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Searching for the Holy Grail: where do we go with the current biomarkers for sepsis?

À procura do Santo Graal: aonde vamos com os biomarcadores na sepse?

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The diagnosis and risk stratification of patients with sepsis is complicated by the varied and nonspecific nature of its presentation. Thus, achieving a more precise early diagnosis and appropriate risk stratification for patients is important for initiating treatment in a timely manner and for the application of targeted therapies for sepsis. The goal for sepsis treatment is to transform a clinical syndrome into one (or more) distinct diseases capable of being adequately characterized and specifically treated.

In this context, the search for sepsis biomarkers has been an integral part of the intensive care research aimed at meeting these needs. More than 200 biomarkers have been studied, but only a few are currently used routinely in the care of sepsis patients.[1] Moreover, because deciphering the large number of biomarkers can be an extremely difficult task, these markers have been organized into five general classes according to their clinical utility: risk prediction, diagnostics, monitoring, stratification and outcome.[2]

In the current issue of RBTI, Martin et al. demonstrated the role of interleukin (IL)-12 as a risk stratification marker for pediatric sepsis patients.[3] Although the authors did not observe any significant differences in the plasma levels of IL-12 between sepsis and septic shock patients, there was an increase in the level of this biomarker in septic shock patients within the first 12 hours of admission to intensive care. Therefore, although these results are likely not useful for the risk stratification of patients, other potential implications can be applied to these results. For example, may IL-12 levels be useful for monitoring septic shock patients or could be used to guide therapeutic decision making for this patient population? Which pathophysiological significance do these results have (i.e., should we block or not block such a response)?

However, some general questions should be addressed concerning future studies involving biomarkers. Why do we undertake such efforts in searching for new biomarkers, and what information are we hoping to obtain from these markers? Do we have enough understanding of the pathophysiology of sepsis to "take a chance" and test all new (and old) cytokines in isolation in an attempt to predict specific situations for a syndrome as complex as sepsis? Do new studies contribute relevant knowledge, or do they just add to the confusion surrounding this disease? Although it is clear that the search for sepsis biomarkers is extremely relevant to patient care (as well as to our understanding of the disease), isolated biomarkers rarely provide solid answers to the questions listed here. Thus, the incorporation of biomarkers into risk stratification systems such as the PIRO system[4] and the addition of biomarkers to existing

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severity scores[5] or panels of multiple markers[6] likely represent the best prospects for the use of biomarkers in the future. This approach will provide an improved understanding of the disease (or diseases) encompassed by the category of sepsis and will likely lead to more effective ways of treating patients in the future.

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