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High-Sensitivity Troponins and Outcomes After Myocardial Infarction

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ABSTRACT

BACKGROUND It remains unknown how the introduction of high-sensitivity cardiac troponin T (hs-cTnT) has affected the incidence, prognosis, and use of coronary angiographies and revascularizations in patients with myocardial infarction (MI).

OBJECTIVES The aim of this study was to investigate how the incidence of MI and prognosis after a first MI was affected by the introduction of hs-cTnT.

METHODS In a cohort study, the authors included all patients with a first MI from the Swedish National Patient Registry from 2009 to 2013. Cox regression was used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs) for risk of all-cause mortality, reinfarction, coronary angiographies, and revascularizations in patients with MI diagnosed using hs-cTnT compared with those diagnosed using conventional troponins (cTn).

RESULTS During the study period, 47,133 MIs were diagnosed using cTn and 40,746 using hs-cTnT. The rate of MI increased by 5% (95% CI: 0% to 10%) after the introduction of hs-cTnT. During 3.9 ± 2.8 years of follow-up, there were 33,492 deaths, with no difference in the risk of all-cause mortality (adjusted HR: 1.00; 95% CI: 0.97 to 1.02). There were, in total, 15,766 reinfarctions during 3.1 ± 2.3 years of follow-up, with the risk of reinfarction reduced by 11% in patients diagnosed using hs-cTnT (adjusted HR: 0.89; 95% CI: 0.86 to 0.91). The use of coronary angiographies (adjusted HR: 1.16; 95% CI: 1.14 to 1.18) and revascularizations (adjusted HR: 1.13; 95% CI: 1.11 to 1.15) increased in the hs-cTnT group.

CONCLUSIONS In a nationwide cohort study including 87,879 patients with a first MI, the introduction of hs-cTnT was associated with an increased incidence of MI, although with no impact on survival. We also found a reduced risk of reinfarction alongside increased use of coronary angiographies and revascularizations. (J Am Coll Cardiol 2018;71:2616–24)

Cardiac troponin assays, which have been used since the 1990s to diagnose myocardial infarction (MI), have enabled more accurate diagnosis, risk stratification, and clinical decision making than older cardiac biomarkers (1). However, because prolonged serial sampling is often needed to achieve diagnostic accuracy for determining or excluding MI, the effectiveness of using conventional cardiac troponin (cTn) assays has been questioned (2). High-sensitivity cardiac troponin (hs-cTn) assays,

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which have been increasingly used in clinical practice for some years, allow more rapid rule-in and rule-out of MI compared with cTn assays (3–5).

Nevertheless, it has been suggested that implementation of hs-cTn assays could diminish the clinical specificity for MI diagnosis and potentially lead to increased use of resources. However, in cohort studies of patients with chest pain in the emergency department, the introduction of hs-cTn assays has been associated with small or no increases in coronary angiographies and revascularizations, and a sharp decline in admission rates for chest pain (6–9). In patients admitted to coronary care units, the 1-year mortality rate was unchanged after the introduction of the high-sensitivity cardiac troponin T (hs-cTnT) assay (10). To the best of our knowledge, no large cohort study has investigated the impact of the introduction of hs-cTn assays on the risk of mortality, reinfarctions, and resource use in unselected MI patients. Therefore, we conducted a nationwide study comprising patients with MI during the years when the hs-cTnT assay was adopted widely in Sweden.

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METHODS

STUDY POPULATION. We included all patients who were hospitalized for a first MI during the period from 2009 to 2013 in Sweden and were diagnosed using either cTn or hs-cTnT at hospitals where the 99th percentile value was used as the decision limit for MI.

DATA SOURCES. We used the Swedish National Patient Registry, which includes all hospitalizations in Sweden, to retrieve the study population, their characteristics, and outcomes. We then added information about medication from the Prescribed Drug Registry, and deaths from the Cause-of-Death Registry. Information on cTn assays; and the locally applied cutoffs for the diagnosis of MI were obtained from the SWEDEHEART registry (the Swedish Web-based system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies), from local representatives of all hospitals, and by online search using the Internet. The registries and the construction of the database are described in detail in the Online Appendix.

TROPONIN ASSAYS. From 2009 to 2012, the current iteration of the hs-cTnT assay (Roche Diagnostics, Basel, Switzerland) was the only higher-precision method used in Sweden. For this assay, the lowest concentration measurable with a 10% coefficient of variation is 13 ng/l, the limit of detection is 5 ng/l and the 99th percentile value among healthy controls is 14 ng/l (11). However, some hospitals in Sweden initially used higher diagnostic cutoffs, in the range of 30 to 40 ng/l, for MI (Online Table 1).

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

cTn = cardiac troponin

HR = hazard ratio

hs-cTn = high-sensitivity cardiac troponin

MI = myocardial infarction

DEFINITIONS. The index date was defined as the date when the patient was hospitalized for MI. Medication at baseline was defined as a minimum of 2 dispensed prescriptions during the 365 days preceding the index date. Medication at discharge was defined as at least 1 dispensed prescription during the 6 months following the index date. International Classification of Disease-9th and 10th Revisions were used to retrieve information about comorbidities (Online Table 2). Diabetes at baseline was defined as ongoing medication with any hypoglycemic agent. In multivariable models, the diabetes definition was extended to include patients who, in addition, had any hypoglycemic agent dispensed 6 months following the index date. The Anatomical Therapeutic Chemical classification codes for medication are listed in Online Table 3.

FOLLOW-UP. Follow-up for all-cause mortality started at the index date and ended at the time of death or March 25, 2016, whichever occurred first. For reinfarction, follow-up started at the time of discharge after MI and ended at the date of readmission for a subsequent MI, at the time of death, or December 31, 2014. For coronary angiography and revascularization, follow-up started at the index date and ended at the time of the outcome, at the time of death, or at 30 days after the index date to account for acute event rates. The patient registry is updated only yearly for hospital stays, accounting for the 1-year difference between follow-up for reinfarction and all-cause mortality, which is reported and registered by Swedish authorities within a few weeks of an individual's death.

OUTCOMES. The primary outcome was all-cause mortality. Secondary outcomes were: 1) reinfarction; 2) coronary angiography; and 3) coronary revascularization. In the outcomes analyses, we excluded 9,747 patients who were diagnosed with MI at hospitals that used the hs-cTnT assay with a higher decision limit for MI than the 99th percentile value (Online Table 1) or were diagnosed with MI in health care settings other than acute care hospitals. In addition, for reasons of comparison, we calculated the national incidence of MI for the years 2007 to 2013 whereby MIs excluded in the outcomes analyses were also counted.

STATISTICAL ANALYSES. Baseline characteristics are described as frequencies and percentages for categorical variables, and means and standard