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Editorial

Biomarkers in the Prognosis of COVID-19 in the Emergency Department: May the Soluble Urokinase Plasminogen Activator Receptor (suPAR) Help?

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Abbreviations

suPAR: Soluble Urokinase-Type Plasminogen Activator Receptor; ED: Emergency Department; ALI: Acute Lung Injury; ARDS: Acute Respiratory Distress Syndrome; COPD: Chronic Obstructive Pulmonary Disease

The biomarker suPAR (soluble urokinase-type plasminogen activator receptor), discovered in 1992, is the soluble form of the cell membrane-bound protein uPAR, which is expressed primarily in immune cells, endothelial cells and smooth muscle cells. uPAR is released in inflammatory or activation processes of the immune system, therefore, in these situations, suPAR reflects the degree of immune activation in the subject [1].

Blood suPAR levels are stable during the day, being possible to be quantified in various biological fluids, including blood [2], plasma [3], urine [4], saliva [5], cerebrospinal fluid [6], ascitic fluid [7], and pleural fluid [8]. The normal level of suPAR in plasma is 2 - 3 ng/mL in healthy subjects, over 3 - 4 ng/mL in unselected patients in the Emergency Department (ED), and over 9 - 10 ng/mL in critically ill patients [9,10].

Several studies have shown that suPAR levels are associated with morbidity and mortality, being a negative predictor of several infectious diseases, including sepsis and pneumonia) [11]. Because the elevation of suPAR is not specific to a single disease and may be associated with the coexistence of several pathologies simultaneously, its application as a prognostic and non-diagnostic marker could be useful. This property could be used for risk stratification in unselected patients [12].

In the Emergency Department there is a great renewal of patients, making it necessary to ensure optimal treatment and observation of all admitted patients. All of this must be based on a correct risk assessment in order to ensure that the most serious patients are prioritized in care and study under more careful observation. To improve the patient management in the ED, several biomarkers have been developed to support the physician. One of this is suPAR, revealing recent its utility as a risk stratifier [12].

New COVID-19 pandemic affected several patients worldwide. The pathological and clinical course of the most severe lung injuries induced by SARS-CoV-2 may be divided into three distinct phases. 1) Robust virus replication associated with fever, cough, myalgia, and other systemic symptoms that generally improve in a few days. 2) Progressive decline in virus titers, recurrence of fever, hypoxemia, and progression to pneumonia-like symptoms. 3) 20% of patients evolve to acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), which often results in death [13]. An excess of inflammatory response is observed [14].

Several authors also observed that disease progression is affected by comorbidities, including chronic obstructive pulmonary disease (COPD), diabetes, hypertension, and malignancy [15]. Literature reveals that suPAR levels are associated with morbidity and mortality in a large number of acute and chronic diseases (including cardiovascular, liver, kidney, and lung diseases). In fact, literature data suggested that suPAR levels in serum of patients with different pathologies are elevated (> 4 ng/ml), with good statistical significance [16].

Attending to the actual situation, where any specific biomarker has been developed to categorize the gravity of COVID-19 in the ED, suPAR may play a role as a COVID-19 prognostic marker and

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