CLINICAL RESEARCH STUDY

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Prognostic Impact of Myocardial Injury Related to Various Cardiac and Noncardiac Conditions

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ABSTRACT

BACKGROUND: Elevated cardiac troponins in clinical conditions other than myocardial infarction are well known. For such occurrences, the term "myocardial injury" has been proposed. The long-term outcome in patients with myocardial injury related to various cardiac and noncardiac clinical disorders is unknown.

METHODS: During January 2010 to January 2011, we prospectively studied hospitalized patients who had cardiac troponin I measured on clinical indication. Patients with cardiac troponin I values >30 ng/L and no evidence of myocardial ischemia were diagnosed as having myocardial injury. Patients were classified into 5 categories of plausible related conditions: cardiac ischemic, cardiac nonischemic, noncardiac, multifactorial, or indeterminate. Follow-up was a minimum of 3 years, with all-cause mortality as the single end-point.

RESULTS: A total of 3762 patients were considered, of whom 1089 (29%) had myocardial injury. The most common associated conditions were noncardiac (n = 346) or multifactorial (n = 359). Cardiac ischemic (n = 183) and cardiac nonischemic (n = 134) conditions occurred less frequently. After a median of 3.2 years, 645 patients (59%) had died. A multivariate Cox regression analysis showed no difference in mortality between patients with cardiac ischemic and cardiac nonischemic conditions (hazard ratio [HR] 0.75; 95% confidence interval [CI], 0.50-1.13; $P = .2$). Patients with noncardiac or multifactorial disorders, however, had significantly higher mortality than those with associated cardiac ischemic conditions (HR 1.39; 95% CI, 1.06-1.80; $P = .02$, and HR 1.94; 95% CI, 1.50-2.51; $P < .001$), respectively.

CONCLUSIONS: In patients with myocardial injury, the most common associated conditions were noncardiac or multifactorial. Of notice, these patients had significantly higher long-term mortality when compared with those with associated cardiac conditions.

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KEYWORDS: Myocardial injury; Prognosis; Troponins

Cardiac troponin I and T are highly sensitive markers of myocardial necrosis[1] and comprise the cornerstone in the diagnosis of myocardial infarction.[2,3] Continuous improvements in the sensitivity of cardiac troponin assays have led to a substantial increase in the detection of cardiac troponins in different populations.[4-6] The occurrence of elevated cardiac troponin values in noncardiac and cardiac conditions other than myocardial infarction is well established.[1,7-11] For such cases, the term myocardial injury with necrosis, or, briefly, myocardial injury, has been proposed.[3] However, at present the prognostic implications of myocardial injury have been investigated only in selected subgroups, often with small patient numbers,[12-16] but the results are hampered by the use of older cardiac troponin assays, retrospective study designs, or cut-off values other than the recommended 99th percentile of the upper reference limit (URL).[12,14,15,17,18]

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In a tertiary hospital setting we prospectively investigated all patients with myocardial injury. Further, we aimed to describe the plausible relationship between myocardial injury and various cardiac and noncardiac conditions, and to investigate the long-term outcome in terms of all-cause mortality.

METHODS

Study Design and Population

The study comprised hospitalized patients at a 1000-bed hospital (Odense University Hospital) from January 6, 2010 to January 5, 2011.[19,20] Odense University Hospital serves as the local hospital for a catchment area of 300,000 residents and is the largest in the Southern Region of Denmark. Consecutive patients having cardiac troponin I measured on clinical indication in any of the hospital's departments were traced through retrieval 3 times daily. In cases of multiple admissions, only the first was considered.

CLINICAL SIGNIFICANCE

- Among hospitalized patients with cardiac troponin I values above 30 ng/L, the majority will have myocardial injury.
- Myocardial injury is more frequently related to plausible noncardiac or multiple conditions when compared with clinical cardiac disorders.
- Cardiac nonischemic conditions are associated with very high troponin concentrations, but the outcome is rather good.
- In contrast, myocardial injury related to noncardiac or multiple conditions carries a very poor long-term prognosis.

Within 24 hours after the initial cardiac troponin I testing, patients had a supplementary history taken by a dedicated study personnel paying special attention to symptoms, clinical characteristics, and comorbidity. The study personnel did not interfere with patient management. Results regarding invasive coronary procedures were collected from the Western Denmark Heart Registry.[21]

On January 6, 2014, fatal cases were retrieved from the Danish Civil Registration System by use of each patient's unique civil registration number. This registration system holds records on all Danish citizens, living and deceased.[22]

Inclusion Criteria

Patients were eligible for study inclusion if a cardiac troponin I blood sample was taken on clinical indication at the request of the attending physician(s) in any of the 27 clinical departments of the hospital.

Exclusion Criteria

1) Age <18 years.
2) Residents from outside the local catchment area.

Definition of Diagnoses

The diagnosis of acute myocardial infarction was established according to the universal definition, that is, a typical increase or fall of cardiac troponin I concentrations with at least one value above 30 ng/L along with evidence of myocardial ischemia.[2] Serial cardiac troponin I samples were taken as described previously.[20] Patients with cardiac troponin I values >30 ng/L and no evidence of myocardial ischemia were diagnosed as having myocardial injury. Patients with cardiac troponin I ≤30 ng/L were categorized as having nonelevated cardiac troponin I values.

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, a URL of 99th percentile of 28 ng/L, and a coefficient of variation <10% at 32 ng/L.[23] A cardiac troponin I value >30 ng/L was considered elevated.

Adjudication of the Diagnosis

Three experienced local cardiologists adjudicated the diagnoses in patients with at least one cardiac troponin I value >30 ng/L. The diagnoses were based on the prospectively obtained source information, routine laboratory data, and patient records. Patients with myocardial injury were categorized into 5 prespecified subgroups reflecting the associated cardiac or noncardiac clinical conditions. The subgrouping is adapted from earlier recommendations[24]:

Group A: Cardiac; secondary to myocardial ischemia (eg, heart failure, tachy-/bradyarrhythmias).

Group B: Cardiac; not related to myocardial ischemia (eg, myocarditis, invasive cardiac procedures).

Group C: Noncardiac (eg, infection, chronic kidney disease).

Group D: Multifactorial; at least 2 cardiac or noncardiac conditions.

Group E: Indeterminate; no plausible associated condition(s) could be identified.

In cases of diagnostic ambiguity, the Task Force cochairman (KT) of the universal definition was consulted to reach consensus. Descriptive and prognostic data of patients with myocardial infarction have been published.[19,20,25]

Statistical Analysis

Categorical variables are presented as frequencies and respective percentages. Group comparisons were done using the Pearson chi-squared test or Fisher's exact test. After visually inspecting for normal distributions, normally distributed continuous variables were displayed by means