Result AHI was compared to %T<90% (figure 1) showing a moderate positive correlation ($r=0.6$). Subgroup analysis demonstrated a moderate correlation in the severe group ($r=0.67$), whereas only a very weak correlation in the moderate and mild groups ($r=0.19$ and 0.16 respectively). There was no significant difference in the %T<90% in the moderate group compared to those with an AHI 30–60 (mean (SD) 14.86 (20.15) and 17.96 (17.91) $P=0.067$) despite these patients having different categories of OSA severity.

Conclusion This study suggests that AHI inadequately reflects degree of hypoxic burden, and therefore is an incomplete measure of OSA disease severity. The results demonstrate patients with moderate OSA have a burden of hypoxia similar to many of those with severe disease. In these patients, AHI may inadequately reflect the risk of future complications resulting from hypoxia. Further research is needed to develop an alternate measure of severity to accurately reflect this risk, a composite of AHI and hypoxic burden would be a first step.

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Probing the pleural space

S11 METABOLOMIC ASSESSMENT OF PLEURAL EFFUSIONS (MAPLE)

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Introduction Literature reports of pleural fluid analysis can be found from the late 19th century onwards. Yet, despite nearly 150 years of practice, pleural fluid analytic tests remain

Abstract S11 Figure 1 A - Principal Component Analysis (PCA) shows PC1 and 2 explaining 28.7% and 11.3% of the variance, respectively. Ellipses represent 95% CI for each sample class; B - Hierarchical Cluster Analysis (HCA) of the top 25 features, using a Euclidean distance model, shows clear clustering of benign asbestos pleural effusions (BAPE) and separation from malignant pleural effusions (malign); C - Receiver operator Curve (ROC) and box and whisker plot of the feature '368.898' (2-benzyl-3-iodopropanoic acid) with an AUC of 0.914 (CI 0.847–0.971); D - Multivariate ROC analysis showing 6 models from 3 to 99 features. Model 1 includes 3 features achieving an AUC of 0.929 (CI 0.834–0.986)

relatively limited in diagnostic accuracy, leading to requirements for further investigations and uncertainty for physician and patient.

Metabolomics combines high-resolution mass spectrometry and multivariate statistical analysis, characterising thousands of compounds within a biological sample. It is ideal for biomarker discovery and elucidation of underlying disease processes, yet few studies have applied metabolomic approaches to pleural disease. However, recent pilot work has demonstrated distinct metabolomic 'features' between malignant and non-malignant pleural effusions.

Methods 121 pleural fluid samples from a repository held at North Bristol NHS Trust underwent metabolomic analysis using flow-infusion electrospray-mass spectroscopy (FIE-MS) at the Institute of Biological, Environmental and Rural Sciences (IBERS) at Aberystwyth University. The pathologies were: mesothelioma, malignancy (all subtypes), and benign asbestos related pleural effusion (BAPE). The resultant data were analysed using the online platform Metaboanalysis 4.0. Partial Least Squares Discriminant Analysis (PLSDA) was used for feature selection based on our criteria of Variable Importance Projections (VIP) greater than 2. Data were then sub selected using these features, and analysed using Principal Component Analysis and Hierarchical Cluster Analysis (HCA). Biomarker potentials of these chosen metabolites were then assessed using AUC-ROC curves.

Results Of 108 identified features, 15 were able to differentiate BAPE from malignant effusions with AUCs of >0.81. The most discriminatory feature, 2-benzyl-3-iodopropanoic acid, a metabolite of uncertain clinical significance found more abundantly in malignant effusions than BAPE, was able to distinguish malignant pleural effusions from BAPE with an accuracy of 91%. When combined with up to 10 other features in a panel of markers, this diagnostic accuracy increases to 98%.

Conclusions We have identified many promising metabolomic features which demonstrate high accuracies in differentiating malignant effusions and BAPE. These features have the potential to be developed into future clinical diagnostic biomarkers of pleural disease, and may further our understanding of the disease processes leading to pleural effusion formation. Validation of these findings and identification of the specific metabolites is underway.

S12

PAI-1 IS THE PREDOMINANT BIOLOGICAL FACTOR ASSOCIATED WITH SEPTATION FORMATION IN PLEURAL INFECTION

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Introduction Plasminogen Activator Inhibitor-1 (PAI-1) plays an essential role in the pathogenesis of lung and pleural injury. PAI-1 levels in pleural infection have been shown to be significantly elevated compared to malignant pleural effusions and heart failure. A significant variation was seen in levels of PAI-1 protein and activity in the pleural fluid from participants with pleural infection recruited to the MIST-2 study. Rabbit models of pleural injury have demonstrated that, along with other pro-inflammatory cytokines, PAI-1 is an important contributor to impaired fibrin clearance and subsequent pleural loculation. To date, this has not been studied in the context of prospectively collected pleural fluid samples from patients with confirmed pleural infection and documented baseline ultrasound septation status.

Methods Pleural fluid samples (n=214) prospectively collected from patients recruited to the Pleural Infection Longitudinal Outcomes study (PILOT) were analysed. Protein measurement assays were performed using a commercial Luminex assay for Serpin E1/PAI-1 (Luminex high performance assay, R&D) as analyte of interest in addition to TNF-alpha, MCP-1/CCL-2, IFN-gamma, urokinase plasminogen activator (uPA) and D-dimer. The independent samples T-test was used to compare mean values for each protein between two groups (septated vs non-septated). A multinomial regression model was performed to assess the independent predictive ability for each protein to septation status as an outcome.

Results Complete ultrasound data was available for 166 cases, and these were used in the final analysis. There was a significant difference in the PAI-1 levels between the septated group (n=122; mean=1790.59 ng/mL, SD=2027.28) and non-septated group (n=44; mean=948.82ng/mL, SD=911.41); t(166)=2.65, p=0.009 (Normal ref 2–46 ng/mL). In the multinomial regression model, PAI-1 was the only significant independent predictor of septation status (β =0.000, p=0.003).

Abstract S12 Figure 1

Conclusion These data confirm that whilst several biological factors may contribute to impaired fibrinolysis and subsequent septation formation in pleural infection, PAI-1 appears to be the most important. These data imply that PAI-1 is likely to be the most useful target for further studies involving intra-pleural fibrinolytic therapy in pleural infection. Further work assessing the effect of baseline PAI-1 levels on clinical outcomes in this dataset is ongoing.