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).

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 intrapleural fibrinolytic therapy in pleural infection. Further work assessing the effect of baseline PAI-1 levels on clinical outcomes in this dataset is ongoing.