Editorial

Early rule out of acute myocardial infarction

Bertil Lindahl, Per Venge

Uppsala University, Uppsala, Sweden

Correspondence to: Per Venge, MD, PhD. Uppsala University, Uppsala, Sweden. Email: per.venge@medsci.uu.se.

Comment on: Boeddinghaus J, Nestelberger T, Twerenbold R, *et al.* Direct Comparison of 4 Very Early Rule-Out Strategies for Acute Myocardial Infarction Using High-Sensitivity Cardiac Troponin I. Circulation 2017;135:1597-1611.

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Any measures taken to safely reduce the numbers of patients in the crowded emergency room are more than welcome. Patients with suspicion of acute myocardial infarctions (AMI) make up a substantial number of such patients, about 10%, and these patients deserve special attention, since rapid actions are often required in whom the diagnosis of AMI is established. Diagnostic algorithms are continuously upgraded by international expert groups to define the criteria for AMI, i.e., to rule-in the patient and refer him/her to appropriate actions. Diagnostic algorithms, however, that safely, effectively and rapidly rule-out patients and thereby allow the disposition of such patients to their homes or elsewhere outside the emergency room are still not widely accepted and applied. In the report by Boeddinghaus *et al.* (1), four different algorithms have been compared in a large multicenter study in Europe and in a subgroup of patients also compared with the European Society of Cardiology (ESC) recommended 0/3 hour diagnostic protocol (2). The algorithms were based on the results of the high sensitivity cardiac troponin I assay produced by Abbott Diagnostics. The choice of the assay was simple, since at the time of the study, this was the only cardiac troponin assay that met the criteria of being truly high-sensitive, i.e., having the capacity to measure cTnI concentrations in almost all healthy persons. The effectiveness of three of the algorithms were very encouraging and ruled-out more than 50% of the patients within one hour with 0.5–0.9% misclassifications and only a handful of major adverse cardiac events (MACE) within the next 2 years. The fourth algorithm that was based on findings of results lower than the Level of Detection (LOD) of the assay, which is <2 ng/L, however, showed, that 16% of the patients could be immediately and safely ruled out with 100% NPV and no adverse outcomes within the following 2 years. Even if 60–70% of the patients with suspicion of AMI can be either ruled-in or ruled-out within one hour, 30–40% of the patients remain in the emergency room and have to be taken care of. The appropriate diagnostic procedures for this group of patients in whom AMI could neither be ruled-in or out are still not well established and requires further studies. One important and interesting question that arises from the report is whether the patients that were misclassified were true misclassifications. Thus, of the seven patients missed by the 1 h algorithms none had any signs of cTnI increase at follow up and only 2 of the 13 patients missed by the single cut-off algorithm of <5 ng/L had increased cTnI concentrations compatible with myocardial injury, the rest had only increase in cTnT. To our minds, these findings highlight the difficulties of the adjudication process and the importance of chosen gold standard for diagnosis for the results, since it is difficult to accept that myocardial necrosis would only give rise to cardiac troponin T and not cardiac troponin I. These results do not question the findings of the present report. On the contrary, they might strengthen the safety of the algorithms, since the number of misclassifications would then be <0.1%. Another, somewhat disturbing finding in the study was the inferior diagnostic performance of the ESC recommended, and commonly used in clinical routine, 0/3 h protocol compared to the four rapid rule-out algorithms, with a sensitivity below 93% and a NPV below 99%. Furthermore, the recommendation in the ESC 0/3 h protocol that a single c-Tn value on admission below the 99th percentile is safe for rule-out of AMI in those with a time from onset of symptoms above 6 h seems doubtful. This is probably due to the difficulty in determining the time of onset of symptoms (or even more

difficult, of the time of onset of infarction) in this group of patients with often recurrent episodes of chest pain.

The power of the results in this report of Boeddinghaus *et al.* should encourage emergency rooms to change their management of patients with suspicion of myocardial infarction, since a wise and careful application of these algorithms could help substantially reduce the pressure on these settings. However, such change requires the access to high-sensitive cardiac troponin assays and each new hs-cTn assay needs to prove that it meets these tough requirements and expectations.

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Footnote

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References

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