

Background: Malignant pleural effusion (MPE) is a common condition that indicates advanced malignancy as it signals incurability, shortened life expectancy, and severely compromised quality of life. While MPE incidence is increasing worldwide, the discovery of prognostic biomarkers remains an unmet clinical need.

Objective: To address that clinical call we designed a study to discover, validate and prospectively assess prognostic and therapeutic biomarkers for MPE and develop score that combines pleural fluid biology with clinical and radiological data.

Methods: Five separate and independent patient cohorts (TIME-1, TIME-2, TIME-3, SIMPLE and Pleural Biobank), from previous clinical trials, have been used in order to establish a prognostic and therapeutic score for MPE. We considered clinical, radiological and biological factors as candidate variables. We assessed performance using both internal and external validation.

Results: A high throughput mass spectrometry was applied to screen samples of the TIME-2 database for differential protein expression between the groups with differences in survival and pleurodesis outcome. Three databases (TIME1,2,3) were used for the validation of the protein expression. Data from 435 patients was used to develop the PROMISE score, which includes eight variables. Internal validation using bootstrap resampling and external validation using 161 patients (SIMPLE and biobank) both suggested good discrimination (c-index 0.78 and 0.89 respectively). In addition, external validation shows the model is well calibrated.

Conclusions: We managed to develop and prospectively validate a prognostic score for MPE patients to estimate risk of 3-month mortality