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MINI-FOCUS: HIGH-SENSITIVITY TROPONIN

Small Changes in Troponin T Levels Are Common in Patients With Non–ST-Segment Elevation Myocardial Infarction and Are Linked to Higher Mortality

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Objectives The purpose of this study was to examine the extent of change in troponin T levels in patients with non–ST-segment elevation myocardial infarction (NSTEMI).

Background Changes in cardiac troponin T (cTnT) levels are required for the diagnosis of NSTEMI, according to the new universal definition of acute myocardial infarction. A relative change of 20% to 230% and an absolute change of 7 to 9 ng/l have been suggested as cutoff points.

Methods In a clinical setting, where a change in cTnT was not mandatory for the diagnosis of NSTEMI, serial samples of cTnT were measured with a high-sensitivity cTnT (hs-cTnT) assay, and 37 clinical parameters were evaluated in 1,178 patients with a final diagnosis of NSTEMI presenting <24 h after symptom onset.

Results After 6 h of observation, the relative change in the hs-cTnT level remained <20% in 26% and the absolute change <9 ng/l in 12% of the NSTEMI patients. A relative hs-cTnT change <20% was linked to higher long-term mortality across quartiles ($p = 0.002$) and in multivariate analyses (hazard ratio: 1.61 [95% confidence interval: 1.17 to 2.21], $p = 0.004$), whereas 30-day mortality was similar across quartiles of relative hs-cTnT change.

Conclusions Because stable hs-TnT levels are common in patients with a clinical diagnosis of NSTEMI in our hospital, a small hs-cTnT change may not be useful to exclude NSTEMI, particularly as these patients show both short-term and long-term mortality at least as high as patients with large changes in hs-cTnT. (J Am Coll Cardiol 2013;62:1231–8)

When the electrocardiogram (ECG) is inconclusive in patients with signs of acute coronary syndrome, the diagnosis of myocardial infarction (MI) relies largely on the level of the heart damage biomarker cardiac troponin (1). The introduction of high-sensitivity cardiac troponin T (hs-cTnT) assays and the lowering of the diagnostic threshold to the 99th cTnT percentile of 14 ng/l (2) have increased the number of patients presenting with an elevated cTnT level that needs further assessment (3,4). This is especially prevalent among older patients in the emergency department, where 36% to 50% of patients >65 to 70 years of age without MI present with an hs-cTnT level >14 ng/l (5,6). When cTnT is elevated at baseline, the change in the cTnT level is often evaluated during 3 to 6 h and sometimes up to 24 h (1).

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A few hours after cardiac necrosis, the levels of cTnT start to increase and reach a plateau phase after 10 to 15 h, followed by a slow decline (7). Consequently, it is often considered that MI can be excluded if the change in the cTnT level remains below 20% to 50% in patients presenting early after the onset of symptoms (8–11). There are, however, several reports indicating that plaque rupture often occurs days before the patient seeks medical attention (12,13), which is

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Abbreviations and Acronyms

CCU = coronary care unit
CPU = chest pain unit
cTnT = cardiac troponin T
ECG = electrocardiogram
HR = hazard ratio
hs-cTnT = high-sensitivity cardiac troponin T
IQR = interquartile range
MI = myocardial infarction
NCCP = noncardiac chest pain
NSTEMI = non–ST-segment elevation myocardial infarction

in line with the finding that many patients with MI present with elevated troponin levels that remain relatively stable during a 2-h to 6-h evaluation period (4,9,11,14). In addition, it is possible that the problem with stable troponin levels has been underestimated, as a change in the cardiac troponin level is often involved in the diagnosis of MI (1). These findings put the negative predictive power of a small troponin change into question.

To examine this further, we have evaluated hs-cTnT changes in patients with a final diagnosis of non–ST-segment elevation myocardial infarction (NSTEMI) in a clinical setting where the change in hs-cTnT was not mandatory for the diagnosis.

Methods

Study design and populations. Only patients admitted to coronary care unit (CCU) and chest pain unit (CPU) at Sahlgrenska University Hospital during the period December 2009 to January 2012, after the introduction of the hs-cTnT assay (Elecsys [Roche, Germany] hscTnT immunoassay), were included in the study and registered according to the previously described SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) study protocol (15,16). The more than 100 variables in the SWEDEHEART registry comply with the International Cardiology Audit and Registration Data Standards (CARDS) (15). A total of 1,567 patients received the final diagnosis of NSTEMI during the study period. Among these, 241 were excluded because of too few hs-cTnT analyses, and 148 were excluded because of >24 h between symptom onset and the first hs-cTnT sample. The remaining 1,178 patients with a total of 4,467 hs-cTnT measurements were included in the study (Table 1, Online Fig. 1). The time of symptom onset was available for 1,069 of the 1,178 patients who were included. The NSTEMI patients were diagnosed by a cardiologist, by reviewing data from a physical examination, imaging, ECG, and laboratory test results collected during the stay in the CCU/CPU.

Because no published measure of the 99th TnT percentile was available when the hs-cTnT assay was introduced into clinical routine in December 2009, the diagnostic hs-cTnT threshold that was based on the imprecision (coefficient of variation <10%) of the previous fourth-generation cTnT assay of 40 ng/l (17) was kept unchanged during the following 26 months when the study group was recruited. Changes in hs-cTnT levels were assessed but a significant change was not required for the final NSTEMI diagnosis if there was other convincing evidence of an ischemic origin of the hs-cTnT elevation. All hs-cTnT analyses during the period of the hospital stay were obtained from the local clinical chemistry database. Blood samples taken up to 24 h before arrival at the CCU/CPU were included to ensure that no blood samples of interest were missed. The first hs-cTnT analysis during this time period was considered the baseline sample. The attending clinician made all the decisions about when to sample hs-cTnT based on clinical need. The clinical characteristics of patients sampled at different times are shown in Online Table 1. Mortality data were collected from AMDAT, the Västra Götaland County mortality registry. There were 227 deaths in the NSTEMI study group after a median follow-up time of 380 days. No patient underwent coronary artery bypass graft surgery during the hs-cTnT sampling series. The percentage of patients who underwent percutaneous coronary intervention during the hs-cTnT series varied between 0.2% and 14%, depending on the length of the hs-cTnT series. These patients are summarized in Online Table 2.

Table 1 Characteristics of the Study Groups

	NSTEMI (n = 1,178)	NCCP (n = 326)
Age, yrs	74 (64–83)	67 (57–75)
Male	716 (60.8)	205 (62.9)
Diastolic BP, mm Hg	85 (74–99)	85 (76–95)
Systolic BP, mm Hg	150 (130–170)	150 (130–170)
ECG characteristics		
Sinus rhythm	925 (78.5)	325 (99.7)
Atrial fibrillation	159 (13.5)	0 (0)
ST-segment depression	356 (30.2)	29 (8.9)
Q-wave	123 (10.4)	16 (4.9)
Admission hs-cTnT, ng/l	94 (43–269)	8 (6–14)
Maximum hs-cTnT, ng/l	344 (125–973)	9 (6–17)
hs-cTnT change 6 h, %	81 (18–324)	60 (20–117)
hs-cTnT change in hospital, %	141 (34–702)	67 (25–166)
hs-cTnT change 6 h, ng/l	70 (22–233)	3 (2–7)
hs-cTnT change in hospital, ng/l	173 (48–601)	4 (2–11)
Creatinine, μmol/l	86 (71–110)	80 (66–93)
Symptom time, h	3.3 (1.4–6.9)	4 (1.7–7.3)
Risk factors		
Diabetes mellitus	276 (23.4)	49 (15.0)
Hypertension	560 (47.5)	151 (46.3)
Smoker	210 (17.8)	46 (14.1)
Body constitution and lipids		
BMI, kg/m^2	23.5 (26.0–29.3)	26.9 (24.3–29.7)
Total cholesterol, mmol/l	4.7 (4.0–5.6)	5.0 (4.2–5.8)
LDL cholesterol, mmol/l	2.8 (2.1–3.6)	2.9 (2.2–3.7)
Previous cardiovascular disease		
Myocardial infarction	447 (37.9)	75 (23.0)
Chronic heart failure	235 (19.9)	32 (9.8)
Previous PCI	224 (19.0)	51 (15.6)
Stroke	140 (11.9)	21 (6.4)
PCI during hospital stay	452 (38.4)	0 (0)

Values are median (interquartile range) or n (%).
BMI = body mass index; BP = blood pressure; ECG = electrocardiogram; hs-cTnT = high-sensitivity cardiac troponin T; LDL = low-density lipoprotein; NCCP = noncardiac chest pain; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention.