Online Appendix 2   BTS Guideline for Pleural Disease

Research Recommendations

Contents

Section A: Spontaneous pneumothorax

Recommended areas for further research for the treatment of spontaneous pneumothorax in adults:

1. Comparing conservative management with ambulatory management for the treatment of primary and (particularly) secondary spontaneous pneumothorax.

2. Stratifying primary spontaneous pneumothorax patients by risk of recurrence to maximise the benefit of early thoracic surgery.

3. Comparing needle aspiration to chest drain for secondary spontaneous pneumothorax.

4. Identifying which patient groups may benefit from elective surgical management after a first episode of pneumothorax.

5. Determining and defining the optimal management strategy for pneumothorax with persistent air leak.

6. Understanding individual patient perceptions of recurrence risk with regards to acceptability of complications and outcomes associated with different forms of surgical access.

7. Determining the optimal type of surgical pleurodesis (e.g. pleurectomy, abrasion, talc) and adjunct (e.g. bullectomy) for the treatment of spontaneous pneumothorax.

Section B: Investigation of the undiagnosed pleural effusion

Recommended areas for further research for investigating undiagnosed pleural effusion in adults:

1. Characterising the radiological features of individual non-malignant causes of pleural effusion to improve radiological assessment of non-malignant pleural effusions.

2. Determining the optimal volume required to establish "actionable cytology" based on currently available molecular profiling, in particular in relation to tumour types associated with higher sensitivity of pleural fluid cytology.

3. Determining the clinical utility of pleural fluid cytology, as defined by combined diagnostic and predictive value, in individual tumour sub-types.

4. Determining the diagnostic value of pleural fluid markers for tuberculous pleural effusion, heart failure and auto-immune pleuritis, to improve the strength of the clinical recommendations.

5. Investigating the diagnostic accuracy of serum biomarkers to diagnose pleural malignancy, pleural infection or autoimmune pleuritis.

6. Prospectively validating a consistent diagnostic cut-point for serum N-terminal pro hormone BNP (NT-proBNP) in the diagnosis of heart failure.

7. Prospectively validating serum T-spot testing in the diagnosis of tuberculous pleural effusion, which should include areas of lower TB prevalence.

8. Comparing rigid versus semi-rigid thoracoscopy to determine if one technique is superior to the other in terms of diagnostic accuracy of pleural biopsy and other clinical outcomes.

9. Investigating the role of tools such as cryobiopsy, narrow band imaging and confocal laser endomicroscopy as adjuncts to standard thoracoscopic pleural biopsies.

10. Investigating the role of image-guided closed pleural biopsy in the diagnostic pathway for patients with suspected pleural disease, particularly its use as a front-line test alongside diagnostic thoracentesis for individuals with identifiable pleural thickening or nodularity on imaging studies.

Section C: Pleural infection

Recommended areas for further research for the treatment of pleural infection in adults:

1. Assessing the potential role of radiology (ultrasound and computed tomography) in risk stratification of patients presenting with pleural infection.

2. Assessing if directed care according to RAPID scores effects clinical outcome

3. Investigating the role of radiological features (both ultrasound and CT) for predicting complicated parapneumonic effusion (CPPE), especially in patient with an indeterminate risk of CPPE or pleural infection on initial pH measurement

4. Investigating the role of novel biomarkers (in particular soluble urokinase plasminogen activator receptor (suPAR)) in pleural infection.

5. Prospectively validating novel biomarkers (in particular suPAR) for their ability to inform immediate management in parapneumonic effusion (PPE).

6. Determining if initial chest tube drainage or surgical drainage is better for the treatment of pleural infection.

7. Investigating the feasibility and role of medical thoracoscopic drainage for pleural infection.

8. Investigating the role of combination tissue plasminogen activator (TPA) and DNASe and saline irrigation for treating pleural infection in adults, specifically relating to reduced dose regimens and concurrent administration.

9. Determining the role of intrapleural irrigation compared with medical or surgical thoracoscopy in the management of CPPE and empyema.

10. Determining the optimal surgical management of advanced stage empyema with trapped lung.

11. Determining the efficacy of decortication surgery versus either drainage or debridement alone for the management of a trapped lung associated with pleural infection.

Section D: Pleural malignancy

Recommended areas for further research for diagnosing and treating pleural malignancy in adults:

1. Determining the relative roles of thoracic ultrasound, CT, MRI and PET-CT for diagnosing malignant pleural disease.

2. Assessing the diagnostic accuracy of specific MRI techniques for the diagnosis of malignant pleural disease.

3. Determining the effect of systemic therapy in patients with MPE, specifically those with treatment-sensitive tumours such as small cell lung cancer, lymphoma and hormone receptor-positive breast cancer.

4. Investigating the effect of systemic anti-angiogenesis agents in patients with MPE, specifically those with non-small cell lung cancer (NSCLC) and epidermal growth factor receptor (EGFR) mutations.

5. Assessing the factors that predict the re-accumulation of pleural fluid following an initial aspiration.

6. Determining patient and carer experience with indwelling pleural catheters (IPCs).

7. Comparing the clinical outcomes of thoracoscopy (local anaesthetic or VATS) with talc poudrage pleurodesis and chest drain with talc slurry pleurodesis in treating patients with malignant pleural effusion.

8. Assessing the clinical benefits of surgery in non-selected adult patients with malignant pleural effusion.

9. Assessing the clinical benefits of combined video-assisted thoracoscopic surgery (VATS) and indwelling pleural catheters (IPC).

10. Determining the optimum management pathway(s) for non-expanded lung.

11. Determining the optimum definition of non-expandable lung, including how radiological abnormalities relate to symptoms and outcomes.

12. Investigating the impact of talc slurry pleurodesis on patient reported outcome measures in patients with minimal non-expandable lung (e.g. <25%).

13. Determining a non-invasive method (other than pleural aspiration and a subsequent chest x-ray) for identifying non-expandable lung prior to intervention.

14. Determining the use of intrapleural fibrinolytics to manage symptomatic loculations in patients with septated malignant pleural effusion, especially in the ambulatory patient group.

15. Investigating the surgical management of patients with septated malignant pleural effusion.

16. Comparing the risks and benefits of indwelling pleural catheter daily drainage and symptom-based drainage for managing patients with malignant pleural effusion.

17. Comparing long term pleurodesis outcomes and quality of life between outpatient talc administered via IPC and inpatient talc pleurodesis.

18. Assessing the clinical effects of novel intrapleural anti-cancer agents in combination with standard care systemic anticancer treatment for the treatment pleural malignancy.

19. Developing a prognostic score that predicts pleurodesis success and investigating if prognostic scores lead to improved clinical outcomes in patients with malignant pleural effusion.