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EDITORIAL COMMENT

Serum biomarkers and the electrocardiogram: Best friends forever?

Biomarcadores séricos e ECG: melhores amigos para sempre?

Pedro Silva Cunha

Arrhythmology, Pacing and Electrophysiology Unit, Cardiology Service, Central Lisbon Hospital and University Center, Lisbon, Portugal

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''When I pronounce the word Future, the first syllable already belongs to the past.''
– Wisława Szymborska, Poems New and Collected

In recent decades, cardiovascular medicine has been actively looking for biomarkers that could be used as additional tools to predict therapeutic failure or morbidity and mortality in patients with heart disease.

The measurement of biomarkers such as troponin and natriuretic peptides has consistently been shown to improve risk prediction in addition to clinical risk stratification models.

Recently, a study investigated the relationship between troponin level, coronary angiography, and all-cause mortality in patients presenting with atrial fibrillation (AF).[1] In this study the presence of elevated troponin levels in patients presenting to the hospital with AF was associated with a high risk of mortality, with higher levels associated with worse prognosis. Importantly, the risk of mortality associated with troponin increase was lower in patients who underwent coronary angiography than in those who did not.

The exact pathophysiology of circulating troponin in AF is still the subject of research, and there are no clear answers. One hypothesis is that myocardial necrosis is caused by rapidly conducted AF in the context of pre-existing coronary artery disease (causing oxygen supply-demand mismatch). But several other pathophysiological mechanisms may be involved, including volume and pressure overload, changes in microvascular blood flow, atrial calcium overload, oxidative stress, and changes in tissue structure.[2,3] Oxygen supply-demand mismatch is probably a credible explanation, as it has been observed that rate control can reduce troponin leak.[4] Nonetheless, there are also circumstances in which troponin release also occurs at normal ventricular rates, and furthermore in several patients with stroke and AF there is evidence of troponin increase in the acute phase.[5]

The role of coronary revascularization is not obvious, as the identified coronary artery disease is not always severe or functionally significant, which makes clear treatment decisions difficult, but this debate is beyond the scope of the present discussion.

In the area of electrical activity analysis, research has shown that the presence of P-wave disturbance is a predictive factor not only of arrhythmia morbidity, but also of overall mortality, stroke and dementia.[6]

Prolonged P-wave duration is a marker of left atrial abnormality, and in a sub-analysis of the Atherosclerosis Risk in Communities study, an association was also found between the presence of P-wave prolongation and the increased risk of sudden cardiac death in the general population.[7] This association was independent of cardiovascular risk factors and conditions including AF.

Recently, a deep convolutional neural network using digital electrocardiogram (ECG) traces, trained on >1 million

E-mail address: psilvacunha@sapo.pt

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12-lead resting ECGs, predicted new-onset AF within one year.[8]

Electrocardiographic analysis during sinus rhythm could thus be an additional tool to predict the development of cardiovascular disease.

In the context set out above, it seems extremely attractive to include the combined assessment of different biomarkers and electrical parameters, so that together they add predictive value to clinical data.

Ocak et al., [9] in their study published in this issue of the *Journal*, analyzed the clinical usefulness of combining P-wave dispersion and cardiac troponin I to predict AF recurrence in patients presenting to the emergency department with paroxysmal AF. P-wave dispersion (PWD) is defined as the difference between maximum and minimum P-wave duration recorded by 12-lead surface ECG.

In this analysis, 65 patients with paroxysmal AF were included, divided into three groups according to baseline troponin I and PWD values. The novelty of this approach is the combination of a serum biomarker with an electrocardiographic parameter.

The multivariate logistic regression analysis, in which age, C-reactive protein, white blood cell count, erythrocyte sedimentation rate, glucose, platelets and gender were analyzed, revealed that higher values of troponin and PWD were independent predictors of AF recurrence.

Troponin I values $\geq$0.11 ng/ml predicted AF recurrence with a specificity of 61.9% and sensitivity of 72.7%, and PWD$\geq$44.5 ms predicted AF recurrence with a specificity of 79.5% and sensitivity of 71.4%.

The combined use of PWD and baseline troponin I values had higher predictive value than PWD or troponin alone.

As the authors report, the study is limited by its small sample size and the inclusion only of patients with the paroxysmal phenotype of AF, and this should be taken into consideration when analyzing the results.

Even with the above limitations, this study is a further step in the inclusion of relatively accessible markers in the risk stratification of patients with AF. Its findings suggest that it will soon be possible to integrate these data routinely into clinical decision-making.

The combination of these two parameters could add significant information on the likelihood of AF recurrence, ultimately resulting in the therapeutic approach being decided based on this prediction, particularly with regard to the maintenance of oral anticoagulation. However, in order for its use as a prediction tool to become routine, it will be necessary to demonstrate its validity in larger numbers of patients.

Conflicts of interest

The author has no conflicts of interest to declare.

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