

the authors update us on biomarkers used in cardiovascular medicine. We would like to thank you for your article and would like to make the following observations.

At present, the study into inflammatory markers has become a new tool which is most useful for establishing the prognosis of patients with acute coronary syndrome (ACS).² The inflammatory substrate involved in ACS is extremely complex, with a large number of factors involved both in its activation and its modulation.² Furthermore, scientific literature reports that the existence of a circadian rhythm in the triggering of cardiovascular accidents can suggest the implication of, or association with, these physiological rhythms that show activity peaks at particular times of the day or night.³ The variation of the inflammatory functions 24 hours a day allows for the identification of the times of the day or night at which the peaks of inflammatory activity can be associated with a higher incidence of cardiovascular events.⁴

It is important to remember that the contributions of the inflammatory processes and their markers in the clinical development of patients with ACS do vary amongst different individuals. According to Martín-Ventura et al,¹ one of the ideal characteristics of a biomarker is its concentration stability throughout the whole day. In recent years, our team has shown the existence of diurnal variations in the concentrations of certain cardiovascular biomarkers in patients with ACS.⁵⁻¹⁰

It is known that protein-C reacts and metalloproteins play a key role in the physiopathology of the atherosclerosis. It has been shown in both molecules in which there are diurnal variations, with higher serum concentrations in the light phases (9.00) than in the dark phases (2.00), which would indicate that the diurnal variability could, at least in part, have central neuroendocrine regulation.⁵⁻⁸

Recent studies from our team have shown the vascular cell adhesion molecule-1 has a higher serum concentration in the dark phases than in the light phases.⁹ These results indicate that the individual variability in the immunitary response and the inflammatory activation that is produced during the ACS noticeably influence the increase in the values of the vascular cell adhesion molecule-1, which would explain the findings of different clinical data regarding its prognostic value, probably derived from the different time and high variability of their determination.⁹ Furthermore, it has been shown that the soluble CD40 ligand presents diurnal variations in patients with ACS, with higher values in the light phases.¹⁰

Keeping in mind the potential association between inflammation and circadian rhythm,

Diurnal Variations in Biomarkers Used in Cardiovascular Medicine: Clinical Significance

To the Editor:

It is with great interest that we read the recent article by Martín-Ventura et al¹ in which

a better understanding of the kinetics of said markers could lead to improvements in their use in cardiovascular diseases. Considering the diversity of the diurnal variations in the intrinsic properties of the cardiovascular system, these should be kept in mind during the design of in vivo experimental studies. Such temporal decisions will undoubtedly reduce the discrepancies between the studies carried out in different laboratories, as well as between animal and human subjects. The majority of these clinical studies are carried out during daytime hours, when the subject is awake. As such, the information available reinforces our opinion when suitably validating the biomarkers and the need to demonstrate their reliability, stability, and lack of variability and standardise the methodology of their measurement.

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