Editorial

The ongoing struggle with empyema management: is surgery really the answer?

Eihab O. Bedawi[1,2], Lonny Yarmus[3], Najib M. Rahman[1,2,4]

[1]Oxford Centre for Respiratory Medicine, Oxford University Hospitals, Oxford, UK; [2]Oxford Respiratory Trials Unit, University of Oxford, Oxford, UK; [3]Division of Pulmonary and Critical Care, Johns Hopkins University, Baltimore, MD, USA; [4]NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK

Correspondence to: Dr. Eihab O. Bedawi, MRCP. Oxford Pleural Unit and Oxford Respiratory Trials Unit, Churchill Hospital, Roosevelt Drive, Oxford, OX3 8DY, UK. Email: eihab.bedawi@ouh.nhs.uk.

Provenance: This is an invited Editorial commissioned by the Section Editor Laura Chiara Guglielmetti (Cantonal Hospital Winterthur, Kantonsspital Winterthur, Winterthur, Switzerland).

Comment on: Semenkovich TR, Olsen MA, Puri V, *et al.* Current State of Empyema Management. Ann Thorac Surg 2018;105:1589-96.

Submitted Sep 26, 2018. Accepted for publication Oct 12, 2018.
doi: 10.21037/jtd.2018.10.54
View this article at: http://dx.doi.org/10.21037/jtd.2018.10.54

Despite having been described over 3,000 years ago, pleural infection continues to be a challenging condition to treat. The last decade has seen a greater understanding of the pathogenesis and microbiology of pleural infection. There are now data to suggest that although the majority of cases are related to pneumonic consolidation, the varied microbiology and radiological findings suggest that primary pleural infection is a distinct entity requiring specific attention. For reasons that remain unclear, although are postulated to relate to a shift in serotypes of aggressive pneumococcal disease (1), there has been a significant increase in the incidence of empyema across all age groups, with up to 80,000 cases a year seen in the UK and USA combined, and a 10-fold incidence increase in paediatric populations in the last 2 decades (2). Unfortunately, outcomes remain poor, with up to a 20% mortality within the first year, 20% requiring surgery due to failed medical therapy and an average hospital stay of 10 days (3). Optimal management of this condition remains undefined, and despite the presence of a number of guidelines, initial treatment (medical or surgical) remains a subject of discussion.

In this edition of the *Journal of Thoracic Disease* (*JTD*), Semenkovich *et al.* aimed to address an important question: what is the optimal management of empyema? The authors investigated current practices through a retrospective analysis of coding data on empyema hospitalisations from an impressively large database (New York State Inpatient Database) over a 5.5-year period. They should be congratulated on assembling a cohort of 4,095 patients, who were analysed for the association between initial coding recorded management and subsequent available outcomes.

In this large dataset, initial treatment varied with 67.8% undergoing chest tube placement, 18.5% undergoing video-assisted thoracoscopic surgery (VATS) treatment with the remaining 13.6% receiving an upfront thoracotomy and open decortication. Treatment outcomes were compared between groups, including success rates, readmission, reintervention and mortality, with treatment success defined as management with a single procedure during the index hospitalisation, no reintervention within 30 days and survival up to 30 days of follow up.

The data reporting on treatment "success" was significantly different according to initial treatment modality with 37% success rate in initial chest tube management, compared with 55% in the VATS group and 58% in initial open decortication. A similar pattern was seen for outcomes of reintervention and mortality, this being seen in 51% and 13% for the chest tube group, 41% and 5% for the VATS group and 36% and 6% for the initial open operation group. They conclude that surgery, in particular VATS, may have a greater role to play in improving outcomes in pleural infection.

Due to the nature of coding studies, no data is available on other potential outcome predictors in pleural infection

and therefore key parameters, which influence outcomes could not be measured. The authors discuss that drawing causative conclusions from retrospective, non-randomised data (an administrative coding database) is problematic. It is therefore crucial to note that this study should inform readers about clinicians' behaviour rather than the relative efficacy of each treatment modality.

It is not immediately clear why the initial chest tube treatment failure rate (in 63%) is higher in this study than that demonstrated in the placebo arms of large randomised controlled trials of pleural infection, where failure occurs in around 30% (4). From this dataset, it is impossible to determine the intent of initial chest tube placement (i.e., intended definitive treatment, an adjunct for fibrinolytics, a temporary source control measure or a bridge to a definitive operation as a result of a patient or resource limitation). These subgroups are likely to have significant variations and therefore it is difficult to draw any further conclusions from the data relating to this group. An important additional finding from this study is that pleural infection remains a very significant health burden—median hospital stay was at least 9 days in these patients, even in those who had initial treatment with VATS or open thoracotomy, emphasising the healthcare burden of this condition.

The results in this study on success rate from VATS and open surgery are impressive in terms of treatment success, with fewer requiring reintervention and lower mortality. Should we then conclude that surgical treatment is clearly the "optimal" first line management strategy? Analysis of the demographic tables demonstrate that those undergoing more invasive surgery were younger with fewer comorbidities, had lower frequency of septicaemia and lower frequency of shock, strongly suggesting that selection bias is operating and may be the cause of the apparent differences seen in the treatment groups. The median age of the VATS group in this study was 56, compared with 64 in the chest tube group (P<0.001), and interestingly is significantly below the median age of 61 years seen in an unselected and well-documented UK sample of 454 participants diagnosed with pleural infection (4). An additional difficulty in appraising surgical treatment success with regard to pleural infection, which the authors allude to, is the variability of practice and patient selection between surgeons and the lack of agreed quality standards (5).

In recent years, pleural infection management has been revolutionized by the advent of intrapleural fibrinolytic therapy with tissue plasminogen activator (tPA) and deoxyribonuclease (DNAse) (6). Although not possible in this dataset, it would have been interesting to see how prevalent this practice was amongst the New York cohort, and to assess any influence on results. Multicentre case series have suggested that this treatment can successfully treat over 90% of patients with pleural infection that 'fail standard treatment' with a chest tube alone (7). The major advantage of this treatment is that it can be given through a small-bore chest tube, with minimal pain for patients and applicable across a wider patient group without the anaesthetic and intraoperative risks associated with surgery. Recent studies have assessed other, less invasive methods of 'medically' treating pleural infection with chest tube and saline irrigation (8) showing positive results, and another study of local anaesthetic thoracoscopy drainage delivered by the physician currently ongoing.

The results of the current study highlight the important fact that mortality rates remain unacceptably high, with 20% 30-day mortality in the chest tube cohort. Early provision of a single definitive treatment is likely to provide the best chance of successful recovery before the empyema reaches the organised phase. Their finding that only 53% of patients overall were treated with a single procedure demonstrates the complexity of treatment of this condition, but adds support to the notion that large prospective randomised trials are urgently required to determine optimal initial treatment. It is possible that a cohort of patients would benefit from early surgery; however, a recent Cochrane review suggested that there is no statistically significant difference in mortality between primary surgical and non-surgical management of pleural empyema for all age groups. A key issue is the ability to stratify patients in terms of risk at presentation, who might therefore benefit from aggressive treatment. Data from the PILOT study due to be published later this year are likely to provide a needed evidence-based approach to support these treatment decisions (9).

It is noteworthy that from a patient's perspective, there is a significant difference between being offered antibiotics and a small chest tube insertion under local anaesthetic versus a major operation. The disadvantages of surgical drainage are substantial and surgical thoracic procedures carry associated anaesthetic/perioperative risks, with a quoted mortality of approximately 2% and major complication rate of approximately 8% in reported VATS series (10). Whilst VATS drainage is associated with a significantly lower rate of adverse events, 4% of patients still experience significant pain at 2 years (11). In this paper, 15% of VATS procedures required conversion to open

thoracotomy, which is highly useful data reflecting current practice, and can be used to inform patients and clinicians of the likely outcome of VATS. However, it should be noted that the literature variably reports conversion rates of up to 59% (12-14).

Semenkovich *et al*. are correct to consider early delivery of aggressive treatment as a potential factor in improving patient outcomes. However, it is worth noting the time to intervention was lowest in the chest tube group, compared to VATS and open surgery (P<0.001). It is therefore not surprising that current guidelines encourage chest tube drainage as the initial treatment step, and suggests that early access to thoracic surgery is often an obstacle. Patients were more likely to receive VATS than open operation in larger hospitals with >300 beds (P<0.001), indicating that surgical expertise is variable and may represent a barrier. Two prospective, randomised trials in children compared VATS with intrapleural fibrinolytics and showed no therapeutic or recovery advantage, at a significantly lower cost in the latter (15,16).

Although surgical treatment is not be based on large randomised trials, large cohort studies have shown that in selected patients it may be associated with improved outcomes (17). It is unclear as yet which patients stand to benefit most from surgical management, and the major concern remains that this vital treatment modality is avoided in those who may need it most—including the elderly. A feasibility study is currently being planned to understand patients' perceptions and their acceptance of being randomised to the three evidence-based treatment options currently at the clinicians' disposal; chest tube with saline, intrapleural fibrinolytics and video-assisted thoracoscopic surgery. The important qualitative outcomes from this study will determine whether a larger multicentre RCT can be conducted to compare these treatment modalities head-to-head.

In this age of tailoring treatment to the individual patient, early surgical intervention may indeed be the answer for a selected group of patients—however, we do not know which patients these are. The practice observed in this study and likely to be mirrored in the wider community, in which the young and fit undergo early surgery, and older more comorbid patients who are likely to carry a greater risk from pleural infection receive a conservative approach, may not be correct. This is especially important given the increasing surgical and anaesthetic experience treating an ageing population. Further efforts are needed to identify pleural infection early, use all available data to risk stratify patients according to clinical risk, followed by a collaborative approach between physician and surgeon in delivering the appropriate treatment as early as possible.

Acknowledgements

None.

Footnote

Conflicts of Interest: Professor Rahman is the first author of the Intrapleural Use of Tissue Plasminogen Activator and DNase in Pleural Infection (MIST-2) study.

References

1 Byington CL, Hulten KG, Ampofo K, et al. Molecular epidemiology of pediatric pneumococcal empyema from 2001 to 2007 in Utah. J Clin Microbiol 2010;48:520-5.
2 Deceuninck G, Quach C, Panagopoulos M, et al. Pediatric Pleural Empyema in the Province of Quebec: Analysis of a 10-Fold Increase Between 1990 and 2007. J Pediatric Infect Dis Soc 2014;3:119-26.
3 Maskell NA, Batt S, Hedley EL, et al. The bacteriology of pleural infection by genetic and standard methods and its mortality significance. Am J Respir Crit Care Med 2006;174:817-23.
4 Maskell NA, Davies CW, Nunn AJ, et al. U.K. Controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med 2005;352:865-74.
5 Scarci M, Abah U, Solli P, et al. EACTS expert consensus statement for surgical management of pleural empyema. Eur J Cardiothorac Surg 2015;48:642-53.
6 Rahman NM, Maskell NA, West A, et al. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med 2011;365:518-26.
7 Piccolo F, Popowicz N, Wong D, et al. Intrapleural tissue plasminogen activator and deoxyribonuclease therapy for pleural infection. J Thorac Dis 2015;7:999-1008.
8 Hooper CE, Edey AJ, Wallis A, et al. Pleural irrigation trial (PIT): a randomised controlled trial of pleural irrigation with normal saline versus standard care in patients with pleural infection. Eur Respir J 2015;46:456-63.
9 Corcoran JP, Psallidas I, Gerry S, et al. Prospective Validation of The RAPID Clinical Risk Prediction Score in Patients with Pleural Infection: The Pleural Infection Longitudinal Outcome Study (PILOT). Am J Respir Crit

Care Med 2018;197:A7767.
10 Allen MS, Deschamps C, Jones DM, et al. Video-assisted thoracic surgical procedures: the Mayo experience. Mayo Clin Proc 1996;71:351-9.
11 Stammberger U, Steinacher C, Hillinger S, et al. Early and long-term complaints following video-assisted thoracoscopic surgery: evaluation in 173 patients. Eur J Cardiothorac Surg 2000;18:7-11.
12 Lardinois D, Gock M, Pezzetta E, et al. Delayed referral and gram-negative organisms increase the conversion thoracotomy rate in patients undergoing video-assisted thoracoscopic surgery for empyema. Ann Thorac Surg 2005;79:1851-6.
13 Luh SP, Chou MC, Wang LS, et al. Video-assisted thoracoscopic surgery in the treatment of complicated parapneumonic effusions or empyemas: outcome of 234 patients. Chest 2005;127:1427-32.
14 Solaini L, Prusciano F, Bagioni P. Video-assisted thoracic surgery in the treatment of pleural empyema. Surg Endosc 2007;21:280-4.
15 Sonnappa S, Cohen G, Owens CM, et al. Comparison of urokinase and video-assisted thoracoscopic surgery for treatment of childhood empyema. Am J Respir Crit Care Med 2006;174:221-7.
16 St Peter SD, Tsao K, Spilde TL, et al. Thoracoscopic decortication vs tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomized trial. J Pediatr Surg 2009;44:106-11; discussion 111.
17 Farjah F, Symons RG, Krishnadasan B, Wood DE, Flum DR. Management of pleural space infections: a population-based analysis. J Thorac Cardiovasc Surg 2007;133:346-51.

Cite this article as: Bedawi EO, Yarmus L, Rahman NM. The ongoing struggle with empyema management: is surgery really the answer? J Thorac Dis 2018;10(Suppl 33):S4122-S4125. doi: 10.21037/jtd.2018.10.54

