Diagnosis of Unstable Angina Pectoris Has Declined Markedly with the Advent of More Sensitive Troponin Assays

CrossMark

Maria D'Souza, MD,[a] Laura Sarkisian, MD,[a] Lotte Saaby, MD, PhD,[a] Tina S. Poulsen, MD, PhD,[a] Oke Gerke, MSc, PhD,[b] Torben B. Larsen, MD, PhD,[c] Axel C.P. Diederichsen, MD, PhD,[a] Nikolaj Jangaard, BScmed,[a] Søren Z. Diederichsen, MD,[a] Susanne Hosbond, MD, PhD,[a] Jens Hove, MD, PhD,[d] Kristian Thygesen, MD, DMSc,[e] Hans Mickley, MD, DMSc[a]

[a]Department of Cardiology, Odense University Hospital, Odense, Denmark; [b]Department of Nuclear Medicine, Odense University Hospital and Center of Health Economics Research, Odense, Denmark; [c]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark; [d]Department of Cardiology, Hvidovre Hospital, Copenhagen, Denmark; [e]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark.

ABSTRACT

BACKGROUND: Since the arrival of the universal definition of myocardial infarction more sensitive troponin assays have been developed. How these occurrences have influenced the proportions and clinical features of the components of acute coronary syndrome have not been studied prospectively in unselected hospital patients.

METHODS: During 2010 we evaluated all patients in whom cardiac troponin I had been measured at a single university hospital. The diagnosis of acute myocardial infarction (ST-elevation myocardial infarction [STEMI] or non-ST-elevation myocardial infarction [NSTEMI]) was established in cases of a rise and/or fall of cardiac troponin I together with cardiac ischemic features. Patients with unstable chest discomfort and cardiac troponin I values below the decision limit of myocardial infarction were diagnosed as having unstable angina pectoris. The definition of acute coronary syndrome included unstable angina pectoris, NSTEMI, and STEMI. Mortality data were obtained from the Danish Civil Personal Registration System.

RESULTS: Of 3762 consecutive patients, 516 had acute coronary syndrome. Unstable angina pectoris was present in 7%, NSTEMI in 67%, and STEMI in 26%. The NSTEMI patients were older, more frequently women, and had more comorbidities than patients with unstable angina pectoris and STEMI. At median follow-up of 3.2 years 195 patients had died: 14% of unstable angina pectoris, 45% of NSTEMI, and 25% of STEMI patients. Age-adjusted log−rank statistics revealed differences in mortality: NSTEMI vs unstable angina pectoris ($P = .0091$) and NSTEMI vs STEMI ($P = .0045$).

CONCLUSIONS: The application of the universal definition together with the use of a contemporary troponin assay seems to have reduced the proportion of patients with unstable angina pectoris to the benefit of patients with NSTEMI. Despite this, NSTEMI patients have a sustained higher mortality than patients with STEMI.
© 2015 Elsevier Inc. All rights reserved. • The American Journal of Medicine (2015) 128, 852-860

KEYWORDS: Acute coronary syndrome; Mortality; Myocardial infarction; Troponin; Unstable angina pectoris

Acute coronary syndrome encompasses unstable angina pectoris together with non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI).[1,2] Over the last decades improvements of cardiac troponin assays have led to greater sensitivity but lower specificity for diagnosing acute myocardial infarction.[3,4] Recently new high-sensitivity troponin assays have been marketed, and it has been proposed that patients who in the past would have been classified as having unstable angina

pectoris will be diagnosed with acute myocardial infarction.[1,3,5] Even so, and in the wake of the universal definition,[6] it is important to know the true proportions of the individual entities of acute coronary syndrome when using a conventional troponin assay. The main purpose of this prospective study is to assess the proportions, the clinical characteristics, and the outcomes of the individual acute coronary syndrome components in an unselected hospital cohort.

METHODS

Study Design

Odense University Hospital serves as a tertiary unit for a total of 1.2 million citizens and has a local catchment area of 300,000 residents. The hospital has 1000 beds and 27 clinical departments. During a 1-year period from January 2010 to January 2011 all hospitalized patients having cardiac troponin I measured on clinical indication were considered.[7,8] Only patients living in the local catchment area were included, to avoid selection bias. Patients aged <18 years were excluded, and a patient could be included only once. During the inclusion period management of patients with acute coronary syndrome was according to guidelines from the European Society of Cardiology.[9,10]

Data Collection

Patients who had cardiac troponin I measured were traced through retrieval 3 times daily at the department of clinical biochemistry of the hospital. Within 24 hours after the initial troponin sampling, patients had a supplementary history taken by a dedicated study staff, paying special attention to symptoms, clinical characteristics, and comorbidity. Data registered were specified in a worksheet (**Appendix**, available online). Results of echocardiographic examinations were retrieved from the hospital's records, and the results of coronary angiographies were collected from the Western Denmark Heart Registry.[11] Cardiovascular prescription medication reimbursed by the patients within 3 months after hospital discharge was identified through the Odense Pharmaco-Epidemiological Database.[12] On January 6, 2014 the number of deaths was retrieved from the Danish Civil Personal Registration System.[13]

Analysis of Cardiac Troponin I

Samples of cardiac troponin I were analyzed by Architect c16000 (Abbott Diagnostics, Abbott Park, Ill), which has a detection limit of 10 ng/L, an upper reference limit of 99th percentile of 28 ng/L, and a coefficient of variation <10% at 32 ng/L.[14] Accordingly, a cardiac troponin I value >30 ng/L was considered the decision limit for the diagnosis of myocardial infarction.

> ## CLINICAL SIGNIFICANCE
>
> - Less than 10% of patients with acute coronary syndrome have unstable angina pectoris.
>
> - During the last decade the proportion of patients with ST-elevation myocardial infarction remains steady, comprising approximately 25% of the acute coronary syndrome population.
>
> - After more than 3 years of follow-up a sustained, much higher mortality is observed in patients with non-ST-elevation than in those with ST-elevation myocardial infarction.

Definition of Unstable Angina Pectoris, NSTEMI, and STEMI

According to the criteria of the universal definition the myocardial infarction diagnosis is established in the presence of an increasing/decreasing pattern in cardiac troponin I values, with at least one measurement above the 99th percentile together with evidence of myocardial ischemia.[6] The timing of cardiac troponin I value measurements was according to the routine procedures of the hospital and has been described previously.[8] Additionally, the type of myocardial infarction was categorized as STEMI or NSTEMI according to the universal definition.[6] Patients with new (or presumably new) left bundle branch block were included in the STEMI group. Unstable angina pectoris was diagnosed in patients with unstable chest discomfort (rest, new onset, or worsening of angina) and the presence of cardiac troponin I values ≤30 ng/L.[15]

Adjudication of the Diagnoses

On the basis of the prospectively obtained source information provided by the worksheet, routine laboratory data and patient records (**Appendix**), an independent clinical event committee consisting of 3 local cardiologists adjudicated the diagnoses of unstable angina pectoris, NSTEMI, or STEMI. In case of diagnostic ambiguity the Task Force co-chairman (KT) of the universal myocardial infarction definition was consulted to reach consensus.

Statistical Analysis

Continuous variables are presented as medians (with interquartile range) or as means (± standard deviation). Categorical variables are listed as frequencies and respective percentages. After visually inspecting for normal distributions, normally distributed continuous variables were displayed by means (± standard deviation), and group comparisons were performed using 1-way analysis of variance. If normal distributions could not be achieved, the nonparametric Kruskal-Wallis test was used for comparisons between the groups, and medians with 25th and 75th percentiles were presented for descriptive purposes. Pearson's χ^2 test was used for intergroup comparison of categorical