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Individualised management of malignant pleural effusion

Malignant pleural effusion (MPE) is a potentially debilitating disorder in which cancer (commonly of the breast or lung) causes accumulation of fluid in the pleural cavity. MPE often results in severe breathlessness, which can be improved by pleural drainage procedures. As a result of the increasing global cancer prevalence and more effective, better tolerated, systemic therapies, the burden of MPE is rising. An increasing number of high-quality, suitably powered randomised trials in MPE have begun to provide a robust evidence base for some of the treatment approaches available.\(^1\)\(^-\)\(^3\) Therefore, dedicated pleural services, providing a wider range of management strategies, including indwelling pleural catheters (IPC) and local anaesthetic thoracoscopy, are becoming widespread.

Because of the expansion of these alternative treatment options, the traditional approach of admitting all patients with MPE for a chest drain and pleurodesis is now outdated. Ambulatory management can be a realistic and appealing treatment strategy for many patients.

Inflammation seems to have a crucial role in MPE by contributing to both morbidity and mortality. Markers of both systemic inflammation (eg, blood neutrophil-lymphocyte ratio)\(^4\)\(^-\)\(^6\) and localised pleural inflammation (eg, pleural fluid lactate dehydrogenase)\(^4\)\(^,\)\(^6\) are associated with a worse prognosis. These findings have led to a need for more accurate prognostic methods to assist clinicians and patients in selecting the most appropriate treatment. Several prognostic scores exist for patients with MPE associated with pleural mesothelioma, which although complex to calculate, can help to predict an individual’s survival.\(^7\)\(^,\)\(^8\)

International collaboration has led to the development of the LENT prognostic score for all cell types of malignant effusions. This score combines markers of local and systemic inflammation along with tumour type and Eastern Cooperative Oncology Group (ECOG) performance score and can help predict survival more accurately than performance status alone.\(^9\) In those patients with the highest scores, treatment could be best focused on symptom control and end-of-life care in the community rather than attempting to achieve a definitive pleurodesis. The LENT score requires more widespread validation and impact analysis before its routine clinical use. However, it has the potential to improve the information available to clinicians during the early assessment of patients with MPE and assist appropriate recruitment to clinical trials.

Localised pleural inflammation is also essential for successful pleurodesis through the formation of adhesions and fibrosis that obliterate the pleural cavity; however, pleural inflammation could also contribute to side-effects such as pain and fever after administration of intrapleural sclerosants. Even within the context of large randomised trials, pleurodesis success rates remain lower than 80%,\(^1\)\(^,\)\(^2\) which has led to the search for more effective treatments and modes of delivery. The potential of harnessing the host immune response to induce pleural inflammation has led to the study of intrapleural bacterial moieties including Corynebacterium parvum, Lipoteichoic Acid-T, and Streptococcus pyogenes (OK-432), with varying degrees of success.\(^9\)\(^-\)\(^1\)\(^1\)

IPCs are increasing in popularity and offer a cost-effective long-term outpatient management strategy for patients with MPE. Findings from the Therapeutic Interventions in the Malignant Effusions-2 trial\(^1\) showed IPCs conferred similar control of breathlessness and quality of life but significantly shorter length of hospital stay than did inpatient talc pleurodesis. IPCs also allow long-term, outpatient access to the pleural cavity, making them an ideal potential portal for local drug delivery. Instillation of sclerosants through an IPC in those patients with complete lung re-expansion is an attractive proposition, which could harness the benefits of both techniques. Trial data regarding the efficacy of this approach is awaited with interest.

There is also a role for IPCs in the context of a so-called trapped lung, whereby the lung fails to completely re-expand after drainage of an effusion. This complication affects 10–20% of patients with MPE, and those with a high pleural tumour burden (resulting in a visceral pleural rind) or a heavily loculated effusion are likely to be at highest risk. The absence of parietal and visceral pleural apposition greatly reduces the chances of pleurodesis success and potentiates the production of pleural fluid to fill the space between the pleural layers (effusion ex-vacuo), which can result in pain during pleural aspirations, rapid recurrence of breathlessness after drainages, and more limited long-term treatment options.

There is a common misconception that active effusion management in trapped lung is futile. However, pleural effusion drainage might relieve pressure on surrounding
structures and improve diaphragmatic motion, thereby enhancing respiratory mechanics and improving symptoms of breathlessness. However, trapped lung often goes under-recognised in clinical practice. The diagnosis might be suspected if a patient shows marked symptoms (chest discomfort and pain) during fluid drainage or if a post-aspiration chest radiograph shows a hydropneumothorax. Alternatively, pleural manometry, which measures the change in pleural pressure during a pleural aspiration, could be used to identify those with trapped lung and establish the extent of residual visceral pleural elasticity, although its routine clinical role is debated.12-13 Early work evaluating M-mode ultrasound to detect trapped lung has also shown some promise.14

In theory, the early identification and management of malignant effusions might help limit the formation of trapped lung by promoting complete lung re-expansion, maintaining visceral pleural elasticity, and minimising the formation of septations and loculations due to repeated invasive procedures. Specific studies assessing this concept, as well as examining improved identification techniques and management options for patients with trapped lung, are much needed to provide robust data regarding this under-researched subgroup.

A proactive approach to MPE treatment in general has several potential benefits in terms of streamlining the patient pathway and avoiding recurrent and prolonged hospital admissions. Early observational data in those with known MPE suggests that the combination of thoracoscopic talc poudrage with an IPC might be an effective management strategy, although randomised data are needed to evaluate this approach in more detail.15 Taking this idea a step further, in those with suspected MPE, a diagnostic thoracoscopy in conjunction with talc poudrage or insertion of an IPC, or both, might be an attractive one-stop approach to diagnosis and management in the future.

As the treatment options for MPE become more complex, the outcome measures used by future clinical trials need to be carefully considered. Rigorously recorded, patient reported outcome measures, such as breathlessness scales, quality-of-life scores, and patient satisfaction, are essential to ensure clinically relevant conclusions are drawn regarding the relative efficacy of the various management strategies.

Several questions remain unanswered regarding the management of MPE. In the future, more creative management strategies that combine the benefits of a few established treatments might help improve care of patients with MPE and facilitate ambulatory management. Provision of a variety of treatment approaches according to an individual’s prognosis, clinical features, and personal preferences is necessary to ensure an individualised, patient-centred approach to care.

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