External validation of a clinical decision rule to identify patients at low risk for acute coronary syndrome who do not need objective coronary artery disease testing

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On behalf of Advanced Predictors of Acute Coronary Syndrome Evaluation (APACE) Investigators

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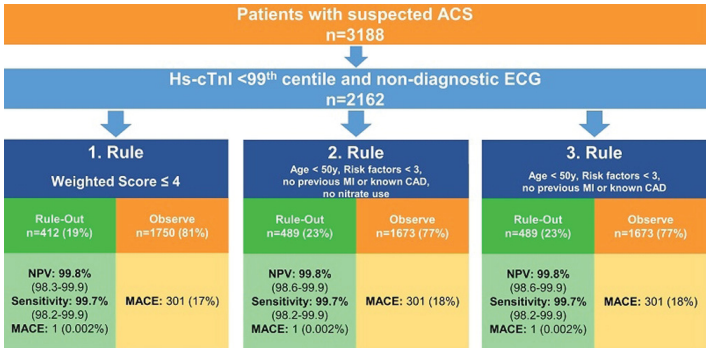
Background: Rapid high-sensitivity cardiac troponin (hs-cTn) based algorithms have substantially improved the early rule-out of acute myocardial infarction (AMI) and thereby facilitated the selection of patients eligible for outpatient management. However, it remains unclear, which patients after rule-out of AMI should still undergo objective anatomic or functional cardiac testing for the detection of relevant coronary artery disease. A pilot study has derived a clinical decision rule for the selection of patients who do not need objective anatomic or functional cardiac testing for coronary artery disease ("No Objective Testing" (NOT) rule).

Purpose: To externally validate the performance of the NOT-rule in a multicentre study.

Methods: Patients presenting to the ED with symptoms suggestive of an acute coronary syndrome (ACS) were enrolled in a large prospective international multicentre study at 12 study sites in five European countries. Two independent cardiologists centrally adjudicated the final diagnosis using all clinical data including cardiac imaging and at least 90-day follow-up. The NOT-rule is applied in patients, in whom a 2h accelerated diagnostic protocol (using hs-cTnI concentrations at 0h/2h and ECG data) has ruled-out AMI and based on clinical variables. In brief, the first rule is a weighted score derived from independent predictors of ACS that classifies patients as low-risk if they score $\leq$4 points. The second rule was simplified and ruled patients out if they were younger than 50 years, had no history of an AMI or known CAD, and no prescribed nitrates. The third rule equals the second except nitrate use was omitted. Primary objective was the safety and efficacy of the NOT-rules for rule-out of major adverse cardiac events (MACE) including AMI, unstable angina pectoris, urgent or emergency revascularisation or cardiovascular death at 30-days of follow-up. Secondary objective was the safety and efficacy for rule-out of MACE at 2-years.

Results: Out of 3188 enrolled patients, 2162 (68%) had hs-cTnI concentrations at 0h and 2h below the 99th centile as well as a non-diagnostic ECG and were therefore eligible for the analysis. MACE at 30-days occurred in 302 (14%) patients. The second and third rule offered highest safety and efficacy for rule-out of MACE at 30-days. Both identified 492 (23%) patients at low-risk with a sensitivity of 99.7% (95% CI 98.2–99.9%) and a negative predictive value (NPV) of 99.8% (95% CI 98.6–99.9%). One MACE was missed within 30-days (revascularisation of a one-vessel CAD). Sensitivity 98.9% (95% CI 97.1–99.7%) and NPV 99.2% (95% CI 97.8–99.7) were also very high for 1-year MACE, as well as 2-year MACE 98.4% (95% CI 96.5–99.4%) and 98.4% (95% CI 96.5–99.3%), respectively.

Conclusions: The NOT rules proved to be a safe tool that identifies nearly one-fourth of patients at very low risk for MACE, who may not need objective anatomic or functional cardiac testing for coronary artery disease.



Performance of NOT rules