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EDITORIAL

Biomarkers and Risk Assessment — an Interdisciplinary Approach

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Biomarkers are measurable features that can serve as indicators of the presence, evolution or severity of a disease. They can also be used to assess the risk associated with a given disease, or to measure the progress of the illness.

Examples of biomarkers may include levels of various substances or proteins in the blood, with measurable levels at different time intervals, or different quantifiable parameters obtained during imaging tests.

Emergency departments and intensive care units, including coronary care units, represent some of the fields where the use of biomarkers is the most useful. Patients in critical conditions or presenting with acute onset of symptoms are more exposed to rapid further deterioration of their clinical status, and careful monitoring of the appropriate biomarkers could be life-saving, allowing rapid adjustment of treatment strategy in these critical cases.

Many studies have been developed in recent years in order to identify new biomarkers associated with acute or critical conditions, and to establish their predictive values. For instance, a large number of biomarkers associated with acute coronary syndromes have been proposed and tested in various scenarios, and complex biomarker panels have been validated for a more accurate diagnosis of acute coronary syndromes.[1,2] Several publications identified the concepts of the vulnerable patient and vulnerable plaque, and described the potential to assess the risk for myocardial infarction associated with the vulnerable patient, based on serum biomarkers, and associated with vulnerable plaques, based on imaging biomarkers.[3,4]

In patients with coronary artery disease undergoing percutaneous coronary interventions, serum biomarkers such as peroxynitrite-matrix metalloproteinase, creatinine and nitrotyrosine have been proved to correlate with myocardial function.[5]

Several articles in this issue of JIM address the relevance of several biomarkers in assessing the risk associated with critical or advanced-stage diseases. A particular critical condition in which biomarkers play a significant role is represented by advanced heart failure, and the role of biomarkers in patients with advanced heart failure has been extensively addressed in this issue of JIM. In the review published by Chiotoroiu *et al.*, the role of biomarkers in assessing the severity of heart failure patients is presented in an integrated approach, from serum- to imaging-based biomarkers. Aiming to summarize the most recent progresses in the field of research oriented towards biomarker discovery for monitoring heart failure patients, the review presents the newly discovered serum biomarkers such as natriuretic peptides, soluble ST2, troponins, myoglobin, C-reactive protein, galectin-3, growth differentiation factor 15, myeloperoxidase, procalcitonin, micro ribonucleic acids and long non-coding ribonucleic acids, as well as their role in predicting the risk associated with different forms of ventricular failure, at the same time with the presentation of newly discovered imaging-derived biomarkers characterizing ventricular dysfunction, obtained using advanced echocardiographic or magnetic resonance techniques.[6]

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In an original study published in this issue of JIM, Șuteu *et al*. studied the role of spirometric parameters and of several serum biomarkers such as brain natriuretic peptide (BNP) in assessing the severity and predicting the risk associated with right ventricular failure. This study used BNP as a measure of ventricular dysfunction, and proved that spyrometry-derived parameters such as forced vital capacity, forced expiratory volume in one second, peak expiratory flow rate and forced expiratory flow at 25–75% of the pulmonary volume are good indicators of the severity of right ventricular failure, correlating well with validated serum or imaging biomarkers such as BNP ($p < 0.0001$) or echocardiographic parameters reflecting right ventricular function ($p = 0.01$).[7]

At the same time, in another study carried out by Muntean *et al.*, published in the current issue of this journal, echocardiography-derived parameters characterizing left ventricular function, such as longitudinal systolic strain and synchronicity index were positively correlated with the severity of pulmonary arterial hypertension in children ($p < 0.0001$), proving the role of imaging-derived biomarkers for assessing ventricular function.[8] These two studies published in this issue by Șuteu *et al*. and Muntean *et al*. succeed to prove that beyond the traditional serum biomarkers, there is a significant role for more complex biomarkers, such as those provided by imaging techniques, for assessing the evolution of patients with left or right heart failure of different etiologies.

Biomarkers are also extremely useful in critical care units, where they are currently used to monitor the response to treatment and to predict the risk associated with the critical condition. In the review published by Bedreag *et al*. in this issue of JIM, the role of homocysteine levels in predicting the evolution of critically ill patients is presented in a complex manner, from pathophysiological mechanisms involved in its action, to interrelation with different other diseases such as cardiovascular or bone diseases.[9] The relationships between homocysteine levels and particular features of the critically ill patients are described together with the potential of control of homocysteine levels in this category. The review includes the presentation of new studies that demonstrated an increase of this biomarker in patients with atherosclerosis or with cardiovascular diseases via complex pathways that involve endothelial dysfunction, LDL oxidation and monocyte aggregation.[9] This, together with the observation described in this work, that the level of HCYS is proportional to the incidence of coronary artery disease, raises the question if this biomarker, useful for critically ill patients, could also be used for assessing the cardiovascular status. As for the relation between HCYS and critically ill patients, seven recent studies are presented that prove the relationship between HCYS levels and the deterioration of the clinical condition in these patients. However, an interesting approach of this article refers to the potential to control this biomarker using supplementation with vitamin B and folate, application that makes this substance not only a biomarker, but a relevant therapeutic target in critically ill patients.[9]

The integration of biomarkers into complex biomarker platforms was recently proposed in different studies, in order to identify new biomarker panels that can prove superior cost-efficiency for the early detection and monitorization of high-risk conditions.[10] Such a complex biomarker panel should integrate relevant data provided by multiple tests (serum tests, imaging tests, etc) with different patient-specific information, data being processed with the help of complex bioinformatics tools. This kind of new biomarker panels are currently under development, and will surely represent a significant step forward in the field of biomarker research.

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