Evidence and pitfalls in diagnosis and prognostication of acute coronary syndrome

Welcome to this second special issue of *Annals of Translational Medicine* (*ATM*) on the acute coronary syndrome (ACS). This second volume is the most logical prosecution of the former and, according to the editors' intent, is aimed to attempt "closing the circle" of the intricate diagnostic and prognostic aspects of ACS.

It can be credibly put forward that the diagnostic approach to patients with suspected ACS has engaged the mind of many physicians more than any other human disease actually did during the past decades (1). This is also due to the fact that heart disease remains the leading cause of death and disability worldwide (2). Throughout years of research in this challenging arena, no unique diagnostic tool was proven to be so efficient and clinically viable to be proposed as the exclusive gold standard. As for many other conditions, the diagnosis of ACS entails the combination of clinical history, signs and symptoms, electrocardiography, imaging testing and, last but not least, laboratory diagnostics (3). We have hence decided to focus this second issue on the many diagnostics tools that have become available in the past years for a more accurate and efficient diagnosis (or rule out) of ACS.

The first article of the volume is a foremost editorial written by Alan Wu about the current and future perspective of laboratory diagnostics for myocardial ischemia (4). The article debates many still unanswered issues, highlighting the analytical drawbacks of commercial assays for cardiac troponin testing, including the heterogeneity of the analytical techniques, the real significance of "high-sensitivity", the poor standardization and comparability across different platforms, as well as the accurate definition of the diagnostic thresholds and other biological issues which ultimately make these assays still challenging.

The second article in this issue by Bonfanti *et al.* (5) provides additional insights on the role of the sensitivity of cardiac troponin immunoassays for prognostication of ACS. Basically, it is clearly demonstrated that the routine use of a contemporary-sensitive troponin I immunoassay may retain a meaningful clinical value for predicting adverse outcomes in a general population of patients admitted to the emergency department (ED), especially when used within a well-defined protocol.

In a following article of this volume, Perales *et al.* explore an intriguing issue in modern cardiology, that is the impact of some gestational risk factors on maternal cardiovascular system (6), highlighting the existence of a significant relationship between gestation and heart disease in pregnancy.

The prediction of adverse outcome after an ACS remains a challenging but essential aspect in both a clinical and healthcare perspective. Despite imaging techniques and selected biomarkers provides useful prognostic information after an episode of myocardial ischemia, Turcato *et al.* show that the use of red blood cell distribution width (RDW), a rather simple and inexpensive measure of anisocytosis, may help stratifying the medium-term risk of mortality and major adverse cardiac events (MACE) in patients who suffered from an episode of myocardial infarction (7).

Alongside cardiac troponin testing, imaging techniques may offer novel diagnostic opportunities in patients with ACS. In the article of De Filippo and Capasso (8), the potential usefulness of non-invasive imaging options such as coronary computed tomography angiography (CCTA) and cardiac magnetic resonance (CMR) is thoughtfully discussed, highlighting that these techniques may be regarded as a valuable aid for the rapid and accurately diagnosis of ACS in patients with low to intermediate cardiovascular risk.

Although it is clear to many that heart disease remains overall the leading cause of death and disability around the globe, Sanchis-Gomar *et al.* (9) performed a comprehensive analysis of current data about the burden of this condition in both industrialized and developing countries. Interestingly, reliable data shows that the frequency of ACS is expected to increase further in developing countries, thus requiring to strengthen primary prevention strategies worldwide, not only in the Western world.

The constant refinement of the analytical techniques for cardiac troponin testing has finally yielded to development and commercialization of the so-called high sensitivity immunoassays (10). As highlighted in previous articles published in this

journal (1,3), the higher analytical sensitivity of the new methods may introduce a paradigm shift in the fast and accurate diagnosis of ACS. Nevertheless, some questions remains especially pertinent to the real cost-effectiveness of using high-sensitivity immunoassays in patients admitted to the ED. Therefore, in a comprehensive state-of-the-art analysis, Galli and Lippi explore the main unquestionable advantages of these novel techniques along with the further economic and technical aspects that may be clarified before definitive implementation in routine clinical practice (11).

The prognostication of heart disease has already been discussed in another regular article of this issue, leading the way to an additional contribution especially devoted to the analysis of the existing measurable biomarkers. Salvagno and Pavan thereby provide an ample revision of current evidence about the use of suppression of tumorigenicity 2 (ST2) and galectin-3 (GAL-3), two important molecules in the pathogenesis of heart dysfunction, the measurement of which may soon become a paradigm of managed care (12).

In the last article of this issue, Leischik *et al.* provide a nice overview about the currently available ultrasound techniques for detection and assessment of coronary heart disease, including tissue Doppler imaging, contrast echocardiography, 3D-echocardiography and speckle tracking echocardiography (i.e., strain/strain rate-echocardiography), emphasizing the advantages and the potential limitation of their use in clinical practice (13).

In conclusion of this preface of this second issue of *ATM* on ACS, we wish to thank again the authors to for their original and valuable contribution, hoping that this latter volume may be of substantial interest for the readership of the journal.

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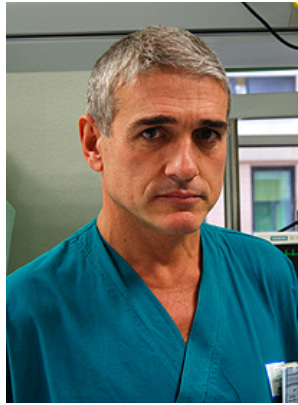
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