The additive value of biomarkers to clinical risk scores in acute coronary syndrome. Are biomarkers really ready for real world usage?

Antonio Tello-Montoliu, Francisco Marín, Vanessa Roldán, et al.

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The additive value of biomarkers to clinical risk scores in acute coronary syndrome. Are biomarkers really ready for real world usage?

To the editor: We read with great interest the study by Ang et al., addressing the value of brain natriuretic peptide (BNP) levels in comparison with the GRACE score for acute coronary syndromes (ACS), and the additional predictive role of BNP on this established risk score.

The latter is of great interest to physicians managing ACS patients. Indeed, several new (and sometimes, not so new) biomarkers have been studied in relation to their prognostic role in ACS, and some give prognostic information in relation to new adverse events. Several biomarkers, like BNP or C-reactive protein (CRP), are currently available in the majority of hospitals and could be readily used in clinical practice. However, except for troponin, neither is currently being used for ACS risk stratification.

Do these new biomarkers really offer much additional information? In the study by Ang et al., BNP showed better discriminatory accuracy than the GRACE score, and the combination of both increased risk prediction, but only with a marginal improvement.

Our group has investigated the addition of various different biomarkers to the TIMI risk score and its effect on the area under curve values (figure 1), in a non-ST-elevation ACS (nSTEACS) population of 415 patients. These data corroborate the small increases of the area under curve value when new biomarkers were added to the clinical risk variables. Figure 1 shows how the C-statistic increases after adding different variables into the model, as represented by TIMI risk score. The addition of new biomarkers, such as hs-CRP, NT pro-BNP and angiogenin (a marker of angionic activity) all confer a slight increase in the C-statistic. Despite the smaller power of prediction of TIMI risk score in comparison with GRACE scale, these studies are in agreement with others.

Thus, could new biomarkers be useful in current clinical practice? In our opinion, new biomarkers may give greater accuracy to the clinical scores for nSTEACS risk prediction, and add new information regarding major adverse events—for example, the prediction of death or heart failure by BNP levels. This information would be complementary to troponin or clinical scales.

However, more interesting is the possibility of classifying patients in new risk group. For example, Ang et al. show how the GRACE-scale high-risk group could be reclassified in two new risk groups, representing the 25% of entire population. The new “very high-risk” group (high BNP + high GRACE scale) was approximately sixfold more likely to experience a cardiovascular adverse event at 10 months.

Similarly, in 358 patients admitted nSTEACS, we found a twofold increase of event rate at 6-month follow-up, depending the number of biomarkers elevated (in this case, troponin, hs-CRP and NT pro-BNP), despite the risk group as defined by TIMI risk score. This finding may be certainly be important given that new high-risk groups could be managed more aggressively in terms of drugs and interventions. These results were confirmed by other authors. For example, Viviotti et al. demonstrate a better outcome of patients (mainly women) who had high BNP and CRP levels and underwent cardiac catheterisation unless their troponin levels were low.

Figure 1 Variation of C-statistic in relation to different variables. DM: diabetes mellitus; ↓ST: downsloping ST-segment; TnT: troponin; BNP: brain natriuretic peptide; TIMI: TIMI risk score. Model 2: TIMI risk score + CRP + BNP; Model 1: TIMI risk score + CRP + BNP + angiogenin.
Nonetheless, not all new biomarkers (for example, placental growth factor 2) have demonstrated their value in risk prediction as convincingly as BNP or CRP. The exploration of different biomarkers from several systems implicated in the complex pathophysiology of nST-EACS could be interesting and may be highly accurate. Until well-established and highly predictive new biomarkers are available, we suggest that the use of other biomarkers, such as BNP (or NT pro-BNP) and/or hs-CRP levels in current clinical practice could be helpful, by giving more information to the physician regarding the risk of adverse events in patients admitted with nST-EACS.

Antonio Tello-Montoliu, 1 Francisco Marín, 2 Vanessa Roldán, 3 Gregory YH Lip 4

1 Department of Cardiology, Hospital Virgen de la Salud, Toledo, Spain; 2 Department of Cardiology, Hospital Virgen de la Arrixaca, Murcia, Spain; 3 Department of Hematology and Oncology, Hospital Morales Meseguer, Murcia, Spain; 4 University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, England UK

Correspondence to Antonio Tello-Montoliu, Department of Cardiology, Hospital Virgen de la Salud, Adv/Barber 35, Toledo, Spain. attelomont@hotmail.com

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The authors’ response: We agree that the role of biomarkers as a complementary tool to available risk scores in ACS risk stratification is becoming increasingly relevant. Although the addition of BNP to the GRACE score only resulted in a small increase in the C-statistics in our study, it must be emphasised that this (C-statistic) may be an oversimplified statistical method for assessing risk prediction.1 Importantly, we demonstrated that the complementary use of both the GRACE score and BNP could reclassify up to 25% of ACS patients. This is of great relevance because it means that refining risk stratification in ACS would enable us to further identify patients in the highest risk group. We know that patients with non-ST-elevation ACS benefit from an early invasive strategy.2 However, delivery of this strategy may not be feasible in the majority of hospitals even in the developed nations. Offering an early invasive strategy to the highest risk group would be the most cost-effective way of improving clinical outcomes in the real world.3 We agree that BNP is the biomarker of choice in this setting because it has been repeatedly shown in numerous studies to predict adverse clinical outcomes in ACS. From the practical viewpoint, the advent of bedside BNP assays means prognostic information can be obtained very rapidly with a simple blood test, therefore, enhancing the process of triaging these patients.

Donald SC Ang, Michelle PC Kao, Allan D Struthers

University of Dundee, Division of Medicine and Therapeutics, Ninewells Hospital and Medical School, Dundee, Scotland, UK

Correspondence to Donald SC Ang, University of Dundee, Division of Medicine and Therapeutics, Level 7, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK; donaldscang@doctors.org.uk

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