CLINICAL RESEARCH STUDY

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Introduction of High-sensitivity Troponin Assays: Impact on Myocardial Infarction Incidence and Prognosis

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ABSTRACT

OBJECTIVE: The study objective was to compare the incidence and prognosis of acute myocardial infarction when using high-sensitivity cardiac troponin assays instead of a standard cardiac troponin assay for the diagnosis of acute myocardial infarction.

METHODS: In a prospective international multicenter study, we enrolled 1124 consecutive patients presenting with suspected acute myocardial infarction. Final diagnoses were adjudicated by 2 independent cardiologists 2 times using all available clinical information: first using standard cardiac troponin levels and second using high-sensitivity cardiac troponin T levels for adjudication. Patients were followed up for a mean of 19 ± 9 months.

RESULTS: The use of high-sensitivity cardiac troponin T instead of standard cardiac troponin resulted in an increase in the incidence of acute myocardial infarction from 18% to 22% (242 vs 198 patients), a relative increase of 22%. Of the 44 additional acute myocardial infarctions, 35 were type 1 acute myocardial infarctions and 9 were type 2 acute myocardial infarctions. This was accompanied by a reciprocal decrease in the incidence of unstable angina (unstable angina, 11% vs 13%). The most pronounced increase was observed in patients adjudicated with cardiac symptoms of origin other than coronary artery disease with cardiomyocyte damage (83 vs 31 patients, relative increase of 268%). Cumulative 30-month mortality rates were 4.8% in patients without acute myocardial infarction, 16.4% in patients with a small acute myocardial infarction detected only by high-sensitivity cardiac troponin T but not standard cardiac troponin, and 23.9% in patients with a moderate/large acute myocardial infarction according to standard cardiac troponin assays and high-sensitivity cardiac troponin T ($P < .001$).

CONCLUSIONS: The introduction of high-sensitivity cardiac troponin assays leads to only a modest increase in the incidence of acute myocardial infarction. The novel sensitive assays identify an additional high-risk group of patients with increased mortality, therefore appropriately classified with acute myocardial infarction (Advantageous Predictors of Acute Coronary Syndromes Evaluation; NCT00470587).

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The incidence of a disease depends critically on the criteria used for its diagnosis. The cornerstones for the diagnosis of acute myocardial infarction are history, 12-lead electrocardiogram (ECG), and biomarkers of myocardial necrosis. Although ECG techniques and ECG criteria for acute myocardial infarction have remained unchanged during the past few decades, the introduction of more sensitive biomarkers of myocardial necrosis, such as the MB fraction of creatine kinase and the cardiac troponins, have had a major influence on the diagnostic criteria of acute myocardial infarction.[1-3] Epidemiologic studies have confirmed the hypothesis of an increase in the incidence of non-ST-elevation myocardial infarctions in parallel with the increased use of more sensitive serologic markers of myocardial necrosis reaching a plateau in 2004.[4,5] Previous studies have shown that lowering the cardiac troponin threshold identifies a subset of patients with chest pain with true myocardial necrosis associated with worse outcomes.[6,7]

CLINICAL SIGNIFICANCE

- The introduction of high-sensitivity cardiac troponin assays into clinical practice modestly increases the incidence of acute myocardial infarction (up to 22%).
- The increase in the detection of diseases with myocardial necrosis from causes other than acute myocardial infarction is profound (up to 50%).
- Patients with small acute myocardial infarctions identified with only high-sensitivity cardiac troponin assays but not standard cardiac troponin assays had a high mortality rate (16% after 30 months).

The recent introduction of high-sensitivity cardiac troponin assays has enabled the measurement of cardiac troponin concentrations that were not reliably detected with prior generations of tests. The new tests have been shown to improve the early diagnosis of acute myocardial infarction.[7,8] The improvements in assay sensitivity have increased the number of positive cardiac troponin tests in patients with suspected acute myocardial infarction,[8-12] and minor cardiac troponin elevations have been observed in various stable clinical settings, including chronic coronary artery disease[13,14] and chronic heart failure,[15] as well as in the elderly.[14]

The impact of the clinical application of the novel high-sensitivity cardiac troponin assays on the incidence of acute myocardial infarction is unknown,[14] as is the prognosis of patients also identified with acute myocardial infarction. The aim of this study was to investigate the change in incidence of acute myocardial infarction and its prognosis in patients with suspected acute myocardial infarction when using a high-sensitivity cardiac troponin assay instead of a standard cardiac troponin assay for adjudication of diagnoses.

MATERIALS AND METHODS

Study Design and Population

Advantageous Predictors of Acute Coronary Syndrome Evaluation is an ongoing prospective international multicenter study designed and coordinated by the University Hospital Basel (NCT00470587).[11,16,17] From April 2006 to June 2009, a total of 1247 consecutive patients presenting to the emergency department with symptoms suggestive of acute myocardial infarction, such as 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. Patients were excluded from analysis if (1) high-sensitivity cardiac troponin T values were missing ($n = 27$); (2) only a value at presentation but no follow-up values were available, and this presentation value was > 0.014 μg/L (no information on dynamics, $n = 39$); and (3) only an admission value (but no follow-up values) was available, this admission value was < 0.014 μg/L, and time since onset of symptoms or peak was < 4 hours ($n = 57$). This left 1124 patients with complete data for analysis.

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. The authors designed the study, gathered and analyzed the data, vouch for the data and analysis, wrote the article, and decided to publish. There were no agreements concerning confidentiality between the sponsors and the authors or institutions.

Routine Clinical Assessment

All patients underwent an initial clinical assessment, including clinical history, physical examination, 12-lead ECG, standard blood tests, and chest radiography. Standard cardiac troponin levels were measured at presentation and after 6 to 9 hours or as long as clinically indicated. The treatment of patients was left at the discretion of the attending physician.

Investigational High-Sensitivity Cardiac Troponin T Analysis

Blood samples for determination of high-sensitivity cardiac troponin T (Roche Diagnostics, Indianapolis, Ind) were collected in serum tubes at presentation to the emergency department. Additional samples were collected after 1, 2, 3, and 6 hours. Serial sampling was discontinued when the diagnosis of acute myocardial infarction was certain and treatment required transferring the patient to the catheter laboratory or coronary care unit. After centrifugation, samples were frozen at $-80°C$ until assayed in a blinded fashion on the Elecsys 2010 (Roche Diagnostics) in a dedicated