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Implications of Introducing High-Sensitivity Cardiac Troponin T Into Clinical Practice

Data From the SWEDEHEART Registry

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ABSTRACT

BACKGROUND Cardiac troponin is the preferred biomarker for diagnosing myocardial infarction (MI).

OBJECTIVES The aim of this study was to examine the implications of introducing high-sensitivity cardiac troponin T (hs-cTnT) into clinical practice and to define at what hs-cTnT level risk starts to increase.

METHODS We analyzed data from 48,594 patients admitted because of symptoms suggesting an acute coronary syndrome and who were entered into a large national registry. Patients were divided into Group 1, those with hs-cTnT <6 ng/l; Group 2, those with hs-cTnT 6 to 13 ng/l; Group 3, those with hs-cTnT 14 to 49 ng/l (i.e., a group in which most patients would have had a negative cardiac troponin T with older assays); and Group 4, those with hs-cTnT ≥50 ng/l.

RESULTS There were 5,790 (11.9%), 6,491 (13.4%), 10,476 (21.6%), and 25,837 (53.2%) patients in Groups 1, 2, 3, and 4, respectively. In Groups 1 to 4, the proportions with MI were 2.2%, 2.6%, 18.2%, and 81.2%. There was a stepwise increase in the proportion of patients with significant coronary stenoses, left ventricular systolic dysfunction, and death during follow-up. When dividing patients into 20 groups according to hs-cTnT level, the adjusted mortality started to increase at an hs-cTnT level of 14 ng/l.

CONCLUSIONS Introducing hs-cTnT into clinical practice has led to the recognition of a large proportion of patients with minor cardiac troponin increases (14 to 49 ng/l), the majority of whom do not have MI. Although a heterogeneous group, these patients remain at high risk, and the adjusted mortality rate started to increase at the level of the 99th percentile in healthy controls. (J Am Coll Cardiol 2015;65:1655–64) © 2015 by the American College of Cardiology Foundation.

Cardiac troponin (cTn) has been the recommended and preferred biomarker for the diagnosis of myocardial infarction (MI) since 2000 (1). Evidence of myocardial necrosis has been defined as the detection of an increase and/or decrease of cTn with at least 1 value above the 99th percentile of a normal reference population (2–4). Guidelines also state that the assay used should have an optimal precision (coefficient of variation ≤10%) at this level (2–4). Due to the lack of adequate precision of many cTn assays, a new generation of sensitive cTn assays has recently been

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

CI = confidence interval

cTn = cardiac troponin

cTnT = cardiac troponin T

ECG = electrocardiogram

HF = heart failure

hs-cTnT = high-sensitivity cardiac troponin T

MI = myocardial infarction

developed to comply with guideline requirements (5–8). The novel fifth-generation high-sensitivity cTnT (hs-cTnT) assay, with a validated improved analytical performance, is a modification of the fourth-generation assay, lowering the decision limit for myocardial injury from 30 ng/l (with the fourth-generation assay) to 14 ng/l with the fifth-generation hs-cTnT assay (5).

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This new assay has a better clinical sensitivity for the detection of myocardial tissue injury, including acute MI (5–11) and is more useful for risk stratification compared with the fourth-generation cTnT assay (12–22). It is, however, important to note that the detection of cTn indicates myocardial injury (not just ischemic injury), regardless of the etiology (23–25). Thus, there are concerns that the new assays may lead to lower specificity and perhaps unnecessary admissions and overuse of resources. Consequently, it is important to describe the clinical effects of introducing hs-cTnT into clinical practice.

The SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry is a nationwide registry that includes almost all patients who are admitted to a coronary care unit or other specialized facility because of symptoms suggestive of an acute coronary syndrome (ACS) (26). The main objective of this new study was to describe the patients who were identified by the hs-cTnT assay with only a minor increase (14 to 49 ng/l), i.e., a group in which most patients would have had a negative result using older cTnT assays. We evaluated baseline characteristics, in-hospital course, final diagnosis, and outcome. Using a very large cohort of patients with symptoms suggestive of an ACS, we also wanted to delineate the association between the level of hs-cTnT and subsequent long-term outcome, focusing on the lower end of the analytical range.

METHODS

For patients who are admitted to the hospital because of symptoms suggestive of an ACS, the SWEDEHEART registry collects information prospectively for 106 variables, including patient demographics, admission logistics, risk factors, medical history, previous medical treatment and investigations, medical treatment in hospital, interventions, hospital outcome, discharge diagnoses, and discharge medications (26). The SWEDEHEART registry is regularly merged with the Swedish population registry, which includes information about the vital status of all Swedish citizens. To ensure the correctness and high quality of the registry data, hospitals are monitored on a regular basis. The degree of agreement between the hospital records and the registry is 96% (26). Patients included in the registry are informed about their participation and maintain the right to decline (26).

STUDY POPULATION. The study included a total of 48,594 consecutive patients who, over a 4-year period (2009 to 2012), were admitted and recorded in the SWEDEHEART registry in 45 Swedish hospitals that had introduced the hs-cTnT assay into their clinical practice. Only centers with more than 100 registered patients with measured hs-cTnT were included. An acute MI was defined according to current guidelines (2,3), and all hospitals used the 99th percentile in healthy controls as decision limits. However, 8 hospitals initially used higher (30 to 40 ng/l) decision limits. All data were made anonymous before statistical analyses were performed. The study was conducted according to the principles of the Declaration of Helsinki and approved by the local ethics committee.

LABORATORY ANALYSIS. The Elecsys troponin T high-sensitive assay (Roche Diagnostics Corporation, Indianapolis, Indiana) was used to determine the maximal hs-cTnT level during hospitalization. The recommended limit of blank and limit of detection of hs-cTnT are 3 ng/l and 5 ng/l, respectively (5). The 99th percentile in healthy controls is 14 ng/l (27), and the coefficient of variation (≤10%) is reached at 13 ng/l (5). The analytical range of measurement is 3 to 10,000 ng/l (5,27). Recently, 2 studies (5,27) demonstrated that cTn concentrations determined by the fourth-generation cTnT and hs-cTnT assay are not comparable at the lower end of the analytical range. Giannitsis et al. (5) showed that a cTn value of 30 ng/l according to the fourth-generation cTnT assay corresponds to ~50 ng/l according to the hs-cTnT assay. This has also been supported by others (27); therefore, we divided our study population into 4 groups according to the maximal hs-cTnT during hospitalization: Group 1 with a maximal hs-cTnT value <6 ng/l (a test result below the limit of detection [<5 ng/l] has, in the majority of cases, been registered as "5" ng/l in the registry); Group 2 with a maximal hs-cTnT value of 6 to 13 ng/l; Group 3 with a maximal hs-cTnT value of 14 to 49 ng/l (i.e., a group in which most patients would have had a negative cTnT using the old cTnT