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# Undetectable High Sensitivity Cardiac Troponin T Level in the Emergency Department and Risk of Myocardial Infarction

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**Short title:** Undetectable Troponins and Risk of MI

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**Abstract**

**Objectives**

To evaluate if an undetectable (< 5 ng/l) high-sensitivity cardiac troponin T (hs-cTnT) level, and an electrocardiogram (ECG) without signs of ischemia can rule out myocardial infarction (MI) in the emergency department (ED).

**Background**

Chest pain is a common symptom often associated with benign conditions, but may be a sign of MI. Since there is no rapid way to rule out MI many patients are admitted to hospital.

**Methods**

All patients who sought medical attention for chest pain, and had at least one hs-cTnT analyzed, during two years at the Karolinska university hospital, Stockholm, Sweden were included. We calculated the negative predictive values of an undetectable hs-cTnT, and ECG without ischemia, for MI and death within 30 days.

**Results**

We included 14,636 patients of whom 8,907 (61%) had an intial hs-cTnT of < 5 ng/l, 21% had 5 to 14 ng/l, and 18% had > 14 ng/l. During 30 days of follow-up 39 (0.44%) patients with undetectable hs-cTnT had a MI, of whom 15 (0.17%) had no ischemic ECG changes. The negative predictive value for MI within 30 days in patients with undetectable hs-cTnT, and no ischemic ECG changes was 99.8% (95% confidence interval (CI) 99.7-99.9). The negative predictive value for death was 100% (95% CI 99.9-100).

**Conclusions**

All patients with chest pain who have an initial hs-cTnT level of <5 ng/l and no signs of ischemia on ECG have a minimal risk of MI or death within 30 days and can be safely discharged directly from the ED.

**Keyword:** Chest pain, Myocardial infarction, High-sensitivity troponin, Emergency department

**Abbreviations:**

hs-cTnT = high-sensitivity cardiac troponin T
ECG = electrocardiogram
MI = myocardial infarction
ED = emergency department
CI = confidence interval
eGFR = estimated glomerular filtration rate
STEMI = ST-elevation myocardial infarction
NSTEMI = non ST-elevation myocardial infarction
PCI = percutaneous coronary intervention

## Introduction

Chest pain is the cardinal symptom of myocardial infarction (MI), and it is one of the most common complaints of patients seeking medical attention in the emergency department (ED), accounting for an estimated 15 to 20 million ED visits per year in Europe and the United States (1-3). Although chest pain is often merely a sign of a completely benign condition, it may indicate that the patient is suffering from a life-threatening disease. As many as 2% of patients with MI are inadvertently discharged directly from the ED, which is associated with a doubling of the risk of death (4). Current guidelines therefore recommend that patients with chest pain who have normal clinical findings, electrocardiograms (ECG), and cardiac injury markers in the ED should have biomarker testing repeated 3-6 h after presentation (2). Commonly this means that the patient is admitted to hospital for further evaluation. However, only 10 to 20% of patients admitted for chest pain are diagnosed with MI during the hospitalization (4-6).

If MI can be ruled out safely and efficiently, without serial testing, or prolonged observation, then hospital admissions, ED overcrowding, and costs could be reduced. Several clinical decision rules have been developed to safely and efficiently exclude MI, which include assessment of pretest probability, biomarker levels, and ECG findings (6-9). However, these algorithms all include serial testing of biomarkers, which may delay patient discharge from the ED.

Recently, high-sensitivity cardiac troponin T (hs-cTnT) has been introduced as a highly sensitive, and early biomarker of myocardial damage (10). In two prospective cohorts of patients admitted to hospital for chest pain undetectable hs-cTnT was found to have a very high negative predictive value for MI (5,11).

We hypothesized that all patients with chest pain who have an initial hs-cTnT level of <5 ng/l and no signs of ischemia on ECG have a minimal risk of MI or death within 30 days and can be safely discharged directly from the ED.

## Methods

### Study population

**Study population.** This study included all patients aged ≥25 years who sought medical attention for chest pain in the ED, and had at least one hs-cTnT level measured while in the ED, at Karolinska University Hospital, Stockholm, Sweden from December 10, 2010 to December 31, 2012. This hospital is located at two sites that are 22 km apart (Huddinge and Solna), and has a total capacity of 1610 beds. The annual number of patients presenting to the adult ED is about 77,000 in Huddinge and 70,000 in Solna. Coronary angiography and percutaneous coronary intervention (PCI) are available at Huddinge during office hours, and at all times at Solna.

Patients who presented to the ED were identified from the hospitals register of patients. Archived laboratory data were retrieved to determine which patients had at least one hs-cTnT level measured while in the ED. Serum creatinine levels measured in the ED were retrieved to assess renal function, and the time spent in the ED was recorded. The patient data were then sent to the National Board of Health and Welfare to obtain data from the Swedish National Patient Register (12) which includes all patients hospitalized in Sweden, regarding prior hospitalizations for MI, stroke, heart failure, or chronic obstructive pulmonary disease, to determine the background characteristics of the study population. Information about current medications was retrieved from the Swedish Prescribed Drug Register (13). The data were then anonymized and returned to the investigators.

Diabetes mellitus was defined as ongoing treatment with any hypoglycemic agent. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease

Epidemiology Collaboration formula. Chronic kidney disease was defined as an eGFR of <60 ml/min/1.73 $m^2$. The study protocol complied with the guidelines of the Declaration of Helsinki and was approved by the Regional Ethical Review Board in Stockholm.

The main group of patients studied were those with a first hs-cTnT level of <5 ng/l (undetectable) measured in the ED, combined with no ST changes indicating myocardial ischemia on ECG (2). Patients with a first hs-cTnT level of <5 ng/l and initial ECG changes indicating MI were excluded from further analysis. In patients with a first hs-cTnT level of ≥5 ng/l, the ECGs were not reviewed. The hs-cTnT levels were analyzed using the Elecsys 2010 system (Roche Diagnostics GmbH, Mannheim, Germany), which has been available at Karolinska University Hospital since December 10, 2010. This method has a detection limit of 2 ng/l, a 99th-percentile cutoff point of 14 ng/l, and a coefficient of variation of <10% at 13 ng/l (14). Patients were categorized into three goups according to the first hs-cTnT level: <5 ng/l, 5 to 14 ng/l, and >14 ng/l.

**Outcome and follow-up.** The primary outcome was fatal or non-fatal type 1 MI, which is defined as MI related to atherosclerotic plaque rupture, fissuring, or erosion which leads to an intraluminal thrombus formation resulting in myocardial ischemia (2), within 30 days of the ED visit. The secondary outomes were MI within 180 days and 365 days of the ED visit, and all-cause mortality within 30, 180 and 365 days of the ED visit. In patients with a first hs-cTnT level of <5 ng/l, the hazard ratio for all-cause mortality was calculated for admitted patients compared with patients discharged directly from the ED.

Patients were followed from the time of the first hs-cTnT level until 30, 90 or 365 days after the ED visit. Data regarding subsequent diagnosis of MI, hospitalizations, discharge diagnoses other than MI, and length of hospital stay were obtained from the Swedish National Patient Register. Causes of death were obtained from the Cause-of-Death Register, which includes all individuals who are residing in Sweden at the time of their death.

**Review of ECGs and diagnoses of MI.** All patients with a first hs-cTnT level of <5 ng/l and a diagnosis of MI within 30 days were identified, and their ECGs were retrieved from the medical records. ECGs were also retrieved for two control patients per case from the cohort of patients who visited the ED because of chest pain, matched for age, sex, and the first hs-cTnT level, who were not diagnosed with MI within 30 days. Two independent senior cardiologists, blinded to the study protocol, were asked to review the ECGs and assess whether there was new ST elevation in two contiguous leads with cut-points of ≥ 0.1 mV in all leads except for in leads $V_2$-$V_3$ where ≥ 0.2 mV in men ≥ 40 years of age, and ≥ 0.25 mV in men <40 years of age, and ≥ 0.15 mV in women were applied; or if there were significant ST depression defined as a horizontal or down-sloping ST segment ≥ 0.05 mV in two contiguous leads; or if there was a left-bundle branch block present which was new compared with previous ECGs, if there were any to compare with (2). The only data available to the senior cardiologists were the age and sex of each patient, and that the main complaint was chest pain. A third senior cardiologist (M.J.H.) also assessed all the ECGs, and if there was disagreement between the assessments by the two independent cardiologists, the assessment by M.J.H. was used for the analyses. At a later stage, the records of all patients with a first hs-cTnT level of <5 ng/l were reviewed to determine whether they met the criteria for MI within 30 days according to troponin levels, other laboratory values, coronary angiography findings, echocardiography findings, and ECG findings.

**Statistical analyses**

We stratified patients into three groups according to level of hs-cTnT (<5, 5 to 14 and >14 ng/l) and calculated the absolute risks, negative predictive values and incidence rates with 95 % confidence intervals for myocardial infarction and death with a follow-up of 30, 180 and 365 days. The first hs-cTnT level recorded from December 10, 2010 to December 31, 2012 was the starting point of the follow up for each patient. Cox proportional hazards model was

used to calculate hazard ratio and 95 % confidence interval for the potential association between the exposure not admitted (reference admitted) and the outcome time to death adjusted for age, sex, diabetes mellitus, prior MI and eGFR. The data management and the calculations for absolute risks, negative predictive values and incidence rates were conducted using World Programming System, version 3.0 (World Programming Ltd., Hampshire, United Kingdom). Cox proportional hazards model was performed using R version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

**Results**

**Patient characteristics.** There were a total of 330,821 visits to the adult ED at Karolinska University Hospital during the study period (Figure 1). Chest pain was the second most common reason for visiting the ED, accounting for 15,549 (4.7%) of patients, of which 14,636 were aged >25 years and had at least one hs-cTnT level measured. Laboratory results showed that 61% of these patients had a first hs-cTnT level of <5 ng/l, 21% had a first hs-cTnT level of 5 to 14 ng/l, and 18% had a first hs-cTnT level of >14 ng/l (Table 1). Patients with a first hs-cTnT level of <5 ng/l were younger; less likely to have chronic kidney disease, chronic cardiovascular disease, or diabetes mellitus; and less likely to be taking medication for secondary prevention of cardiovascular disease (Table 1). With increasing levels of hs-cTnT patients were older, more often men, and had more comorbidities.

**Admissions, second hs-cTnT levels and discharge diagnoses.** A total of 5,418 (37%) patients were admitted to hospital, of whom 35% had a first hs-cTnT level of <5 ng/l (Table 2 and Figure 1). The hospitalization rate was 21% in patients with a first hs-cTnT level of <5 ng/l, 44% in patients with a first hs-cTnT level of 5 to 14 ng/l, and 82% in patients with a first hs-cTnT level of >14 ng/l (Table 2). Among patients with a first hs-cTnT level of <5 ng/l, 1,704 (89%) had a second hs-cTnT level measured, which was <5 ng/L in 1362 (90%) patients, 5 to 14 ng/l in 111 (7.3%) patients, and >14 ng/l in 44 (3.0%) patients. Patients with

a first hs-cTnT level of <5 ng/l and no MI within 30 days were hospitalized for a total of 3,262 days, with a mean duration of hospital stay of 1.5 ± 3.0 days, and 1482 (77%) of these patients were discharged on the same or next day. The most common discharge diagnoses in patients with a first hs-cTnT level of <5 ng/l were nonspecific chest pain (50.0%), atrial fibrillation or supraventricular tachycardia (5.6%), and angina (5.1%) (Table 3). A diagnosis of MI was unusual (2.0%) in patients with a first hs-cTnT level of <5 ng/l, but was more common with higher hs-cTnT levels, reaching 30% in patients with a first hs-cTnT level of >14 ng/l (Table 3). Among patients with a first hs-cTnT level of <5 ng/l, the time spent in the ED was similar for those who were discharged compared with those who were hospitalized, 208 (±101) minutes vs. 203 (±111) minutes. Time in the ED in relation to level of troponin and final diagnosis of MI is described in Table 1, supplemental material.

**Myocardial infarction and death.** A total of 746 (14%) patients were discharged from the index hospitalization with a diagnosis of MI. Forty-four patients with a first hs-cTnT level of <5 ng/l were diagnosed with MI within 30 days. Two of these patients had a periprocedural MI and three did not meet the current criteria for MI (2).

These five patients were excluded from further analysis. Twenty-four of the remaining patients had significant ECG changes, of whom 15 (62%) were diagnosed with ST-elevation myocardial infarction (STEMI) and 9 (38%) were diagnosed with non-ST-elevation myocardial infarction (NSTEMI) (Figure 2). No patient had a left-bundle branch block on the ECG.

In 15 of the remaining 39 patients, there were no significant changes on the first ECG performed in the ED (Table 4 and Figure 2). These patients were older, more often men (73%), and had prior cardiovascular disease (20%) more frequently than patients with hs-cTnT < 5 ng/l and no MI. In addition they were often (40%) active smokers. The first hs-cTnT level was measured within 2 h of the onset of symptoms in 11 (73%) patients, and >3 h

after the onset of symptoms in 2 (13%) patients. One patient was discharged directly from the ED and was readmitted with a diagnosis of STEMI after 18 days. In two patients, a second ECG within 1 h of the first ECG showed ST elevation, and in another patient the ED physician judged the ECG to be consistent with a diagnosis of STEMI. These four patients underwent primary PCI. In the 11 patients who did not undergo immediate cardiac catheterization, the maximum hs-cTnT level ranged from 18 to 157 ng/l. In 5 (45%) of these 11 patients, the maximum hs-cTnT level was <30 ng/l (Table 4).

A first hs-cTnT level of <5 ng/l in combination with no signs of ischemia on ECG had a negative predictive value for MI of 99.8% (95% confidence interval [CI]: 99.7–99.9) and an absolute risk for MI of 0.17% (95% CI: 0.09–0.27) (Table 2). MI occurred in 39 patients with a first hs-cTnT level of <5 ng/l at 30 to 365 days after discharge from the ED, which is an incidence of 7.36 (95% CI: 5.55–9.58) per 1000 person-years. In patients with a first hs-cTnT level of 5 to 14 ng/l, the absolute risk of MI within 30 days was 3% and the negative predictive value for MI within 30 days was 97%. In patients with a first hs-cTnT level of >14 ng/l, the absolute risk of MI within 30 days was 26% and the negative predictive value for MI within 30 days was 74% (Table 2).

In patients with a first hs-cTnT level of <5 ng/l and no signs of ischemia on ECG, the negative predictive value for death within 30 days was 100% (95% CI: 99.9–100) (Table 2), and there were 38 deaths during the 365 days after discharge from the ED. The underlying cause of death was cardiovascular disease in 2 (5%) patients, cancer in 32 (84%) patients, and another cause in 4 (11%) patients.

Among patients with a first hs-cTnT level of <5 ng/l, there was no significant difference in the risk of death within 365 days between those who were discharged directly from the ED and those who were admitted to hospital after adjustment for age, sex, diabetes mellitus, prior MI, and eGFR (hazard ratio; 0.73; 95% CI: 0.48–1.12).

**Discussion**

In a large cohort of 14,636 consecutive patients who sought medical attention for chest pain in the ED, we found that a first hs-cTnT level of <5 ng/l combined with no signs of ischemia on ECG had a 99.8% negative predictive value for MI and a 100% negative predictive value for death within 30 days.

Cardiac troponins have been used as a cornerstone of diagnosis of MI, together with clinical assessment and ECG findings, for more than 15 years (15). However, a limitation of former generations of troponin assays have been that they required at least 6 hours from the onset of symptoms before they would be detectable (14). Repeated testing were therefore often required, leading to unnecessary hospitalizations for investigation of chest pain. Recently, high-sensitivity cardiac troponins have been introduced in clinical practice (10,16). They increase the diagnostic accuracy, by identifying a larger proportion of patients with MI at the time of presentation to the ED. As elevation of high-sensitivity cardiac troponin levels are detectable at a much earlier stage than earlier generations of troponin assays (10,14,16), they have been suggested to have the potential to rule out MI at an earlier stage (5-8,10,11,16).

Two recent studies investigated the negative predictive value of an intial undetectable hs-cTnT for MI (5,11). In both of these studies, patients were recruited prospectively at the discretion of the ED physician, serial hs-cTnT levels were measured, and only hospitalized patients were included. In another study, a second troponin measurement was taken 1 h after the first, and was used to rule out patients with MI (8). In all three studies, the negative predictive value for MI was almost 100% if hs-cTnT was undetectable. In contrast to those three studies, the current study included all patients who presented to the ED with a main complaint of chest pain, and used the first hs-cTnT level and ECG findings to rule out MI, without assessment of the pretest probability of MI and without serial measurements of hs-

cTnT levels. This simple strategy confirmed the findings of the two previous studies that an undetectable first hs-cTnT level rules out MI with almost 100% accuracy.

Chest pain was the second most common reason for presentation to the ED during the study period, and 61% of patients with a main complaint of chest pain had a first hs-cTnT level of <5 ng/l. Hospitalization occurred in 21% of these patients, accounting for one-third of all patients admitted to hospital because of chest pain. This indicates that 594 patients with a first hs-cTnT level of <5 ng/l would have to be admitted to detect one additional MI. More than two-thirds of the patients with a first hs-cTnT level of <5 ng/l who were admitted to hospital were dischaged on the same or next day, and 50% had a discharge diagnosis of unspecified chest pain. Although some of these patients may have had other conditions requiring hospitalization such as heart failure, atrial fibrillation, or pulmonary embolism, we believe that hospitalization could have been avoided in the majority of these patients, resulting in an annual decrease of 500 to 1000 admissions to our hospital. Considering that an estimated 15 to 20 million patients seek medical attention at an ED for chest pain every year in Europe and the United States, the potential savings for healthcare providers are enormous (1-3).

Only 15 of all patients who presented to our ED during the study period were diagnosed with MI despite having an undetectable first hs-cTnT level combined with no signs of ischemia on the intial ECG. The first hs-cTnT level was measured <2 h after the onset of symptoms in 11 of these patients. If a second hs-cTnT level would have been obtained 3-4 hours after onset of symptoms most likely it would have been significantly elevated in most of these patients.

As chest pain is one of the most common symptoms in patients seeking medical attention in the ED, our strategy may help to reduce overcrowding of the ED. However, our results did not show that low-risk patients who are admitted to hospital spend more time in

the ED than those who are discharged directly from the ED.

There were only 2 cardiovascular deaths in patients with undetectable hs-cTnT levels during the year that followed the visit to the ED. This indicates that hs-cTnT may not only be a predictor of early but also long-term prognosis (17).

There may have been several patients among those with undetectable levels of hs-cTnT who were discharged from the ED who if they were admitted to hospital would have had elevated hs-cTnT levels subsequently. We calculated the risk of death within the year after the visit to the ED for patients who were admitted compared with patients who were discharged directly from the ED and found no difference.

It is very important to determine whether patients with a very small elevation of the first hs-cTnT level benefit from being diagnosed with MI. There were two procedure-related MIs in our study population. As MI after PCI has a worse prognois than PCI without MI (18), a diagnosis of MI based on a very small elevation of the hs-cTnT level may increase the risk to the patient. In almost half of the patients diagnosed with MI who had a first hs-cTnT level of <5 ng/l combined with no signs of ischemia on ECG, the maximum hs-cTnT level was <30 ng/l. With earlier generations of troponin assays, these patients would probably not have been diagnosed with MI (14).

To the best of our knowledge, this is the first study of such a large cohort of consecutive patients (14,636 patients) who sought medical attention for chest pain, and had information on hs-cTnT levels, at an ED over 2 years. Patient follow-up was complete because follow-up data were obtained from national registers.

In conclusion, we found that a first hs-cTnT level of <5 ng/l combined with no signs of ischemia on ECG ruled out MI with nearly 100% accuracy regardless of prior disease, timing of measurement of the hs-cTnT level, age, sex, or other risk factors for MI.

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**Figure legends**

**Figure 1, Study population**

Figure 1 demonstrates the selection of the study population, and number of patients at different levels of high-sensitivity cardiac troponin T which are reported in ng/l. ED means, emergency department; hs-cTnT, high-sensitivity cardiac troponin T, and y.o., years old.

**Figure 2, Patients with undetectable hs-cTnT and MI within 30 days**

Figure 2 demonstrates all 39 patients with an intial hs-cTnT < 5 ng/l and an ECG without ST-elevation or depression, but MI within 30 days of follow-up. MI, means myocardial infarction; ECG, electrocardiogram; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; LAD, left anterior descending artery; LCX, left circumflex; RCA, right coronary artery, and hs-cTnT, high-sensitivity cardiac troponin T.

**Table 1** Characteristics of the Study Population According to the First High-Sensitivity Cardiac Troponin T Level

| | | High-Sensitivity Cardiac Troponin T level (ng/l) | | |
|---|---|---|---|---|
| | All patients | <5 | 5–14 | >14 |
| **Number of patients** | 14,636 | 8907 | 3150 | 2579 |
| Percentage of study population | 100 | 61 | 21 | 18 |
| Age (years) | 55 (19) | 47 (15) | 63 (16) | 71 (15) |
| Female sex, n (%) | 48 | 53 | 41 | 37 |
| eGFR | | | | |
| >60 ml/min/1.73 $m^2$ (%) | 88 | 98 | 85 | 57 |
| 30–60 ml/min/1.73 $m^2$ (%) | 10 | 2.4 | 15 | 32 |
| 15–30 mL/min/1.73 $m^2$ (%) | 2.1 | 0.03 | 0.74 | 11 |
| eGFR (ml/min/1.73 $m^2$) | 90 (25) | 99 (18) | 82 (21) | 65 (28) |
| Diabetes mellitus (%) | 9.5 | 4.7 | 14 | 21 |
| COPD (%) | 3.4 | 1.7 | 5.2 | 7.9 |
| Prior MI (%) | 8.5 | 4 | 14 | 39 |
| Prior stroke (%) | 4.9 | 2.1 | 7 | 13 |
| Prior hospitalization for CHF (%) | 5.7 | 1.4 | 8.2 | 22 |
| Aspirin | 19 | 9.7 | 30 | 40 |
| Beta-blockers | 23 | 13 | 36 | 47 |
| ACE/ARB | 24 | 13 | 35 | 46 |
| Statins | 19 | 11 | 28 | 34 |

eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; CHF = congestive heart failure; ACE/ARB = angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker.

Age and eGFR are shown as mean (standard deviation).

Table 2. Absolute Risks and Negative Predictive Values for Myocardial Infarction or Death at 30, 180, and 365 Days after Discharge from the ED, According to the First High-Sensitivity Cardiac Troponin T Level, in 14,612* Patients who Sought Medical Attention for Chest Pain at Karolinska University Hospital from December 2010 to December 2012

| | High-Sensitivity Cardiac Troponin T level (ng/l) | | |
|---|---|---|---|
| | <5 | 5–14 | >14 |
| Number of patients | 8883* | 3150 | 2579 |
| Proportion admitted (%) | 1917 (21) | 1397 (44) | 2104 (82) |
| **Myocardial infarction** | | | |
| ***30 days*** | | | |
| Number of events | 15 | 97 | 676 |
| Absolute risk | 0.17 (0.09–0.27) | 3.08 (2.48–3.68) | 26.2 (24.5–27.9) |
| Negative predictive value | 99.8 (99.7–99.9) | 96.9 (96.3–97.5) | 73.8 (72.1–75.5) |
| ***180 days*** | | | |
| Number of events | 33 | 115 | 724 |
| Absolute risk | 0.37 (0.24–0.54) | 3.65 (2.99–4.30) | 28.1 (26.3–29.8) |
| Negative predictive value | 99.6 (99.4–99.7) | 96.4 (95.7–97.0) | 71.9 (70.2–73.7) |
| ***365 days*** | | | |
| Number of events | 54 | 134 | 753 |
| Absolute risk | 0.61 (0.45–0.78) | 4.25 (3.55–4.96) | 29.2 (27.4–31.0) |
| Negative predictive value | 99.4 (99.2–99.5) | 95.7 (95.0–96.5) | 70.8 (69.0–72.6) |
| **Death** | | | |
| ***30 days*** | | | |
| Number of events | 2 | 13 | 66 |
| Absolute risk | 0.023 (0.001– | 0.41 (0.19– | 2.56 (1.95–3.17) |

| | | | |
|---|---|---|---|
| | 0.054) | 0.64) | |
| Negative predictive value | 100 (99.9–100) | 99.6 (99.4–99.8) | 97.4 (96.8–98.1) |
| ***180 days*** | | | |
| Number of events | 15 | 66 | 216 |
| Absolute risk | 0.17 (0.083–0.25) | 2.09 (1.59–2.59) | 8.38 (7.31–9.44) |
| Negative predictive value | 99.8 (99.7–99.9) | 97.9 (97.4–98.4) | 91.6 (90.6–92.7) |
| ***365 days*** | | | |
| Number of events | 38 | 108 | 342 |
| Absolute risk | 0.43 (0.29–0.56) | 3.43 (2.79–4.06) | 13.3 (12.0–14.6) |
| Negative predictive value | 99.6 (99.4–99.7) | 96.6 (95.9–97.2) | 86.7 (85.4–88.0) |

*Twenty-four patients with a first high-sensitivity cardiac troponin T level of <5 ng/l were excluded because they had ECG changes suggestive of myocardial infarction at the time of presentation to the emergency department. Absolute risks and negative predictive values are given as percentage (95% confidence interval).

**Table 3** The 12 Most Common Discharge Diagnoses for Patients Admitted to Hospital, According to the First High-Sensitivity Cardiac Troponin T Level

| High-Sensitivity Cardiac Troponin T Level (ng/l) | | | | | |
|---|---|---|---|---|---|
| <5 (n = 1,917) | | 5–14 (n = 1,397) | | >14 (n = 2,104) | |
| Chest pain (%) | 50 | Chest pain | 34 | MI | 30 |
| A-fib/SVT (%) | 5.6 | Angina | 8.1 | Chest pain | 13 |
| Angina (%) | 5.1 | A-fib/SVT | 7.5 | Heart failure | 8.7 |
| Abdominal pain (%) | 2.8 | MI | 5.1 | A-fib/SVT | 7.2 |
| Myalgia (%) | 2.4 | Unstable angina | 3.2 | Angina | 4.2 |
| MI (%) | 2.0 | Heart failure | 3.1 | Pneumonia | 4.1 |
| Pneumonia(%) | 1.8 | Pneumonia | 2.3 | Unstable angina | 2.4 |
| Syncope (%) | 1.8 | Syncope | 1.9 | Myocarditis | 1.6 |
| Hypertension (%) | 1.6 | Myalgia | 1.7 | PE | 1.2 |
| Unstable angina (%) | 1.5 | Hypertension | 1.4 | Syncope | 1.2 |
| PE (%) | 1.3 | PE | 1.3 | Aortic stenosis | 1.1 |
| Palpitations (%) | 1.0 | Dyspnea | 1.2 | Hypertension | 0.9 |

Chest pain was defined as international classification of diseases (ICD) code (version 10) R07.4, R07.3, Z03.4, or Z03.5; atrial fibrillation (A-fib) as I48.9; supraventricular

tachychardia (SVT) as I47.1; myalgia as M79.1; syncope as R55.9; hypertension as I10.9; unstable angina as I20.0; pulmonary embolism (PE) as I26.9; palpitations as R00.2; pneumonia as J18.9; abdominal pain as R10.4, K29.7, or K85.9; dyspnea as R06.0; aortic stenosis as I35.0; myocarditis as I40.9; and myocardial infarction (MI) as I21.4, I21.9, or I21.1.

**Table 4** Details of 15 Patients with Chest Pain and a First High-Sensitivity Cardiac Troponin T Level of <5 ηg/l Combined with No Signs of Ischemia on ECG, who had a Final Diagnosis of Myocardial Infarction

| Sex | Age | Previous Medical History | Current Medical History | Time from Onset of Symptoms to 1st, 2nd and 3rd Hs-cTnT Level | ECG Assessment by the ED Physician | Clinical Course |
|---|---|---|---|---|---|---|
| Male | 48 | This patient had COPD, never smoked, and had a BMI of 31 kg/m$^2$. | Sudden onset of chest pain and tachycardia in the morning. | <1 h: <5 ng/l<br>6–7 h: 33 ng/l<br>12–13 h: 23 ng/l | SR, 108 beats/min, no signs of ischemia. | Coronary angiograhy was performed on day 3 and a stent was placed in the LAD. The final diagnosis was NSTEMI. |
| Female | 52 | This patient had hypertension, was an ex-smoker, and had a BMI of 22 kg/m$^2$. | Sudden onset of chest discomfort in the morning. | 2–3 h: <5 ng/l<br>8–9 h: 18 ng/l<br>14–15 h: 9 ng/l | SR, 97 beats/min, nonspecific ST-segment changes in leads V4–V6. | Coronary angiography on day 4 was normal. The final diagnosis was NSTEMI. |
| Male | 39 | This patient had hypertension, was an | Sudden onset of chest pain and nausea during | 1–2 h: <5 ng/l<br>7–8 h: 1,930 | SR, 55 beats/min, ST-segment elevation | Primary PCI was performed and a stent was placed in the RCA. The final diagnosis |

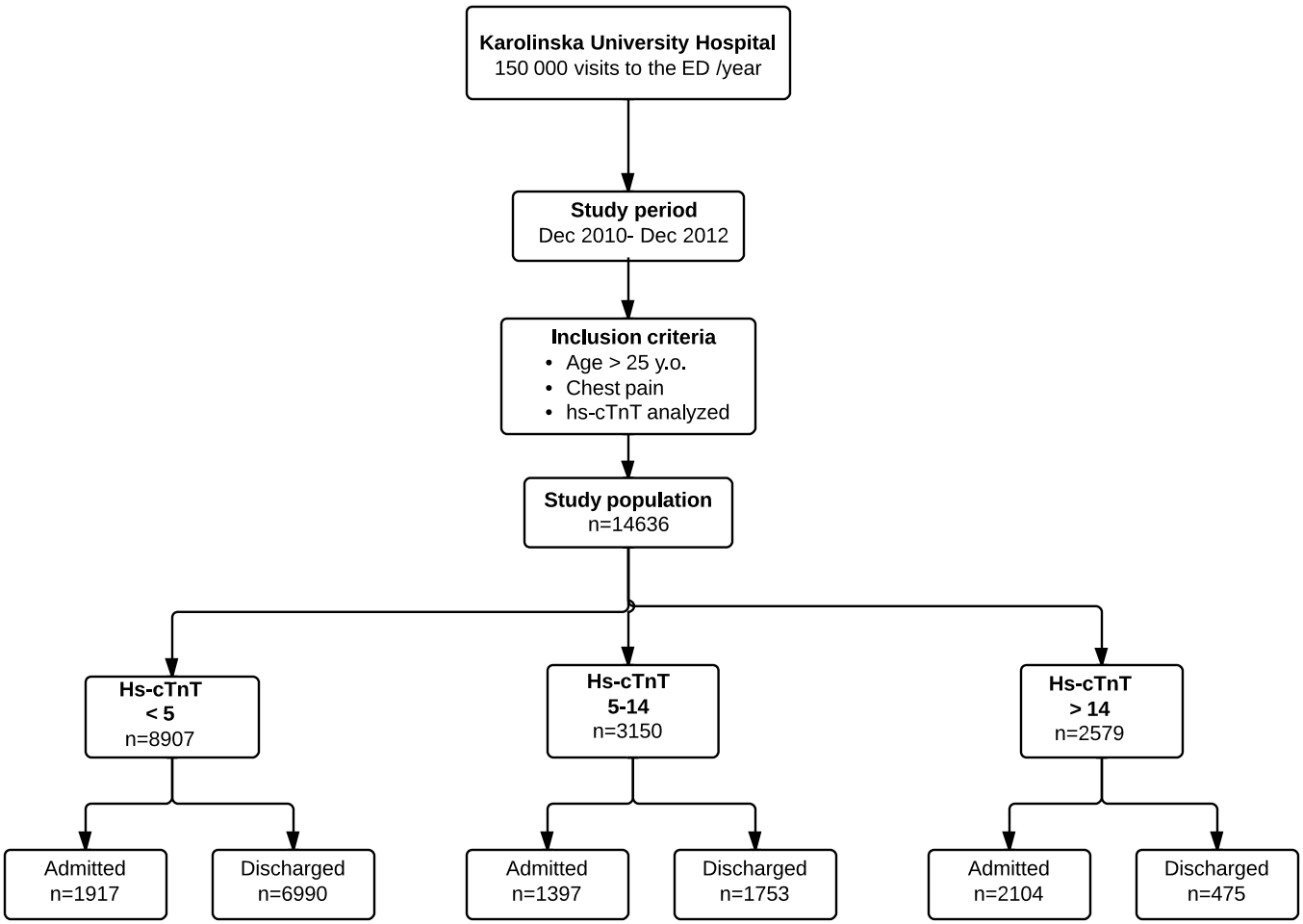
| | | | | | | |
|---|---|---|---|---|---|---|
| | | ex-smoker, and had a BMI of 28 kg/m$^2$. | physical activity. | ng/l | in leads II and avF. | was STEMI. |
| Male | 64 | This patient was a previously healthy smoker and had a BMI of 28 kg/m$^2$. | Sudden left-sided stabbing sensation in the chest. | <1 h: <5 ng/l | SR, 85 beats/min, no signs of ischemia. | This patient was discharged from the ED, but returned after 18 days with STEMI, which was treated with primary PCI with stenting of the LAD. |
| Male | 57 | This patient had a prior CABG, never smoked, and had a BMI of 25 kg/m$^2$. | Sudden onset of chest pain and nausea in the morning. | 1–2 h: <5 ng/l<br>7–8 h: 0.16 ng/l*<br>13–14 h: 0.34 ηg/l* | SR, 63 beats/min, Q-wave in lead III. | Coronary angiography was performed on day 3 and a stent was placed in the RCA. The final diagnosis was NSTEMI. |
| Male | 59 | This patient had hypertension, was a current smoker, and had a BMI of 27 | Sudden onset of chest pain during the night. | 1–2 h: <5 ng/l<br>7–8 h: 81 ng/l<br>13–14 h: 149 ng/l | SR, ST-segment depression in leads I and aVL. | Coronary angiography was performed on day 3 and a stent was placed in the RCA. The final dignosis was NSTEMI. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | kg/m$^2$. | | | | |
| Male | 62 | This patient was a non-smoker and had a BMI of 28 kg/m$^2$. | Sudden onset of recurrent chest pain. | 1–2 h: <5 ng/l<br>7–8 h: 21 ng/l<br>13–14 h: 21 ng/l | SR, 107 beats/min, no signs of ischemia. | Coronary angiography was performed on day 2 and a stent was placed in the LAD. The final diagnosis was NSTEMI. |
| Female | 72 | This patient was a current smoker and had a BMI of 22 kg/m$^2$. | Sudden onset of left-sided chest pain in the morning. | <1 h: <5 ng/l<br>6–7 h: 4,560 ng/l | SR, 45 beats/min, no signs of ischemia. | A second ECG performed 1 h after the first ECG showed ST-segment elevation in the inferior leads. Primary PCI was performed and a stent was placed in the LCX. The final diagnosis was STEMI. |
| Male | 68 | This patient had hypertension, was a non-smoker, and had a BMI of 31 kg/m$^2$. | Sudden onset of chest pain, diaphoresis, nausea, and dyspnea. | 2–3 h: <5 ng/l<br>8–9 h: 18 ng/l<br>14–15 h: 15 ng/l | SR, 110 beats/min, no signs of ischemia. | Coronary angiography was performed on day 4, and was normal. The final diagnosis was NSTEMI. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Male | 64 | This patient was a current smoker and had a BMI of 31 kg/m$^2$. | Sudden onset of chest pain and diaphoresis at noon. | 1–2 h: <5 ng/l<br>7–8 h: 158 ng/l<br>13–14 h: 888 ng/l | SR, 60 beats/min, T-wave inversion in leads V1 and V2. | A second ECG performed 30 min after the first ECG showed ST-segment elevation in the inferior leads. Primary PCI was performed and a stent was placed in the RCA. The final diagnosis was STEMI. |
| Male | 56 | This patient was a current smoker and had a BMI of 20 kg/m$^2$. | Sudden onset of chest pain during physical activity. | 1–2 h: <5 ng/l<br>7–8 h: 29 ng/l<br>13–14 h: 56 ng/l | SR, no signs of ischemia. | Coronary angiography was performed on day 5, and was normal. The final diagnosis was NSTEMI. |
| Female | 68 | This patient had 3 prior MIs and a prior CABG, was an active smoker, and had a BMI of 17 kg/m$^2$. | Sudden onset of left-sided chest pain during physical activity. | >3 h: <5 ng/l<br>>9 h: 40 ng/l | SR, 60 beats/min, no signs of ischemia. | Coronary angiography was performed on day 2 and showed no significant stenosis. The final diagnosis was NSTEMI. |
| Female | 56 | This patient was an | Sudden onset of chest | <1 h: <5 ng/l | SR, 76 beats/min, no | ECG later on the day of admission showed |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | active smoker and had a BMI of 27 kg/m$^2$. | pain during the night. | 6–7 h: 19 ng/l | signs of ischemia. | ST-segment elevation. Coronary angiography showed no significant stenosis. The final diagnosis was STEMI. |
| Male | 54 | This patient had hypertension, was an ex-smoker, and had a BMI of 26 kg/m$^2$. | Sudden onset of chest pain in the morning. | 1–2 h: <5 ng/l<br>7–8 h: 157 ng/l<br>13–14 h: 92 ng/l | SR, non-significant ST-segment elevation in leads V3–V6. | Coronary angiography was performed on day 3 and showed no signficant stenosis. The final diagnosis was NSTEMI. |
| Male | 72 | This patient had a prior stroke, was a non-smoker, and had a BMI of 24 kg/m$^2$. | Sudden onset of chest pain during the night. | >3 h: <5 ng/l<br>>9 h: 12 ng/l<br>> 15 h: 29 ng/l | SR, no signs of ischemia. | Coronary angiography was performed on day 3 and showed no signficant stenosis. The final diagnosis was NSTEMI. |

BMI = body mass index; BP = blood pressure; RR = respiratory rate; ECG = electrocardiogram; SR = sinus rhythm; LAD = left anterior descending artery; PCI = percutaneous coronary intervention; LCX = left circumflex artery; STEMI = ST-segment elevation myocardial infarction; MI = myocardial infarction, *This patient had cardiac troponin I analyzed after he was admitted to the cardiac care unit.



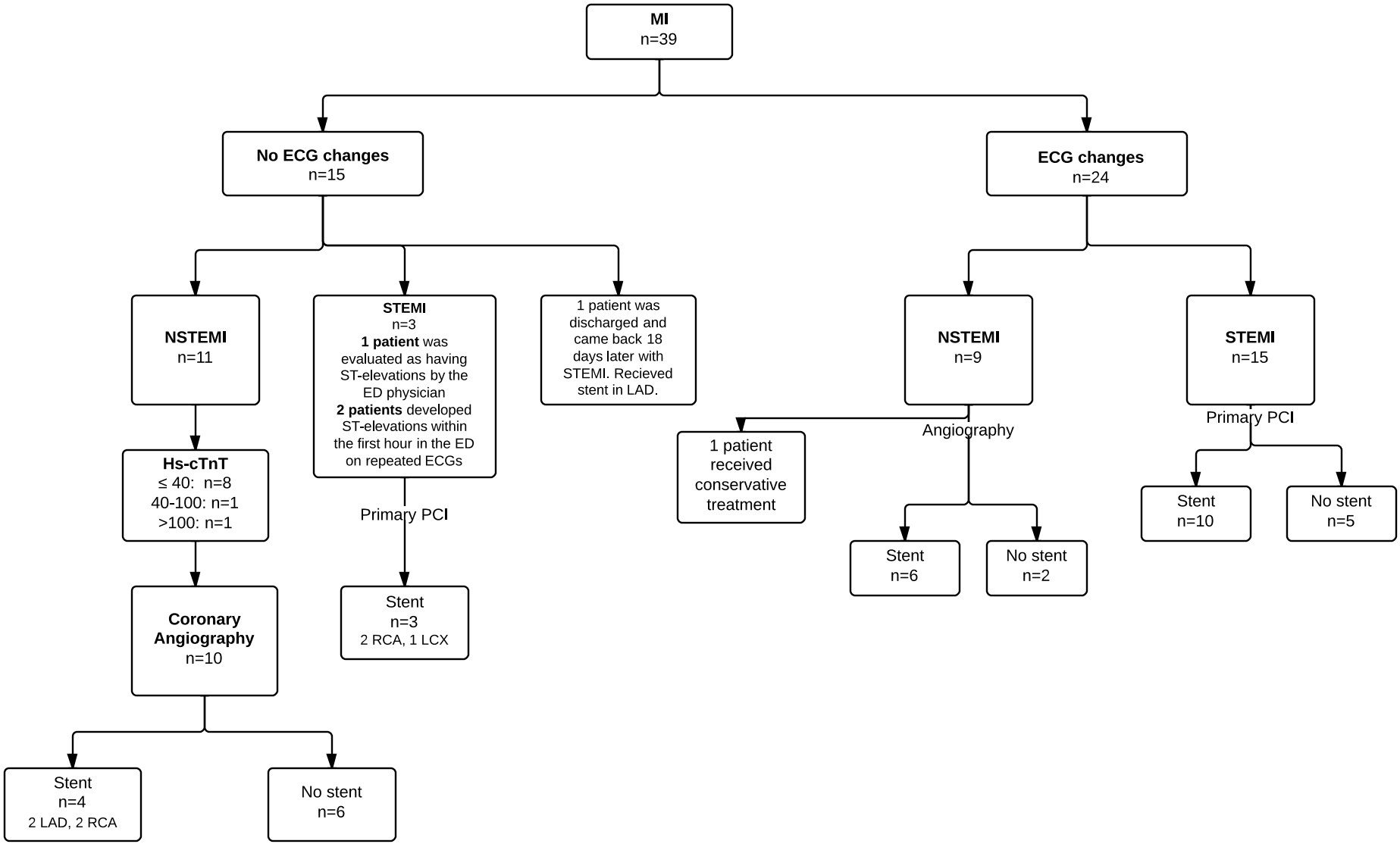


**Table 1, supplemental material. Time Spent In the Emergency Department in Relation to High-sensitivity Cardiac Troponin T Level and Discharge or Admission**

| | All patients | Hs-cTnT < 5 | | | | Hs-cTnT 5-14 | | | | Hs-cTnT > 14 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | All | Admitted | Discharged | MI as discharge diagnosis | All | Admitted | Discharged | MI as discharge diagnosis | All | Admitted | Discharged | MI as discharge diagnosis |
| Time in minutes (SD) | 209 (107) | 207 (103) | 203 (111) | Ta | 123 (94) | 217 (115) | 211 (111) | 221 (109) | 156 (184) | 204 (112) | 196 (109) | 238 (120) | 150 (90) |

Hs-cTnT, high-sensitivity cardiac troponin T; SD, standard deviation; MI, myocardial infarction. Time is reported as mean (standard deviations).