

Preface

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Biomarkers in the emergency department. Handle with care

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The term ‘biomarker’, portmanteau of ‘biological marker’, refers to a quantitative measure that may allow the screening, diagnosis, classification, prognostication and therapeutic monitoring of a given pathological condition [1, 2]. The use of biomarkers testing has hence become commonplace in modern science and medicine, with usage rates in emergency settings that can be as high as 30% of the total laboratory volumes [3]. Although we would all agree that the availability of efficient biomarkers has the potential to revolutionize the clinical decision process in emergency settings, especially in the emergency department (ED), the diagnostic performance of novel tests is seldom not as straightforward as in other healthcare environments as there are several clinical, analytical and practical aspects that highlight some major areas of uncertainty and would, at least partially, erode their diagnostic efficiency.

One of the main drawback is indeed represented by the patients themselves. Estimations based on current age-specific ED admission rates suggest that the aging of the population will cause a substantial increase in the number of ED visits from elderly patients [4]. The analysis of trends also shows that visit lengths and likelihood of hospitalization will consistently increase over the ensuing decades [5]. These clear trends pose serious challenges to the appropriate use of laboratory diagnostics in the ED, since most biomarkers have been identified, developed and validated in ideal settings, i.e., in patients free from important comorbidities and therapies. A paradigmatic example is that of troponin testing for the diagnosis of myocardial injury, especially myocardial infarction (MI). Several lines of evidence now attest that the 99th percentile of the reference range of both high-sensitivity troponin I and T immunoassays increases as a physiological consequence of aging [6]. The three most common diagnoses in the ED are unspecified chest pain, congestive heart failure and pneumonia [7], all conditions in which requesting troponin is commonplace. As such, the use as a decisional level of a unique threshold value (i.e., the 99th

percentile established in the whole population) instead of age- and gender-related cut-offs would considerably increase the number of patients showing values above the cut-off, (‘false positive’ MI cases and) then contributing to overcrowding. Another important aspect is the potential presence of comorbidities. As the population gets older, the likelihood of heart failure, diabetes, cancer, autoimmune diseases and other frequent disorders will grow exponentially. Since these conditions are well established causes of increased troponin values [8], validated diagnostic algorithm should be considered in order to prevent the chance of overdiagnosing MI. The rate and modality of ED access are also rapidly changing, with a consistent increase of utilization from migrant populations, whose care is strongly influenced by a number of factors, such as biological heterogeneity, health seeking behaviors and language barriers. In this evolving environment, the diagnostic performance of some biomarkers may be seriously challenged by the use of universal decisional thresholds.

Beside important clinical considerations, there are also some analytical and practical problems that may be seen as unique to diagnostics in ED patients. The first issue is obviously the turnaround time (TAT). We all know that ‘*Time is Heart & Brain*’. The current deadlines for door-to-balloon and door-to-needle (for MI and stroke, respectively) are lower than 90 min and 4.5 h, respectively. This not only would require a faster triage in the emergency room, but also the availability of rapid laboratory techniques for efficient diagnosis and risk assessment of patient candidates for urgent revascularization. Similar conclusions can be drawn for patients admitted to the ED with severe infections or acute heart failure, in whom the timely availability of procalcitonin or natriuretic peptides may be vital for the diagnosis and the therapeutic decision making. Nevertheless, distance may be regarded as a serious challenge in a rapidly evolving scenario, such as that of laboratory diagnostics, in which small laboratories are increasing consolidated within larger facilities [9]. On one hand, this would require the adoption of suitable analytical techniques to fulfil the local organization, including highly automated and efficient assays to withstand larger volumes of testing

in shorter times. On the other hand, the introduction of point of care testing (POCT) may be advisable in those healthcare settings in which laboratory resources would not be readily available [10], provided that essential quality specifications are fulfilled [11]. With continuous identification and commercialization of innovative biomarkers, the need for clear-cut standardization or harmonization is also vital, in order to provide consistent answers to increasing demands of urgent care throughout different organizations and healthcare settings [12].

A final issue is the often discounted importance of a sufficient knowledge of a given biomarker biology. Whatever biological marker does not make a diagnosis by itself, but requires deeper evaluation of a number of demographic and clinical variables to bridge the gap between theory and practice [13]. Therefore, the use of biomarkers entails a forward stepwise logistic approach, wherein clinical history, signs and symptoms should drive laboratory testing and not the contrary, in order to prevent misleading utilization and saving human and economical resources [14].

There is indeed some wiggle room to tackle the roots of biomarker utilization in the ED, and a constructive interdisciplinary cooperation remains the preferable option. The GREAT (Global Research on Acute Conditions Team) is an International Network between experts operating in the management of acute clinical conditions in the field of Emergency Medicine (GREAT Association [15]), which integrates research inputs from basic sciences (including laboratory medicine) and political sciences to optimize both patient care and preventive measures which may extend beyond the provision of healthcare services. This issue of *Clinical Chemistry and Laboratory Medicine* is a collection of lectures of the IV Italian Congress of the GREAT Network, held in Rome, 14–18 October 2013. The leading topics that will be discussed include the appropriate use of consolidated and emergent biomarkers of myocardial injury, heart failure, dyspnea, electrolyte and metabolic disorders, localized and systemic infections (i.e., systemic inflammatory response syndrome), along with practical considerations about the perspectives of POCT in emergency settings. We wish to thank all the authors to this issue for their unique and comprehensive contributions and hope that our readership will find interest in the contents.

Conflict of interest statement

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