TIME to change: management of pleural disease

S19 INTERVENTIONS FOR THE MANAGEMENT OF MALIGNANT PLEURAL EFFUSIONS

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10.1136/thoraxjnl-2015-207770.25

Aims Malignant pleural effusion (MPE) is a common clinical problem and a number of treatment options are available to manage these patients.

We undertook a systematic review of the literature and meta-analysis in order to ascertain the optimal management strategy for adults with symptomatic MPE.

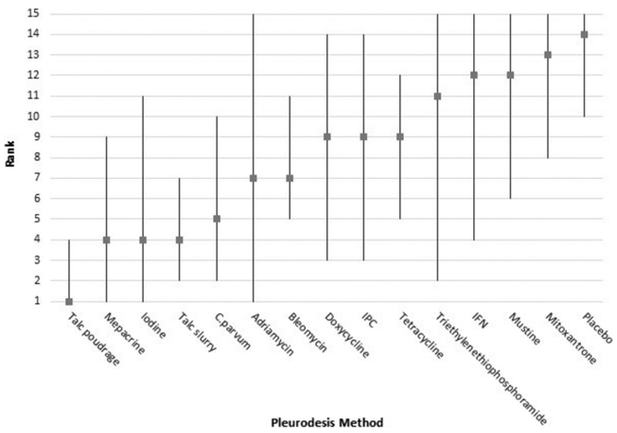
Methods We searched CENTRAL, MEDLINE, EMBASE, CINAHL; SCI-EXPANDED and SSCI (ISI Web of Science) databases to May 2015. We included randomised controlled trials of intrapleural interventions for adults with symptomatic MPE. Two review authors independently extracted the data and assessed the studies' risk of bias.

The primary outcome measure was pleurodesis failure rate. Secondary outcome measures were adverse effects and complications, patient reported control of breathlessness, quality of life, cost, mortality, duration of inpatient stay and patient acceptability.

We performed network meta-analysis with random effects to analyse the primary outcome data and those secondary outcomes with enough data. If this was not possible, we reported the results by narrative synthesis.

Results Of the 1888 records identified, 62 randomised trials, including a total of 3428 patients, were eligible for inclusion. All studies were at high risk of bias for at least one domain and the majority were unblinded.

Network meta-analysis evaluating the rate of pleurodesis failure suggested Talc Poudrage to be the most effective method (estimated rank 1 [95% CI 1, 4]). The estimated ranks of the other evaluated methods are shown in the Figure. The estimates were imprecise as evidenced by the wide credible intervals. Both statistical and clinical heterogeneity was high.



Abstract S19 Figure 1 Estimated ranks (95% Cr-I) for each of the pleurodesis methods from the main network meta-analysis

The secondary outcomes were inconsistently reported. Network meta-analysis was only performed for pain, fever and mortality and minimal evidence was obtained suggesting differences between treatments for these outcomes. Indwelling pleural catheters were examined in two RCTs, both reporting improved breathlessness when compared to Talc Slurry pleurodesis, despite lower pleurodesis success rates.

Conclusions Based on the available evidence, Talc Poudrage may be the optimal method for obtaining a pleurodesis in MPE. However, there is minimal evidence to suggest large differences between the next most effective methods. Global experience of these agents and their adverse events must also be considered when selecting a sclerosant.

S20 PRIMARY RESULT OF THE 1ST THERAPEUTIC INTERVENTIONS IN MALIGNANT EFFUSION (TIME1) TRIAL: A 2 × 2 FACTORIAL, RANDOMISED TRIAL OF CHEST TUBE SIZE AND ANALGESIC STRATEGY FOR PLEURODESIS IN MALIGNANT PLEURAL EFFUSION

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10.1136/thoraxjnl-2015-207770.26

Background Optimal management of pleurodesis for malignant pleural effusion (MPE) has not been defined either in terms of optimal analgesia or chest tube size. Non-steroidal anti-inflammatory drugs (NSAID) are highly effective analgesics, but are avoided in pleurodesis as they may reduce pleurodesis efficacy. Smaller (<14 French) chest tubes may be less painful compared to larger chest tubes, but their efficacy in MPE pleurodesis has not been proven. This study investigated chest tube size (large versus small) and analgesia (NSAID versus opiate) in this setting.

Methods A 2 × 2 factorial, phase 3 randomised controlled trial in 320 patients with MPE undergoing pleurodesis. Patients were randomised to opiate/NSAID and 24 French drain/12 French drain. Co-primary outcomes were; pain while tube *in situ*, measured on 100 mm visual analogue scale (VAS) over 5 days (superiority comparison) and pleurodesis efficacy at 3 months (non-inferiority comparison, margin of non-inferiority 15%). Secondary outcomes included use of rescue analgesia, pleurodesis success to 6 months, adverse events and mortality.

Results 320 patients were randomised (63% male, mean age 71.8 years), with similar baseline characteristics. Mean VAS scores in opiate and NSAID groups were similar (adjusted mean difference, -1.5 mm (95% confidence interval [CI], -5.0 to 2.0; p = 0.40). Patients receiving NSAID required more rescue analgesia (38% vs. 26%). Pleurodesis failure occurred in 33/144 (23%) NSAID patients compared with 30/150 (20%) of participants receiving opiate, meeting criteria (15%) for non-inferiority (difference 3%; (90% CI -5% to 10%)). Smaller chest tubes

were modestly less painful than larger tubes (adjusted mean difference, -6.0 mm (95% CI, -11.7 to -0.2; p = 0.04)) and were associated with a higher pleurodesis failure rate which failed to meet non-inferiority criteria (pleurodesis failure 15/50 (30%) and 12/50 (24%) respectively, difference 6% (90% CI, -9% to 20%)). Adverse events did not differ between analgesic groups, but complications during insertion occurred more commonly with smaller drains (adjusted odds ratio, 1.91; 95% CI 0.71 to 5.13, p = 0.20).

Conclusion NSAID and opiate analgesia were not significantly different in treatment of post-pleurodesis pain and neither was associated with impaired efficacy of pleurodesis. Smaller chest tubes were associated with less pain, but may be associated with reduced pleurodesis success compared with larger tubes. These results challenge current guidelines for pleurodesis of MPE, which advocate avoidance of NSAID and use of small chest tubes.

S21 EARLY CONTRAST ENHANCEMENT: A PERFUSION-BASED MAGNETIC RESONANCE IMAGING BIOMARKER OF PLEURAL MALIGNANCY

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10.1136/thoraxjnl-2015-207770.27

Introduction and objectives Radiological detection of pleural malignancy (PM) remains challenging. In early-stage Malignant Pleural Mesothelioma (MPM) a pleural effusion may be the only significant abnormality, indistinguishable from benign asbestos-related pleural effusion (BAPE). PM is associated with neovascularisation. We report the diagnostic performance of a novel perfusion-based Magnetic Resonance Imaging (MRI) biomarker of PM – Early Contrast Enhancement (ECE).

Methods 24 patients with suspected PM were recruited prospectively. All underwent contrast-enhanced Computed Tomography (CT) scanning, 3T Pleural MRI and Thoracoscopy.

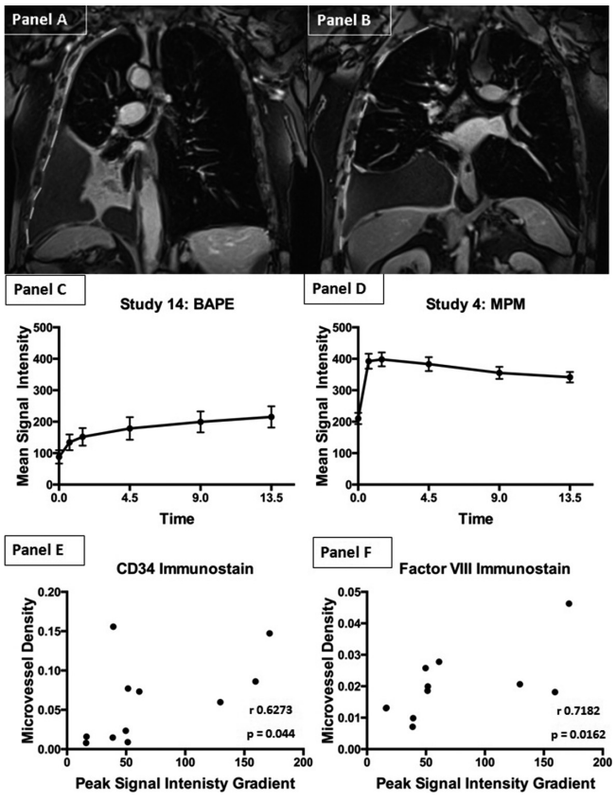
18/24 had complete MRI examinations: T1-weighted 3D-spoiled-gradient-echo sequences acquired at baseline, 40 s, 80 s and 4.5, 9 and 13.5 min after intravenous Gadobutrol contrast. Mean signal intensity (SI) of representative parietal pleura was derived from 15 regions of interest placed by two respiratory physicians. ECE was defined objectively by an early peak in mean SI (≤4.5 min) on the resulting SI/time curve (Figure 1). Morphology suggestive of PM on CT and MRI was recorded by two thoracic radiologists. Diagnostic performance and inter-observer agreement for ECE, MRI and CT morphology were compared. All analyses were blinded.

Pleural SI data were correlated against Microvessel Density (MVD) measured in paraffin-embedded pleural biopsies stained with CD34 and Factor VIII immunostains.

Results Mean patient age was 73 (SD 8) years. 18/24 were asbestos-exposed and 12/18 had pleural thickening ≤5 mm. ECE was present in 10/11 patients with PM (MPM (n = 10); lung cancer (n = 1)). The false negative case had MPM. ECE was absent in 6/7 patients with benign pleural disease (BAPE (n = 4), fibrothorax (n = 2), TB (n = 1)). The false positive case had TB.

Overall diagnostic accuracy of ECE, MRI and CT morphology: sensitivity 91%, 91%, 90%; specificity 86%, 71%, 50%; negative predictive value 86%, 83%, 80%; positive predictive value 91%, 83%, 69% respectively. Inter-observer agreement was 0.766 for ECE, 0.727 for MRI and 0.753 for CT.

Figure 1 shows the relationship between MVD and Pleural SI.



Abstract S21 Figure 1 Example of 3D T1-weighted Pleural MR images acquired 4.5 minutes post-Gadobutrol in 2 different patients – one with BAPE (Panel A) and one with early-satge MPM (Panel B). Panels C and D show the accompanying partietal pleura SI/time curves for each patient (Panel C: patient with BAPE – ECE absent, panel D: patient with MPM – ECE present). Panels E and F demonstrate the relationship between peak signal intensity gradient in patients with pleural malignancy and Microvessel Density measured in diseased tissue with CD34 immunostain (Panel E) and Factor VIII immunostain (Panel F)

Conclusions ECE appears an accurate and reproducible, perfusion-based, objective biomarker of PM, out-performing subjectively-defined CT and MR morphology. ECE assessment can be performed in patients with minimal pleural thickening, suggesting potential utility as a biomarker of early-stage MPM or low-volume metastatic PM.

S22 VATS FOR PRIMARY SPONTANEOUS PNEUMOTHORAX – A COHORT STUDY OF 1415 PATIENTS

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10.1136/thoraxjnl-2015-207770.28

Background Video-assisted thoracic surgery (VATS) is an increasingly common treatment for recurrent or persistent primary spontaneous pneumothorax (PSP). Surgery usually involves a diffuse treatment of the pleura and possible targeted surgical techniques on areas of bullous disease. There is no robust evidence to guide the use of specific surgical techniques. The purpose of this large observational cohort study was to examine the recurrence rates associated with VATS and identify predictors of outcome.