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New ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

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Summary

This review highlights an important novel aspect of the 2011 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the recommendations of a rapid rule-out protocol (0h and 3h) when high-sensitive cardiac troponin assays are available. The controversy relates to the scientific question how reliably patients can recall the onset or maximum of acute chest pain and the general question how conservative clinical practice guidelines should be.

Several important arguments support the novel recommendations, particularly when accepting that guidelines should highlight treatment principles rather than individualised details. I hope that many physicians caring for patients with acute chest pain will actually take the time to read the new 2011 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Certainly, application of the principles highlighted in there will help them in their daily clinical work.

Key words: *myocardial infarction; diagnosis; troponin; guidelines*

Introduction

Recently, the new 2011 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation have been presented [1]. Two of the new aspects introduced in the 2011 document have sparked intense discussions: the use of the novel more potent (and expensive) oral antiplatelet agents (prasugrel and ticagrelor) and the recommendations of a rapid rule-out protocol (0h and 3h) when high-sensitive cardiac troponin (hs-cTn) assays are available. This editorial will focus on the later. The controversy relates to the scientific question how reliably patients can recall the onset or maximum of acute chest pain and the general question how conservative clinical practice guidelines should be.

Diagnosis of acute myocardial infarction (AMI)

Patients with symptoms suggestive of AMI account for about 10% of all emergency department (ED) consultations, however only 10–20% of them eventually suffer from AMI [1]. Electrocardiography (ECG) and cTn form the diagnostic cornerstones and complement clinical assessment in the evaluation of chest pain patients [2–4]. A limitation of standard cTn assays is a delayed increase of circulating levels for 3 to 4 hours requiring serial sampling for 6 to 12 hours in a significant number of patients [2, 3, 5]. Delays in diagnosing disease ("rule-in") holds back prompt use of modern day therapies with proven benefit [2, 3]. Delays in excluding disease ("rule-out") interferes with evaluation of alternative diagnoses and contributes to overcrowding in the ED and costs estimated to exceed several billion US dollars per year [6].

Hs-cTn assays

The recent introduction of hs-cTn assays has enabled measurement of cTn concentrations not reliably detected with prior generations of tests [7]. The new tests have been shown to improve the diagnostic accuracy in the early diagnosis of AMI, and it has been suggested that particularly the rule-out of AMI might be feasible more rapidly with the new tests as a very high negative predictive value of cTn levels below the 99th percentile were consistently reported in large prospective studies already at presentation [8, 9]. Current research by our group and others investigates the best possible clinical use of hs-cTn levels in this setting, including the effect of age and comorbidities on cut-off levels as well as the most appropriate metrics (absolute versus relative changes in cTn) to differentiate conditions with acute cardiomyocyte damage (= cTn release) such as AMI from conditions with chronic cardiomyocyte damage [10–15]. As it is currently unknown how to best take advantage of the novel hs-cTn tests in clinical practice, there is an on-going debate whether and to what extent a shortening of the time interval to the 2nd sample is feasible and safe.

Chest pain onset

The onset of chest pain in patients with AMI is considered the onset of cardiomyocyte damage and therefore ultimately the pathophysiological mechanism that results in the release of cTn into the circulation. It is poorly known how well patients are able to recall the onset and/or maximum of acute chest pain. Previous guidelines argued that the uncertainty regarding the accuracy of this information mandates a uniform 6h (to 12h) rule-out protocol with 6h (to 12h) continuous ECG monitoring and serial blood sampling irrespective of the time interval from chest pain onset to ED presentation. The current 2011 ESC guidelines take a different position, in fact, a position that many clinicians worldwide had already adopted in recent years. In patients who provide a precise estimate of the onset of acute chest pain, the time interval from chest pain onset to blood sampling can help to interpret cTn findings. E.g., AMI can rather reliably be ruled out in a patient with chest pain onset 12 hours before ED presentation and a normal cTn level in the blood sample taken at ED presentation. In contrast, the negative predictive value for AMI is much lower for a normal cTn level at presentation in a patient whose acute chest pain started just 20 minutes prior to ED presentation.

Rapid rule-out algorithm

Accordingly, the current 2011 ESC guidelines suggest that AMI can be safely ruled out once hs-cTn levels are normal in a patient presenting with a chest pain onset more than 6 hours prior to ED presentation. In addition, the 2011 ESC guidelines suggest that these patients, if pain-free and perceived to be at low risk of dying within the next months by a validated risk score (with less than 140 points in the GRACE risk score), can be discharged from the ED for further outpatient management.

Although most experts may agree that these assumptions very likely are true, critics emphasise that these statements are built on little published data. The same is true for the second part of the rule-out protocol: In patients with chest pain onset less than 6 hours before ED presentation, a second normal hs-cTn level taken 3 hours after ED presentation (and 3 hours after the first hs-cTn level) rules out AMI, and again, if pain-free and with less than 140 points in the GRACE risk score, allows discharge from the ED for further outpatient management.

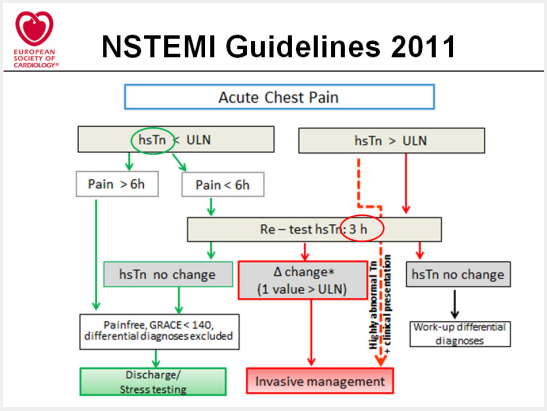

Figure 1

ESC 2011 rapid rule-out algorithm using hs-cTn levels (adapted from [1]; © European Heart Journal, reprinted with permission).

Timely or premature

Does the available evidence suggest that these guidelines are timely or premature? I would like to argue that they are very timely, despite the fact that certainly on-going research will help to further fine-tune them. First, economic constraints and questionable economic incentives have long pushed physicians in many countries to apply rule-out protocols that are faster than the 6 (to 12h) rule-out suggested consistently by the previous ESC and AHA/ACC guidelines. E.g., economic pressures have lead many EDs in the United States to adopt an imaging protocol using CT-angiography to rule-out high-grade coronary lesions in the epicardial coronary segments assessable by this technique in patients with normal cTn levels at presentation. However, these protocols are substantially less well validated than the new ESC 2011 rapid rule-out protocol. In fact, even more methodological concerns apply to these alternative protocols, including the inherent long-term health hazards of radiation exposure with CT-scanning, particularly in younger patients presenting with acute chest pain and perceived to be at low risk of AMI. Second, guidelines should not be confused with tailored treatment algorithms for individual patients. Guidelines should highlight important principals that then allow the treating physician to manage the individual patient as good as possible. I am convinced that the principals highlighted in the current ESC 2011 guidelines are important and correct. The controversy of principles versus individualised treatment plan becomes particularly obvious when taking into account that due to tradition, different professional or financial incentives, and multiple other reasons important details in clinical practice regarding the management of patients with acute chest pain vary widely even among European countries. E.g., for the rule-out of AMI most patients in the United Kingdom are transferred to an observational unit after the initial period in the ED, while in most other countries the complete rule-out process will take place in the ED. Many countries have introduced de facto or virtual “chest pain units” within the ED with clear-cut rule-out protocols.

One important methodological issue might deserve clarification: no prospective interventional studies at all have assessed the use of hs-cTn assays for clinical decision making yet and the few data published so far are derived from prospective observational studies. Clarification of this point does not change the bottom line of the article, but is important in view of the critics that call the rapid rule-out aspect of the 2011 recommendations premature.

In summary, I honestly hope that many physicians caring for patients with acute chest pain will actually take the time to read the new 2011 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Definitely, application of the principles highlighted in there will help them in their daily clinical work.

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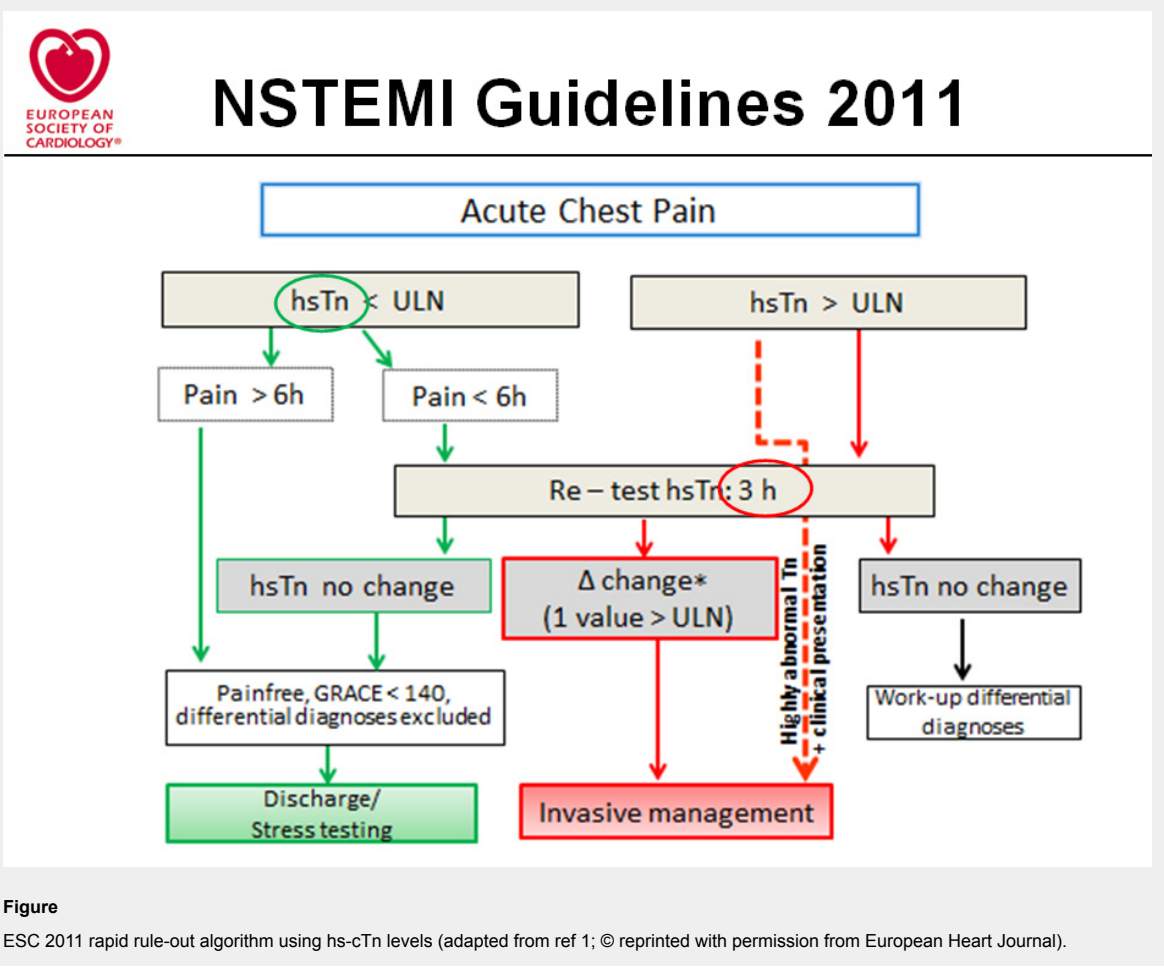
Figures (large format)



Figure

ESC 2011 rapid rule-out algorithm using hs-cTn levels (adapted from ref 1; © reprinted with permission from European Heart Journal).