ORIGINAL INVESTIGATION

HEALTH CARE REFORM

One-Hour Rule-out and Rule-in of Acute Myocardial Infarction Using High-Sensitivity Cardiac Troponin T

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Background: High-sensitivity cardiac troponin (hs-cTn) assays seem to improve the early diagnosis of acute myocardial infarction (AMI), but it is unknown how to best use them in clinical practice. Our objective was to develop and validate an algorithm for rapid rule-out and rule-in of AMI.

Methods: A prospective multicenter study enrolling 872 unselected patients with acute chest pain presenting to the emergency department. High-sensitivity cardiac troponin T (hs-cTnT) was measured in a blinded fashion at presentation and after 1 hour. The final diagnosis

dation cohort, 259 patients (60%) could be classified as "rule-out," 76 patients (17%) as "rule-in," and 101 patients (23%) as in the "observational zone" within 1 hour. Overall, this resulted in a sensitivity and negative predictive value of 100% for rule-out, a specificity and positive predictive value of 97% and 84%, respectively, for rule-in, and a prevalence of AMI of 8% in the observational zone group. Cumulative 30-day survival was 99.8%, 98.6%, and 95.3% ($P < .001$) in patients classified as rule-out, observational zone, and rule-in, respectively.

Conclusions: Using a simple algorithm incorporating

sample is feasible and safe. The aim of our study therefore was to develop and validate an algorithm for rapid rule-in and rule-out of AMI using high-sensitivity cardiac troponin T (hs-cTnT) baseline levels and absolute changes within 1 hour.

METHODS

STUDY DESIGN AND POPULATION

Advantageous Predictors of Acute Coronary Syndrome Evaluation (APACE) is an ongoing prospective international multicenter study designed and coordinated by the University Hospital Basel (clinicaltrials.gov Identifier: NCT00470587).[8,18] From April 2006 to June 2009, a total of 1247 unselected patients presenting to the ED with acute chest pain symptoms suggestive of AMI such as acute chest pain and angina pectoris with an onset or peak within the last 12 hours were recruited. Patients with terminal kidney failure requiring dialysis were excluded. The study was carried out according to the principles of the Declaration of Helsinki and approved by the local ethics committees. Written informed consent was obtained from all patients.

Patients with ST-segment elevation myocardial infarction (n=50) were excluded from this analysis because cardiac biomarkers are of limited clinical value in these patients. Among the remaining 1197 patients, samples at presentation as well as after 1 hour for measurement of hs-cTnT were available in 872 patients. The most common reasons for missing values after 1 hour (n=327) were early transfer to the catheterization

To determine the final diagnosis for each patient, adjudication of final diagnoses was performed centrally in the core laboratory (University Hospital Basel) for all patients according to levels of hs-cTnT. More specifically, 2 independent cardiologists (T.R., M.R., P.H., and M.P.) reviewed all available medical records (including patient history, physical examination, results of laboratory testing including hs-cTnT levels, radiologic testing, ECG, echocardiography, cardiac exercise test, lesion severity, and morphology in coronary angiography) pertaining to the patient from the time of ED presentation to 60-day follow-up. In situations of diagnostic disagreement, cases were reviewed and adjudicated in conjunction with a third cardiologist (C.M.).

Acute myocardial infarction was defined and hs-cTnT levels interpreted as recommended in current guidelines.[2,4,20,21] In brief, AMI was diagnosed when there was evidence of myocardial necrosis with a notable rise and/or fall in a clinical setting consistent with myocardial ischemia. The 99th percentile (14 ng/L) was used as cutoff for myocardial necrosis. Absolute cTn changes were used to determine significant changes based on the diagnostic superiority of absolute over relative changes.[18] On the basis of studies of the biological variation of cTn[22,23] as well as on data from previous chest pain cohort studies,[9,24] a significant absolute change was defined as a rise or fall of at least 10 ng/L within 6 hours, or, in an assumption of linearity, as an absolute change of 6 ng/L within 3 hours, 4 ng/L within 2 hours, or 2 ng/L within 1 hour. If discordant findings occurred, the longest time interval available was required to fulfill the change criteria.

Unstable angina (UA) was diagnosed in patients with nor-