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EDITORIAL – THORACIC ONCOLOGY

The C-Reactive Protein/Albumin Ratio May Predict the Long-Term Outcome in Patients with Malignant Pleural Mesothelioma

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Malignant pleural mesothelioma (MPM) is one of the most lethal neoplasms. To address survival benefit, multimodal treatment with extrapleural pneumonectomy (EPP),[1] chemotherapy,[2] and radiotherapy[3] was conducted in accordance with the stage of the disease. Despite recent advances in the above treatments, the long-term outcome of MPM remains insufficient. Furthermore, it is inconclusive which treatment is appropriate for survival. Although EPP is usually performed for resectable MPM with stages I–III disease, a recent randomized controlled trial suggested that EPP cannot contribute to survival elongation and negatively affects quality of life compared with non-surgical treatments.[4] Moreover, it is unclear which subgroups of patients may benefit from these treatments.

Various biomarkers have been suggested to estimate the prognostic outcome of MPM. The expression level of various microRNAs (miRs), as well as the miR score, may predict survival outcomes,[5] and various markers related to inflammation and nutrition can serve as candidates. Previous studies have suggested that elevated levels of pretreatment C-reactive protein (CRP) may correlate with poorer outcomes.[6] The neutrophil to lymphocyte ratio is also suggested to be a potent prognostic marker.[7] Moreover, the prognostic nutritional index[8] and the controlling nutritional status (CONUT)[9] may predict survival outcomes in patients with MPM.

The serum CRP/albumin ratio (CAR) is one of the indicators reflecting inflammation and nutrition, and, according to previous reports, CAR is useful for estimating survival outcomes in many types of malignancies. Moreover, various meta-analyses suggest the usefulness of CAR as a prognostic marker in cancers.[10,11] However, the association between CAR and prognosis in MPM have not been investigated.

Takamori et al. analyzed the significance of CAR pretreatment as a prognostic marker in MPM.[9] For 100 MPM patients who underwent chemotherapy alone, neoadjuvant chemotherapy followed by surgery, and surgery alone, they retrospectively investigated the association between CAR and prognosis. They used the propensity score-matching method with regard to clinical stage, type of histopathology, performance status, and type of treatment to reduce clinicopathological biases, and concluded that CAR is an independent prognostic factor for overall survival (OS) and disease-free survival (DFS)/progression-free survival (PFS). Their study is important because it is the first study to demonstrate the importance of CAR as a prognostic indicator in patients with MPM. In clinical practice, CAR is considerably useful as it can be calculated conveniently using routine data from blood examinations.

In conclusion, Takamori et al. summarize the reasons why CAR correlates with long-term survival. They claim that proinflammatory cytokines, which induce CRP production, can promote tumor progression and metastasis. Furthermore, they mention that serum albumin reflects nutritional status, which is associated with immune status. Although common, these mechanisms are considered reasonable. Conversely, it is unclear how we can practice CAR pretreatment in clinical practice. How patients with elevated CAR associated with poor survival outcome should be treated in the future is an important issue.

In addition to the limitations referred to by the authors on the heterogeneity of background and reasonability of

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cut-off values, several limitations have been considered. First, the number of enrolled patients was not large. After multivariate analyses, they concluded that a high CAR was an independent predictor of shorter OS and DFS/PFS after surgery; however, only 35 patients underwent surgery. Second, patients were recruited between 1995 and 2015, a rather long period, which certainly associates with historical biases regarding treatment strategy, treatment protocols, and peri-therapeutic management. The authors had documented their primary treatment strategy and implications from each treatment during the study period.

In summary, the study by Takamori et al. suggests the clinical importance of CAR pretreatment as a prognostic marker in patients with MPM. However, further multi-institutional research with a larger cohort is desirable to establish the usefulness and reliability of CAR.

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