasing QOL (Sabur et al., 2013). Several methods are available to treat MPEs. Most treatments involve draining the fluid and preventing reaccumulation (Lombardi et al., 2010). The standard treatment is pleurodesis in which a sclerosing agent is injected, causing scarring and preventing MPE recurrence. An alternative and increasingly used therapy is indwelling pleural catheters (IPC) in which patients and caregivers can drain fluid as needed (Fleming, Alvarez-Secord, Von Gruenigen, Miller, & Abernethy, 2009). No treatment method has shown a superior control of symptoms for a reasonable duration of time. A review of the literature was conducted to identify and summarize management strategies contributing to symptom relief and increased QOL. The following medical subject heading (MeSH) phrases were used: “pleural effusion, malignant/complications” OR “pleural effusion, malignant/drug therapy” OR “pleural effusion, malignant/prevention and control” OR “pleural effusion, malignant/radiotherapy” OR “pleural effusion, malignant/rehabilitation” OR “pleural effusion, malignant/surgery” OR “pleural effusion, malignant/therapy.” Relevant studies (N = 36) were identified through PubMed and then analyzed according to Grading of Recommendations Assessment, Development, and Evaluation, or GRADE, criteria (Atkins et al., 2004).
permeability and leakage of vascular fluid (Lombardi et al., 2010); as a result, fluid accumulates in the pleural space. Symptoms of MPEs include dyspnea, shortness of breath, chest pain, and other issues that decrease functional status.

Current Therapies

Ideal management of MPEs should lead to symptom relief and improved QOL, given the poor prognosis of patients with MPEs. Procedures that contribute to improved QOL have immediate symptom relief (particularly of dyspnea), minimal side effects, and low rates of recurrence, as well as require the least amount of time spent in the hospital or clinic (Thomas & Musani, 2013). Patients’ performance status, life expectancy, social support, and wishes for treatment must also be high priorities when determining the best treatment strategy.

Managing MPEs usually begins with thoracentesis (Hunt et al., 2012) in which fluid is removed from the pleural space via needle, allowing lung re-expansion. An ultrasound, chest x-ray, or chest computed tomography scan is done prior to thoracentesis to confirm the presence and location of the effusion (Heffner, 2015). Thoracentesis is performed to relieve symptoms, as well as to collect fluid samples for cytologic evaluation to identify malignant etiology (Hunt et al., 2012). Thoracentesis procedures may also be used to evaluate for lung entrapment and whether symptoms are relieved by fluid drainage. Although thoracentesis is successful in relieving symptoms, the fluid reaccumulates within 30 days in most cases (Lombardi et al., 2010). Thoracentesis also does not achieve long-term control of the effusion or symptom relief. In addition, it presents a risk for infection, adhesions, puncture of the lung, and loculations, which are thick fibrin layers within the pleural space that create pockets of fluid and make draining and administering a sclerosing agent difficult (Lombardi et al., 2010; Okur et al., 2011). Multiple thoracenteses are not generally recommended, but they may be considered in patients who have a life expectancy of less than three months and cannot tolerate a more invasive treatment method (Lombardi et al., 2010).

Pleurodesis is another procedure that may be performed to prevent fluid reaccumulation and is considered the standard treatment for MPEs despite its adverse effects (Lombardi et al., 2010). During the procedure, a sclerosing agent is injected into the pleural space to cause inflammation, which results in adhesion of the pleural layers, preventing fluid accumulation (Lombardi et al., 2010; Thomas & Musani, 2013). With pleurodesis, symptoms of breathlessness are often relieved. Various sclerosing agents have significantly wide-ranging success rates, including interferon alpha-2b (Intron® A) (62%-100%), povidone-iodine (Betadine®) (64%-96%), t alc (70%-100%), and paclitaxel (Taxol®) (85%-93%) (Zarogoulidis et al., 2013).

The methods of pleurodesis have been refined and narrowed down to thorascopic pleurodesis via video assistance and chest tube pleurodesis (Thomas & Musani, 2013). Pleurodesis has demonstrated high success rates (as much as 75%-95% in some studies), but it often is associated with lengthy hospital stays, repeated interventions, symptoms (e.g., fever, chest pain), and recurrence of the MPE (Hunt et al., 2012; Thomas & Musani, 2013). Studies have revealed recurrence rates of as much as 50% by six months postprocedure (Fysh et al., 2012). With pleurodesis often involving prolonged hospital stays, high recurrence rates, and complications, it often is not the treatment of choice in patients with short life expectancies (Thomas & Musani, 2013).

IPCs, which are also known as tunneled pleural catheters and tunneled catheter drainage systems, are more widely used as treatments in patients with MPEs and shorter life expectancies (Tremblay & Michaud, 2006). They consist of plastic tubes inserted into the pleural space that remain in place for intermittent drainage of fluid. IPCs are popular because their insertion can be done as an outpatient procedure, and they offer immediate relief, can be controlled by patients and families, and are able to be used in patients who are not candidates for pleurodesis (Fysh et al., 2012). IPCs can also be used in patients with trapped lung syndrome—a condition in which the lung does not fully expand and that disqualifies patients for pleurodesis. IPCs also have adverse side effects (e.g., infection, protein depletion), and the high cost of the procedure may be a deterrent (Fysh et al., 2012). Although IPCs do not work when the pleural space has loculations, intrapleural (IP) fibrinolytics (e.g., streptokinase) have been used as a treatment option to manage loculations (Okur et al., 2011). IP fibrinolytics cause lysis of the fibrinous structures in the pleural space to enhance drainage and lung re-expansion (Okur et al., 2011).

Less common therapies for MPEs are decortication, which involves resection of the lung, and pleuropertitoneal shunting, which involves the placement of a pump (Denver shunt) or passive drain (LeVeen shunt) to allow for fluid drainage from the pleural space into the peritoneal cavity (Thomas & Musani, 2013). See Zarogoulidis et al. (2013) for a common algorithm used in choosing a treatment method.

Discussion

Pleurodesis, specifically with talc slurry, has been the standard treatment for MPEs. IPCs have become the treatment of choice because they are associated with shorter hospital stays, immediate symptom relief, and few complications. The literature review reflected the increasing use of IPCs and included eight studies analyzing the effects of IPCs, five of which compared IPCs to talc pleurodesis (TP). Overall, IPCs were found to be linked with significant symptom improvement, better effusion control, reduction in hospital days, fewer complications, lower rates of recurrence, and increased QOL. The relevant literature also showed that IPCs had higher rates of pleurodesis, as well as that IPCs demonstrated efficient effusion control and significant symptom improvement.

One difficulty that arose when comparing studies was the variety of terms used for reporting successful effusion control and symptom control. Some studies measured success by a designated interval of time before the effusion recurred. Other studies measured success as a percentage of effusion reduction (i.e., complete response equals total disappearance of the effusion). The highest rate of effusion control and symptom improvement was in a well-designed pre- and post-test study of IPCs (Tremblay & Michaud, 2006). It demonstrated that 88% of patients had significant to total improvement in symptoms after only
two weeks and experienced low rates of recurrence, giving IPCs an overall success rate in about 90% of patients (Tremblay & Michaud, 2006). The most common significant difference in studies comparing IPCs to TP was the length of hospital stay. In the studies reviewed, patients with IPCs spent significantly less time in the hospital; the range of hospital days for patients with IPCs was 1–3 days as compared to 4.5–10 days for patients with TP. Patients with IPCs also incurred fewer complications than patients with TP in every study except one. The most common complications for patients with IPCs were loculations in which the drain had to be removed or a fibrinolytic agent instilled through the catheter (Davies et al., 2012). Complications among the TP group were more widespread (Fysh et al., 2012). In all reviewed studies comparing patients with IPCs to patients with TP, patients with TP had higher recurrence and re-intervention rates.

In two studies using pleurodesis with povidone-iodine combination, a high success rate was demonstrated (Caglayan et al., 2008; Mohsen et al., 2011). However, in a study comparing pleurodesis with povidone-iodine via chest tube and small-bore catheter, complications occurred in about one-third of both groups (Caglayan et al., 2008). Compared to TP, the povidone-iodine combination has similar success rates but with fewer complications and significantly less length of hospital stay (Mohsen et al., 2011). In a study comparing IP fibrinolytics to pleural drainage only before TP, IP fibrinolytics led to better drainage rates, high rates of pleurodesis and lung re-expansion, and low rates of recurrence (Okur et al., 2011). IP fibrinolytics had lower complication rates and led to greater lung re-expansion (Okur et al., 2011).

In studies using IP cisplatin (Platinol®) to control MPEs, one study demonstrated that IP cisplatin and OK-432 (picibanil) followed by hyperthermotherapy were more effective in controlling MPEs and had fewer side effects (Chen et al., 2012). In another study, the combination of IP cisplatin and bevacizumab (Avastin®) was compared with IP cisplatin alone (Du et al., 2013). The drawback to this combination was a significantly higher rate of hypertension in the group taking the combination of IP cisplatin and bevacizumab (Du et al., 2013). A study involving single-incision pleurectomies showed a high success rate and no recurrences (Kara et al., 2013); however, the study had a small sample size and vague results. QOL was shown to improve with symptom improvement and effusion control (Demmy et al., 2012; Fysh et al., 2012; Sabur et al., 2013). Six studies measured QOL improvement, and all demonstrated significant improvement after MPE intervention with no major differences noted among intervention types.

**Conclusion**

MPEs often occur among patients with advanced cancer and short life expectancy. Treatment for MPEs should be aimed at palliation, leading to immediate symptom relief and improved QOL. The ideal treatment strategy should have minimal side effects, require little to no time in the hospital, and have low rates of recurrence. Although IPCs are widely used for MPE management, TP continues to be considered as the first-line treatment (Thomas & Musani, 2013). No standardized protocol exists for palliating MPEs (Lombardi et al., 2010). This literature review revealed that many management options for MPEs exist, as well as that they continue to be tested. Studies that measured the impact of interventions on QOL demonstrated that any treatment method improves QOL. Just one study found that, compared to TP, IPCs significantly improved QOL (Sabur et al., 2013). IPCs were also found to have better success rates with fewer complications and recurrences; in addition, IPCs can be performed on an outpatient basis. These results support the increasing use of IPCs for managing MPEs. IPCs are not effective in the presence of loculations. However, IP fibrinolytics were shown to have high success rates and increase the effectiveness of pleural drainage, but their instillation must be an inpatient procedure. Research is needed regarding the effectiveness of IP fibrinolytics prior to IPCs.

Many obstacles exist to conducting research involving people with advanced cancer and poor prognoses. However, future research should continue to focus on management strategies that can be administered on an outpatient basis and lead to immediate symptom improvement and improved QOL.

**References**


Tremblay, J., & Michaud, A. (2006). The drawback to this combination was a significantly higher rate of hypertension in the group taking the combination of IP cisplatin and bevacizumab (Du et al., 2013). A study involving single-incision pleurectomies showed a high success rate and no recurrences (Kara et al., 2013); however, the study had a small sample size and vague results. QOL was shown to improve with symptom improvement and effusion control (Demmy et al., 2012; Fysh et al., 2012; Sabur et al., 2013). Six studies measured QOL improvement, and all demonstrated significant improvement after MPE intervention with no major differences noted among intervention types.


