The analytical and clinical aspects pleural fluid analysis

Etiological diagnosis of pleural effusion (PE) remains a challenge for clinicians. Although thoracoscopy has high diagnostic accuracy in patients with undiagnosed PE, it has some limitations, such as invasiveness and the requirement for special training. Pleural fluid analysis shows a high diagnostic accuracy in undiagnosed PE. Compared with thoracoscopy, pleural fluid analysis has the advantages of noninvasiveness, low cost, no requirement for special training, and objectivity. PE can be categorized into transudate and exudate according to the underlying etiology. Transudates are caused by systemic disorders, such as cardiac failure and liver cirrhosis, and exudates are associated with local inflammation of the pleura. The first step in the etiological diagnosis of pleural effusion is separating transudates from exudates. The landmark work in separating exudates and transudate is the Light's criteria (1). The most common causes of exudate are malignancy, pneumonia, and tuberculous pleurisy. Additional biomarkers beyond the Light's criteria are needed to verify the underlying causes of exudate. In this special series of pleural fluid analysis, some issues in the pleural fluid analysis were discussed.

The diagnostic accuracy of tumor markers for malignant pleural effusion (MPE) is controversial, and the results from the available studies are always inconsistent. Consequently, systematic reviews and meta-analyses are needed to ascertain the diagnostic accuracy of a given marker. In this special series, the diagnostic accuracy of pleural endostatin for MPE was investigated by a meta-analysis. The results indicate that the endostatin's diagnostic accuracy for MPE is low (doi: 10.21037/jlpm-20-91).

Machine learning (ML) represents a novel and promising strategy for investigating the diagnostic accuracy of multiple biomarkers (2). A previous study showed that ML improved the diagnostic accuracy of conventional biomarkers for tuberculosis pleural effusion (TPE) (3). In this special series, the diagnostic accuracy of tumor markers for malignant pleural mesothelioma (MPM) was evaluated. Similar to the findings in TPE, results indicated that ML improves the diagnostic accuracy of tumor markers for MPM (doi: 10.21037/jlpm-20-90).

In patients with PE caused by cardiac failure or tuberculosis, pleural biomarkers [e.g., interleukin-27 (4) and natriuretic peptides (5)] show high diagnostic accuracy. By contrast, the available diagnostic accuracy of biomarkers for parapneumonic effusion (PPE) [e.g., C-reactive protein (6) and procalcitonin (7)] is insufficient. In addition, the role of biomarkers in the treatment monitoring of PPE remains controversial. In this special series, a comprehensive review from Lee *et al.* summarizes the current status of biomarkers in the management of PPE (doi: 10.21037/jlpm-2021-01).

The preanalytical errors in pleural fluid biochemistry remain largely unknown. For example, stored pleural fluid specimens are used in the majority of available studies, but the long-term stability of biomarkers in stored pleural fluid specimens has not been determined. In this special series, Kopcinovic and Culej review the preanalytical factors that can affect the reliability of pleural fluid analysis (doi: 10.21037/jlpm-2021-02).

Taken together, this special series focuses on the analytical and clinical aspects of pleural fluid analysis, with the overall aim of providing novel insights into the field of pleural fluid analysis for both clinicians and laboratory specialists.

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