CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Sensitive Troponin Assay and the Classification of Myocardial Infarction

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ABSTRACT

BACKGROUND: Lowering the diagnostic threshold for troponin is controversial because it may disproportionately increase the diagnosis of myocardial infarction in patients without acute coronary syndrome. We assessed the impact of lowering the diagnostic threshold of troponin on the incidence, management, and outcome of patients with type 2 myocardial infarction or myocardial injury.

METHODS: Consecutive patients with elevated plasma troponin I concentrations (≥50 ng/L; n = 2929) were classified with type 1 (50%) myocardial infarction, type 2 myocardial infarction or myocardial injury (48%), and type 3 to 5 myocardial infarction (2%) before and after lowering the diagnostic threshold from 200 to 50 ng/L with a sensitive assay. Event-free survival from death and recurrent myocardial infarction was recorded at 1 year.

RESULTS: Lowering the threshold increased the diagnosis of type 2 myocardial infarction or myocardial injury more than type 1 myocardial infarction (672 vs 257 additional patients, $P < .001$). Patients with myocardial injury or type 2 myocardial infarction were at higher risk of death compared with those with type 1 myocardial infarction (37% vs 16%; relative risk [RR], 2.31; 95% confidence interval [CI], 1.98-2.69) but had fewer recurrent myocardial infarctions (4% vs 12%; RR, 0.35; 95% CI, 0.26-0.49). In patients with troponin concentrations 50 to 199 ng/L, lowering the diagnostic threshold was associated with increased healthcare resource use ($P < .05$) that reduced recurrent myocardial infarction and death for patients with type 1 myocardial infarction (31% vs 20%; RR, 0.64; 95% CI, 0.41-0.99), but not type 2 myocardial infarction or myocardial injury (36% vs 33%; RR, 0.93; 95% CI, 0.75-1.15).

CONCLUSIONS: After implementation of a sensitive troponin assay, the incidence of type 2 myocardial infarction or myocardial injury disproportionately increased and is now as frequent as type 1 myocardial infarction. Outcomes of patients with type 2 myocardial infarction or myocardial injury are poor and do not seem to be modifiable after reclassification despite substantial increases in healthcare resource use.

 • *The American Journal of Medicine (2015) 128, 493-501*

KEYWORDS: Myocardial infarction; Outcomes; Troponin; Type 2

Funding: British Heart Foundation Intermediate Fellowship (FS/10/024/28266) and Clinical Research Fellowship (SS/CH/09/002).

Conflict of Interest: ASVS, SW, and NLM have received honoraria for Abbott Diagnostics, and NLM has acted as a consultant for Beckman-Coulter and Abbott Diagnostics. ASJ has consulted for most of the major diagnostic companies.

Authorship: All authors had access to the data and played a role in writing this manuscript.

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http://dx.doi.org/10.1016/j.amjmed.2014.10.056

The Universal Definition of Myocardial Infarction proposes a classification for patients with myocardial infarction based on cause to accommodate more sensitive markers of myocardial necrosis.[1] The classification differentiates between type 1 myocardial infarction, due to thrombosis of an atherosclerotic plaque, and type 2 myocardial infarction, due to an imbalance of myocardial blood supply and demand that may arise in many acute medical and surgical conditions. The expert consensus further defines evidence of myocardial necrosis in the absence of clinical evidence of myocardial ischemia as myocardial injury. Although this classification has been used in recent clinical trials to refine clinical outcomes,[2–4] type 2 myocardial infarction and myocardial injury are difficult to distinguish or diagnose definitively, and the frequency in clinical practice and implications of these diagnoses are uncertain.[5,6]

After improvements in assay performance, a sensitive troponin assay was introduced into our institution.[7,8] The validation and subsequent implementation of this assay provided an opportunity to assess the impact of lowering the diagnostic threshold on the incidence, management, and clinical outcome of patients with type 2 myocardial infarction and myocardial injury.

CLINICAL SIGNIFICANCE

- Lowering the diagnostic threshold for troponin preferentially increases the number of patients identified with type 2 myocardial infarction or myocardial injury.
- Patients reclassified as having type 2 myocardial infarction or myocardial injury remained in the hospital for longer and were more likely to undergo cardiac investigations but, in contrast to type 1 myocardial infarction, were discharged without additional cardiac therapies and clinical outcomes remained poor and unchanged.

MATERIALS AND METHODS

Study Population

We identified consecutive patients admitted to our regional cardiac center (Royal Infirmary, Edinburgh, UK), with plasma cardiac troponin I concentrations ≥50 ng/L irrespective of clinical presentation during the validation and implementation of a contemporary sensitive troponin assay. We report a prespecified analysis from a published cohort study evaluating the impact of implementation of a contemporary sensitive troponin assay on patients with suspected acute coronary syndrome.[7] In this analysis, we include all patients in whom troponin was measured as part of routine clinical care whether or not they presented with suspected acute coronary syndrome.

Clinical characteristics as described previously,[7] including the primary presenting symptom, referral to specialist cardiology services, cardiac investigations, percutaneous or surgical coronary revascularization, and the use of medical therapies, were obtained through "TrakCare" (InterSystems Corp, Cambridge, Mass), an electronic patient record system used by all hospitals in the National Health Service (NHS), Lothian, United Kingdom. Exclusion criteria included patients admitted for elective nonemergency procedures, patients resident outside of Lothian, and those with incomplete hospital records.

Troponin Assay

Plasma troponin I concentrations were measured using the ARCHITECT$_{STAT}$ assay (Abbott Laboratories, Abbott Park, Ill). The study was divided into 2 phases: validation and implementation. Although plasma troponin was measured using the reformulated sensitive assay throughout both phases, only concentrations above our previous diagnostic threshold (≥200 ng/L) were reported in the validation phase, whereas concentrations above the revised diagnostic threshold (≥50 ng/L) were reported during the implementation phase.[7]

Classification of Myocardial Infarction

Patients were classified as having a type 1 myocardial infarction when myocardial necrosis occurred in the context of an isolated presentation with suspected acute coronary syndrome with chest pain or evidence of myocardial ischemia on the electrocardiogram.[1] Patients with symptoms and signs of myocardial ischemia on the electrocardiogram that were thought to be due to increased oxygen demand or decreased supply (eg, tachyarrhythmia, hypotension, or anemia) and myocardial necrosis were classified as having a type 2 myocardial infarction. Myocardial injury was defined as evidence of myocardial necrosis in the absence of any clinical features of myocardial ischemia. Myocardial infarction presenting as a sudden unexpected cardiac death (type 3) after percutaneous coronary intervention (type 4) and coronary artery bypass grafting (type 5) were also defined. Each case was reviewed and classified independently by 2 cardiologists, and any discrepancies were resolved by consensus through in-depth review of source data. A total of 400 consecutive patients were classified by 2 internal medicine physicians to determine the generalizability of classification.

Outcomes

Clinical outcomes were identified using national and local population registries, the General Register of Scotland and TrakCare, respectively. The primary outcomes were recurrent type 1 myocardial infarction and all-cause mortality at 1