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Editorial

GDF-15 as a risk stratification biomarker for cardiovascular disease

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The assessment of a possible acute myocardial infarction (AMI), including risk stratification of patients presenting with acute chest pain, accounts for numerous patient hospitalizations and remains a major clinical challenge [1]. Biomarkers play a pivotal role in assisting the establishment of the diagnosis, as well as in predicting future cardiovascular risk [2]. In general, biomarkers, changed our diagnostic and therapeutic approach of ACS. New generation highly sensitive troponins facilitate an early and accurate diagnosis of ACS. On the other hand, because of the higher sensitivity, more patients are gradually rated as higher risk compared to the past, resulting in a more aggressive therapeutic approach, generating a lot of controversies [3]. Emerging biomarkers could also be helpful especially in the risk stratification of these patients, supporting the optimization of the treatment plan. As a consequence it is becoming crucial to validate their specific predictive value in the particular real-world setting of acute chest pain before implementing them as diagnostic or prognostic tools [4].

Growth differentiation factor-15 (GDF-15) is a member of the transforming growth factor β family [5]. It was originally cloned on the basis of its enhanced expression during macrophage activation and has been associated to inflammatory states in many tissues [6]. GDF-15 is highly regulated under stressed condition and can be utilized as a biomarker for several diseases. There are multiple studies connecting GDF-15 with different roles in its target issues, including heart, kidney, brain and tumors. However, the results are sometimes not consistent or even contradictory. Various studies have already reported on GDF-15 in the settings of cardiovascular disease. GDF-15 provides prognostic information beyond established clinical and biochemical markers in STEMI patients treated with thrombolysis [7], as well as in the settings of chronic heart failure [8] and in patients presenting with chest pain and suspected MI [9] supporting the predictive value of this biomarker.

In the present study J. Walter et al., assess the prognostic performance of GDF-15 concentrations in unselected patients presenting with suspected acute myocardial infarction (AMI) using adjudication based on high-sensitivity cardiac troponin (hs-cTn). In this cohort of 718 patients, 23% had an AMI diagnosis and the median follow-up time was more than 3 years. GDF-15 predicted survival with very high accuracy and identified more AMI patients with very low death risk than the established GRACE risk score showing an independent and high discriminative ability for 2-year death. Interestingly, both in AMI and in non-AMI patients GDF-15 concentrations remained predictive and surpassed the predictive ability of hsTnI. Moreover, the authors were able to identify a cut-off of 1560 ng/L as a threshold of increased mortality. Therefore, the present study by J. Walter et al. further supports GDF-15 as a predictor of future unfavorable events in patients presenting with acute chest pain and possible AMI, building on previous studies that reported on that [7,9].

Nevertheless, despite evidence from epidemiological studies that show circulating GDF-15 levels are strongly associated with worsening cardiovascular prognosis, the exact function of GDF-15 on the cardiovascular systems is still not clearly understood. Whether GDF-15 is a causative mediator or a risk biomarker of CVD remains uncertain. More work is needed to further clarify the underlying molecular mechanisms of GDF-15 in other pathophysiological states. Recent identification of the endogenous receptor for GDF-15 may allow investigators to shed more light on the mechanism of action of GDF-15 in metabolism [10].

In summary, as supported by the present study J. Walter et al., GDF-15 might be a useful tool for risk stratification of patients presenting with signs and symptoms of acute coronary syndrome, in an era where there is still an unmet need for better prognostication models. Impending benefits of using GDF-15 in risk stratification and triaging of chest pain patients have to be further explored in future randomized interventional studies.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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