Myocardial infarction – diagnostic support:

Myocardial infarction is a diagnosis based on a dynamic increase in troponin levels and at least one of the following symptoms/signs: Symptoms (usually chest pain), ischemic ECG changes, development of pathological Q wave or loss of viable myocardium/regional wall motion abnormalities on imaging (1).

High-sensitive Troponin T (HsTnT) assays detect myocardial damage. The upper normal level is ***14 ng/L.***

This value is based on the 99th percentile among healthy individuals below 70 years of age; however, of all patients over the age of 65 without coronary syndrome at Sahlgrenska Hospital emergency ward, 1/3 have HsTnT levels above 14 ng/L (2).

Elevated levels are seen in:

- **Acute Coronary Syndrome** –Type 1 Myocardial infarction
- **Supply/demand imbalance in myocardial perfusion** – Secondary Myocardial infarction (Type 2)
    - Tachycardia, Aortic dissection, Aortic valve disease, Hypertrophic cardiomyopathy, Shock (Cardiogenic, hypovolemic, septic), Respiratory insufficiency, Anemia, Coronary spasm, Abuse-related endothelial dysfunction – e.g. cocaine.
- **Myocardial effects not related to ischemia**
    - Myocardial contusion, Cardiac interventions (Ablation, Pacemaker implantation, Heart biopsy, Electroconversion), Rhabdomyolysis, Myocarditis, Drug toxicity (e.g. adriamycin), Renal insufficiency, Cardiac insufficiency, Hypertensive crisis, Pulmonary embolism, Acute neurological disease (e.g. Stroke/subarachnoid hemorrhage), Takotsubo cardiomyopathy, Infiltrative disease (sarcoidosis, amyloidosis, etc.), Burn injuries, Sepsis.

Indication for testing:

Suspected acute coronary syndrome.

At triage in Sahlgrenska University Hospital, HsTnT is only performed on patients presenting with chest pain. In all other cases, HsTnT is performed only if ordered by a physician.

Handling of patients:

As always, a clinical evaluation based on the patient's anamnesis, risk factors and ECG (possibly UCG) shall be made.

- In case of definite suspicion of Acute Coronary Syndrome (ACS): To Intensive Coronary Care Unit (CICU) for monitoring. In case of HsTnT elevation, proceed as in NSTEMI. If no elevation is seen, retest after 3 and 6 hours. If the level remains normal, myocardial infarction can be excluded. Consider non-invasive evaluation of ischemia.

- In case of minor suspicion of ACS and elevated HsTnT: retest after 6 hours. If the elevation is clearly dynamic (= more than 60 % difference from first test): To CICU for monitoring, investigation and treatment as in ACS.

- In case of minor suspicion of ACS and elevated HsTnT + other explanation (see conditions above): Treat the basic disorder.

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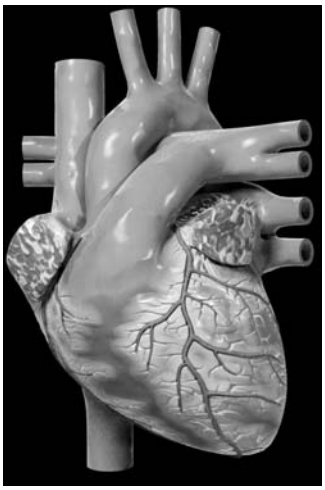
Altered level of normal for Troponin T



On January 30, 2012, the Department of Clinical Chemistry and the Section of Cardiology changed the level of normal for the heart damage marker Troponin T to <14 ng/L, for Sahlgrenska University Hospital as a whole, to harmonize this level with national and international guidelines. A treatment program linked to this new level is available at "http://korturl.com/TNTHS."

Summary

Troponin T (TnT) is a myocardium-specific protein, the release of which into the blood stream increases in all types of myocardial damage. TnT is analyzed in suspected acute coronary syndrome where ECG results are inconclusive. In these cases, myocardial infarction and acute cardiac damage can be excluded, if the TnT level remains below 14 ng/L after 6 hours of monitoring. On the other hand, a TnT level above 14 ng/L does not always indicate acute cardiac damage or myocardial infarction, but should be evaluated on the basis of other clinical findings. A change in the TnT level to above the upper limit of normal (>60 % change) enhances the suspicion of acute cardiac damage, but the absence of an increase does not exclude acute cardiac damage, as a change <20 % is seen in many patients with myocardial infarction over 6 hours of monitoring.

Troponin T levels

If ECG results are inconclusive, the diagnosis of myocardial infarction (Non-STEMI) is often based on a dynamic TnT elevation above the 99th percentile (1). The 99th TnT percentile corresponds to a TnT concentration below which 99 % of a healthy population is found (1). A major reason for international cardiology associations to choose the 99^{th} TnT percentile as the limit for action is its capacity to rule out acute myocardial damage within 3-6 hours (14) and to identify patients with a poor prognosis. However, the 99^{th} percentile provides poor diagnostic precision. Among patients with chest pain and a TnT level above the 99^{th} percentile, only 50 % have a myocardial infarction (2). With the previous action limit of 40 ng/L, about 85 % of patients with chest pain had a myocardial infarction (2).

The 99th TnT percentile has been determined in several studies at 12-14 ng/L for younger patients (Table 1). However, the 99^{th} percentile is strongly age-related, particularly among emergency care patients above the age of 65, of whom approximately 1/3 have a TnT level above >14 ng/L (Table 1) (5,6). In a majority of emergency care patients below the age of 65 with elevated TnT levels, the reason for the elevation can be easily identified (Table 2) (5). On the contrary, in emergency care patients older than 65, the TnT elevation cannot be explained by investigations that are available to the emergency ward physician in the absolute majority of cases (5).

A non-specific, elevated TnT level is prognostically unfavorable, regardless of the underlying cause, and associated with clearly increased mortality in groups with TnT levels >14 ng/L (7,8). How these patients should be handled is still unclear, as there is no (13) or only a weak (7) association with a future myocardial infarction. On the other hand, several studies show that a TnT concentration <14 ng/L after 6 hours of monitoring excludes acute myocardial damage and myocardial infarction (5,6,9,10). These patients also have a good prognosis (7,8).

Troponin T changes

Among older patients and in the conditions listed in Table 2, non-specific TnT elevations are common. In patients with an elevated TnT level but only a minor suspicion of myocardial infarction, the TnT change is often evaluated during monitoring. However, the absence of a TnT elevation does not mean that a myocardial infarction can be entirely excluded, for several reasons:

1. A change in the TnT level may develop slowly if the acute myocardial damage is older than 24 hours.
2. About 30 % of patients with Non-STEMI experience less than a 20% TnT increase over 6 hours of monitoring (SU 2010-2012). This also applies if the symptoms have lasted less than 12 hours. Similar findings have been published recently (9,10).
3. The upper level of normal (97.5th percentile) for TnT changes is 60 % for patients without a myocardial infarction treated in a cardiology ward (5). Similar TnT changes are seen among healthy individuals (11,12).
4. Several common conditions produce dynamic TnT elevations (Table 2), which further confuses the picture.

Thus, there is considerable TnT change overlap between patients with developing myocardial infarction and other patients.

Although the TnT dynamics are used in the clinical evaluation, so far there are only a few scientific evaluations of which levels should be used and to what extent the TnT change contributes to the correct diagnosis. In a recently published study, different breakpoints for TnT changes were investigated with regard to the capacity to identify Non-STEMI. A TnT change >40 % over 6 hours of monitoring yielded the maximum separation between Non-STEMI and non-specific TnT changes (2). However, about 42 % of all patients with Non-STEMI had a TnT change <40 % (2). When the first TnT level was >14 ng/L, a relative change >40 % resulted in separation that was about as good as that obtained with an absolute change >9ng/L. In a similar study, an absolute TnT change >7 ng/L over 2 hours of monitoring resulted in a maximum separation between myocardial infarction and non-specific TnT elevations (3). Changes in the TnT concentration are therefore an unreliable marker of acute cardiac damage and the level of change to be applied still remains unclear.Additional biomarkers probably need to be applied in the evaluation of unclear TnT elevations.

Instructions for testing: See “List of analyses” at www.kliniskkemi.se.

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Table 1: TnT distribution in different populations

Population (number, mean age	Percentage with TnT >14 ng/L	99th TnT percentile (ng/L)	Reference
Patients without heart conditions (533, 37 yrs)	1	14.2	3
Random selection >45 yrs (545, 58 yrs)	NI*	29.9	4
Random selection >45 yrs, healthy (200, NI*)	1	14.4	4
Random selection <65 yrs (195, 57 yrs)	2	20.5	5
Random selection >65 yrs, (208, 71 yrs)	3	21.2	5
Emergency pat's wo ACS§ <65 yrs (458, 41 yrs)	2	18.6	5
Emergency pat's <65 yrs wo condition in Table 2 (446, 41 yrs)	0.4	12	5
Emergency pat's wo ACS§ >65 yrs (230, 76 yrs)	36	157	5
Emergency pat's > 65 yrs wo condition in Table 2 (205, 75 yrs)	27	81.9	5
Chest pain >70 yrs wo myocardial infarction (406, 78 yrs)	Approx. 50	NI*	6

* NI: No Information; § ACS: Acute Coronary Syndrome

Table 2: Conditions associated with Troponin T elevation	
Dynamic	**Stable**
Acute myocardial infarction	High age
Acute cardiac insufficiency	Renal insufficiency
Pulmonary embolism	Stable cardiac insuffiency
Acute myocarditis	Hypertrophic cardiomyopathy
Rapid tachyarrhythmia	
Exacerbation of COPD	
Stroke	
Aortic dissection	
Endocarditis	
Takutsubo cardiomyopathy	
Sepsis	
Hypotension/Shock	
Extreme exercise	