



EDITORIAL

Utility of calcium and phosphorus metabolism biomarkers in the stratification of acute coronary syndrome[☆]



Utilidad de los biomarcadores del metabolismo del calcio y fósforo en la estratificación del síndrome coronario agudo

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Cardiovascular disease is currently the main health problem in Europe, and the leading cause of mortality and origin of healthcare costs. Patients with acute coronary syndrome (ACS) constitute a population with great variability in terms of both the clinical presentation (this posing a genuine diagnostic and initial management challenge) and outcome—with differences in mortality risk of long-term ischemic recurrence.¹

In this issue of *Medicina Intensiva*,² the authors carry out an original study to establish the clinical profile and prognostic implications of the presence of high concentrations of biomarkers related to calcium/phosphorus metabolism, such as parathyroid hormone (PTH), calcidiol and calcitriol, in patients admitted to hospital due to ACS. There have been a number of interesting findings:

1. High PTH levels are frequent in patients admitted due to ACS, being observed in one out of every four cases.
2. Patients with high PTH levels present more cardiovascular risk factors, suffer more extensive infarction, with higher risk, more heart failure, increased inflammatory response, and a poorer outcome after discharge.

3. However, the authors also acknowledge that PTH was not an independent predictor of poor outcome following adjustment to the GRACE scale (a routine instrument used for risk stratification in patients of this kind), thus suggesting that most of the data supplied by these biomarkers are already included in this scale that is commonly used in routine clinical practice.
4. Furthermore, neither calcidiol nor calcitriol were found to be useful in the risk stratification of patients with ACS.

An interesting and current debate therefore arises regarding the relationship between these biomarkers and cardiovascular disease—particularly ACS. In this respect, it is essential to underscore the association between high PTH levels (in patients with hyperparathyroidism) and cardiovascular risk factors, particularly arterial hypertension and diabetes.^{3,4} It is also suggested that the surgical correction of hyperparathyroidism has a positive impact upon patient outcome, with a decrease in the number of cardiovascular events.⁵ However, scant clinical evidence is available in established coronary disease or ACS. Only publications involving small numbers of stable patients and other studies in patients with ACS have described an increased number of cardiovascular adverse events during the clinical course of the patients. On the other hand, Martin-Reyes et al.⁶ have evidenced the relationship between high PTH levels and more complex coronary disease, with a higher SYNTAX score and greater calcification.

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The results of these studies establish a correlation between the biomarkers and the clinical findings, though the true relationship and its clinical repercussions remain to be firmly established.

In this same sense, PTH and vitamin D have been studied in the context of heart failure (HF), with discordant results. While Gruson et al.,⁷ in a prospective cohort of patients with chronic HF, have shown the calcidiol/PTH ratio to be independently associated to cardiovascular mortality, Meems et al.,⁸ in a study involving a large sample of patients with HF, concluded that after controlling for confounding factors, the plasma levels of calcidiol, calcitriol or PTH were not associated to the risk of developing HF. In a subgroup of patients subjected to hemodialysis, a calcidiol/PTH ratio of >1 was associated to an increased risk of cardiovascular events, and was considered to be useful in estimating risk in such patients.⁹ On the other hand, in patients receiving double antiplatelet therapy due to coronary disease, those with high PTH levels show modifications in reactivity of the antiplatelet drugs that act upon the ADP receptor—thus indicating the possible existence of interactions with these drugs.¹⁰

The study commented herein, involving patients with ACS in which calcium/phosphorus metabolism biomarkers are analyzed, with the positive results described above, also has some limitations: (1) The number of patients is small, and therefore few events are analyzed—a fact that complicates the drawing of definitive clinical conclusions; and (2) Although the patients with high PTH have a greater incidence of cardiovascular events, on adjusting to the GRACE scale, no independent effect upon patient prognosis is evidenced. Likewise, no association is observed to either calcidiol or calcitriol. This makes it difficult to establish relations of clinical relevance. On the other hand, the possible relationship between the calcium/phosphorus metabolism biomarkers and renal function and the development of cardiovascular events remains to be established.

There is no doubt that this interesting study—which should be regarded as of an exploratory nature—paves the way for new clinical investigations seeking to clarify the relationship among cardiovascular disease, ACS and calcium/phosphorus metabolism biomarkers. If clinical implications are effectively confirmed, these biomarkers in turn will lead to new options in the risk stratification and clinical management of these patients.

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