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Editorial

Rule-out myocardial infarction in the high-sensitivity cardiac troponin era

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Each year, millions of patients go for the emergency departments (ED) worldwide complaining of acute chest pain, which is the second most common reason for ED visits in the US [1]. Around 20% of these patients will have an acute coronary syndrome (ACS) needing hospital admission [2].

The clinical approach of patients with chest pain in the ED represents a diagnostic challenge. Acute coronary syndromes are classified into ST-elevation myocardial infarction (STEMI), defined as acute chest pain and persistent (>20 min) ST-segment elevation on the electrocardiogram (ECG) and generally reflects an acute total coronary occlusion. Patients with acute chest pain with ECG changes but no persistent ST-segment elevation, and associated with increased biomarkers of cardiomyocyte necrosis are termed as non-ST elevation myocardial infarction (NSTEMI). Unstable angina (UA) is defined as myocardial ischemia at rest or minimal exertion in the absence of cardiomyocyte necrosis [3]. The STEMI accounts for 30% of patients with ACS, however, the vast majority will have an NSTEMI or UA [4]. Patients with ACS correspond to approximately 20% of those with acute chest pain admitted to the ED [2]. The missed diagnosis of acute cardiac injury in this population is about 2% in the pre-troponin era, which generates a great concern for the dire consequences of discharge patients with the missed diagnosis of ACS from the ED, because of the high mortality risk, which represents a serious public health problem.

As a consequence, in the last 30 years, we have observed the development of a large number of protocols and recommendations to rule-in and rule-out patients with ACS, such as the admission of patients with chest pain at a monitored bed in a coronary care unit or in a chest pain unit, prolonged length of observation (12 to 24 h) to exclude an AMI, utilization of high-cost non-invasive and invasive diagnostic tests. All of these recommendations have led to an economic overburden on the health care system and ED overcrowding due to unnecessary investigations and hospital stay [5,6]. This represents a cost of $10 to $12 billion dollars per year in health care expenditures in the US [7]. The introduction of high-sensitivity cardiac troponin (hs-cTn) assays has revolutionized the assessment of patients with acute chest pain, allowing earlier diagnosis of myocardial infarction, shorter stays in the ED and reduced admissions for chest pain for those rule-out with myocardial injury [5,8]. These biomarkers are nowadays considered the gold-standard biomarkers for the detection of myocardial injury and several protocols have been developed for the early diagnosis of AMI, allowing to rule-out a myocardial infarction in up to 3 h of observation. Although a great number of diagnostic strategies have been developed based on hs-cTn tests, the research from Wildi et al. [9] published in this issue of the International Journal of Cardiology are impressive and highlights the efficiency of current diagnostic strategies for detection of an AMI with an extremely low rate of missed diagnosis. This issue is of paramount importance for clinicians decided the best diagnostic approach using hs-cTn, as well as in terms of public health, for the selection of the best diagnostic strategy to implement in an ED for detection of AMI, combining the high sensitivity, specificity and low rate of missed diagnosis. In summary, the APACE study (Advantageous Predictors of Acute Coronary Syndrome Evaluation) is an ongoing prospective international multicenter diagnostic study enrolling 3696 patients presenting with suspected of AMI in the ED. The authors compared the safety and efficacy of 14 different hs-cTnI (Abbott, Architect®) and hs-cTnT (Roche, Elecsys®) based strategies: dual-marker strategy (combining copeptin and hs-cTn), undetectable levels (LoD), ESC 0 h/1 h-algorithm, 0 h/2 h-algorithm, 2 h-ADP-algorithm, NICE (United Kingdom National Institute for Health and Care Excellence) algorithm, ESC 0 h/3 h-algorithm. The primary safety endpoint was defined as the sensitivity and negative predictive value (NPV) for AMI of each strategy. The primary efficacy endpoint was defined as the percentage of patients triaged towards rule-out of AMI. The secondary safety endpoint was the sensitivity and NPV for major cardiac adverse events (MACE) in the rule-out group of each strategy within 30 days. The authors observed that AMI was the final diagnosis in 16% of patients. In the comparison of 14 different hs-cTn-based strategies, there was observed that for hs-cTnT, the safety was very high and comparable for all strategies, except for the dual-marker approach. Using hs-cTnI the results were similar with high safety and comparable for all strategies, except the dual-marker approach and the NICE-algorithm. The efficacy varied markedly and was lowest for the LoD-algorithm. The incidence of

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30-day MACE was low among patients triaged towards rule-out AMI based on the investigative strategies. The incidence of 30-day MACE ranged from 0.1 to 1.8% for hs-cTnT and from 0% to 3.7% using hs-cTnI. The missed diagnosis of an AMI was <1% for all strategies, except for the dual-marker strategy using copeptin associated both with hs-cTnT (3.4%) and hs-cTnI (9.6%). Applying the 2 h-ADP-algorithm for hs-cTnT and the LoD, 0 h/2 h-algorithm, and 2 h-ADP-algorithm for hs-cTnI, no patient with AMI was missed. Gathering all the results, it should take into consideration that the rule-out AMI algorithms should always be used in conjunction with all available clinical information, including chest pain characteristics, the ECG and physician's expertise, the authors emphasized. Based solely on the rule-out AMI algorithms, all these strategies combined safety and efficacy and can be considered for routine clinical practice, except for the dual-marker algorithm and NICE-algorithm using hs-cTnI, concluded the authors.

The implementation of diagnostic strategies in acute chest pain through the utilization of highly sensitive biomarkers for myocardial injury (hs-cTnT an hs-cTnI) to rule-out an AMI may allow early discharge of low-risk patients with acute chest pain from the ED, leading a reduction in health care costs by preventing unnecessary admissions and high-cost tests. Besides, this diagnostic approach may help clinicians to discharge patients with confidence because of the extremely low-rate of missed diagnostic and 30-day MACE. We look forward to new publications from the APACE investigators exploring new hypothesis and the economic impact of diagnostic strategies in ACS.

Disclosure

The author declares no conflict of interest.

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