Acute coronary syndrome: many doubts, some answers

Welcome to this special issue of *Annals of Translational Medicine* (*ATM*). The acute coronary syndrome (ACS) is now recognized as the leading cause of death and disability worldwide. Incidentally, acute cardiac ischemia has been considered for decades as the culprit of a lifelong atherosclerotic chronic disease (1), which may persists undetected for long, but that can ultimately emerge in the form of an acute myocardial infarction (AMI), causing catastrophic consequences on heart structure and function, up to sudden death and/or severe and permanent hemodynamic deterioration (2). The clinical approach to patients with an ACS has engaged the minds of many scientists, but still many questions about the pathophysiology, diagnostics and therapeutic management of this condition remain unanswered (3). It is exactly for these reasons that this special issue of the journal has been though and scheduled.

In the first article of this issue of the journal, Lippi *et al*. explore the potential association between blood lipids and cardiac troponins in a large inpatients cohort, in order to define as to whether any relationship exists between dyslipidemia, coronary atherosclerosis and elevation of cardiac biomarkers (4). Interestingly, it was finally observed that the values of high-density lipoprotein cholesterol (HDL-C) are significant predictors of both cardiac troponin I (cTnI) and cardiac troponin T (cTnT) irrespective of age, sex and other blood lipids. Since the measurement of cardiac troponins is the biochemical gold standard for identifying and prognosticating myocardial injury, the most important consequence of this finding is that the correction of low values of HDL-C by either lifestyle changes or pharmacologic treatment may be indicated in all patients with undesirable values and regardless of their baseline cardiovascular risk.

In a following article (5), Franchini *et al*. provide additional evidence that the ABO blood group plays a significant role in the pathogenesis on many human conditions, which include—but are not limited to—ACS (6), cancer (7) and overall mortality (8). In accord with previous evidence, non-O blood groups were confirmed to be associated with a greater risk of cardiovascular disease compared to subjects bearing the O blood group.

The third article of this issue is aimed to investigate the potential association between hematological abnormalities and the outcome of patients with ACS admitted to the intensive care unit (ICU) (9). In this large population study, Huang and Hu interestingly conclude that basophil percentage, potassium, white blood cell (WBC) count and mean corpuscular hemoglobin concentration (MCHC) were independently associated with hospital morality, whereas WBC, red blood cell distribution width (RDW), MCHC, potassium and percentages of neutrophils and lymphocytes were associated with 1-year mortality. This conclusion further confirms that the use of easy and inexpensive hematologic parameters, such as those routinely provided with the complete blood count (CBC), may be reliably used for prognostication of ACS patients.

The clinical heterogeneity of ACS is indeed one of the leading challenges for a timely and accurate diagnosis of this condition, wherein up to 40% of these patients have non diagnostic ECG at presentation. In a subsequent article of this issue, Cervellin *et al*. provide an overview on the value of the clinical presentation in patients with a suspected ACS. Special focus is placed on clinical history, the main characteristics of chest pain, related symptoms, the likelihood of atypical presentations, as well as on precipitating and relieving factors, drugs, clinical rules and significance of clinical Gestalt (10).

In the following article of this issue, Franchini *et al*. provide a comprehensive overview about the putative genetic background of ACS, as has been recently made available by whole genome scanning and genome wide association studies (GWASs) (11). Briefly, it is now almost certain that the predisposition to developing ACS results from the multifaceted interplay of common genetic variants implicated in lipid metabolism, proliferation and inflammation. Although many of these polymorphisms have small impact on coronary risk when taken alone, they may synergically associate, thus raising the individual threshold risk over a certain limit that considerably increases the likelihood of an acute ischemic cardiac event.

As previously emphasized, many doubts remain about the most accurate and efficient algorithm for diagnosing ACS. Indeed, the introduction of the novel high-sensitivity immunoassays for measuring cardiac troponins has contributed to catalyze many changes and a paradigm shift (12). Nevertheless, as emphasized in the article of Cervellin *et al*. (13), the relatively short history of algorithms for cardiac troponin testing has led to a chaotic scenario, dominated by many different and often contradictory diagnostic approaches. In their article, the available recommendations are hence discussed and a "common sense" algorithm, which includes the many protocols that have been proposed so far, has been developed with the

aim of being validated in future clinical studies.

The last article of this issue of the journal by Danese *et al*. (14) is aimed to provide a comprehensive historical overview on the many diagnostic biomarkers of ACS that have been proposed and clinically validated so far. The conclusion is however rather predictable, wherein cardiac troponins measured with high-sensitivity immunoassays should now be regarded as "the best there is" and probably, as "the best there will be" for a rather long time (15).

In conclusion of this preface, we wish to thank all the authors to this issue of *ATM* for their original and valuable contributions, hoping that this special issue of the journal may be of substantial interest for its readership. We also would like to announce that a follow-up issue on the intriguing topic of ACS is underway, containing additional articles and overviews. We are looking forward to publish it as soon as possible, thus providing more answers to the many challenging doubts in the pathophysiology, diagnostics and therapeutic management of ACS.

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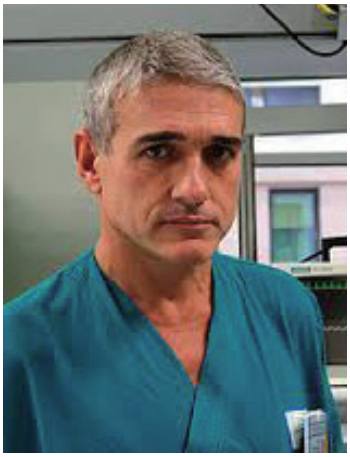

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