LETTERS TO THE EDITOR

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Growth-differentiation factor-15 for risk stratification in patients with acute chest pain

We read with interest the article by Eggers et al., reporting the value of growth-differentiation factor-15 (GDF-15) for risk stratification in patients with acute chest pain. The authors found that GDF-15 was an independent predictor of a combined endpoint of death or myocardial infarction at 6 months. Their findings suggest that GDF-15 levels might be useful for early risk assessment of patients presenting to the emergency department with acute chest pain.

Eggers et al. reported that GDF-15 added incremental prognostic information to the ECG and cardiac troponin I (cTnI) levels. The c-statistic of the pre-test model including the ECG and cTnI data was 0.74, as compared with 0.83 after the addition of GDF-15. When ascertaining the incremental prognostic value of a new test, it should be evaluated whether such test predicts outcomes even after all other pre-test data are considered in an optimized model. Unfortunately, a pre-test model including only ECG and cTnI is far from optimized because many important clinical variables were not considered. In particular, age is a strong independent predictor of mortality in patients with acute chest pain. In the study by Eggers et al., there was a striking graded association between GDF-15 levels and age; in the subgroup of patients with normal GDF-15 levels (<1200 ng/L), mean age was 56 years, as compared with 67 years in the group with moderately elevated GDF-15 levels (between 1200 and 1800 ng/L), and 75 years in the group with highly elevated GDF-15 levels (>1800 ng/L) (P <0.001); moreover, age was significantly related to GDF-15 in the multiple linear regression analysis. A high correlation between age and GDF-15 levels might cause problems of collinearity in the multivariate logistic regression analysis that should be ruled out.

In the same line, the prevalence of diabetes—an important predictor of events in patients with acute chest pain—was 6, 13 and 29% in the groups having normal, moderately elevated, and highly elevated GDF-15 levels, respectively (P <0.001). Furthermore, other relevant clinical variables that may be associated with outcome (such as history of myocardial infarction or heart failure) had also a significant and graded association with GDF-15 levels. These remarkable associations between GDF-15 and potential clinical confounders were also reported in previous studies.

Thus, it would be advisable to test whether GDF-15 still provides significant incremental prognostic information when clinical variables (especially age) are taken into account in an optimized pre-test model.

References


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We agree with Dr Bouzas-Mosquera and his colleagues that clinical variables are important for risk stratification in patients with chest pain suggestive of an acute coronary syndrome (ACS). In the present chest pain population, as well as in patients with confirmed ACS, growth-differentiation factor-15 (GDF-15) levels were independently related to several clinical risk markers, most consistently with age and diabetes. Moreover, we have repeatedly observed independent associations of GDF-15 with biomarkers of inflammation (C-reactive protein), cardiac dysfunction (N-terminal pro-B-type natriuretic peptide), and renal dysfunction. Notably, these and other baseline variables explain only between 32 and 60% of the variability in the GDF-15 levels, indicating that this new biomarker carries unique additional information. In fully adjusted models, GDF-15 emerges as a strong and independent predictor of adverse cardiovascular events.

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