Troponin

- Jesse RL. On the Relative Value of an Assay Versus That of a Test (JACC 2010)
  - "When TN was a lousy assay it was a great test, but now that it’s becoming a great assay, it’s getting to be a lousy test."
**Definition of myocardial infarction**

<table>
<thead>
<tr>
<th>Criteria for acute myocardial infarction</th>
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<td>The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for MI:</td>
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<td>- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:</td>
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<td>† Symptoms of ischaemia.</td>
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<td>† New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).</td>
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<td>† Development of pathological Q waves in the ECG.</td>
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<td>† Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.</td>
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<tr>
<td>† Identification of an intracoronary thrombus by angiography or autopsy.</td>
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<td>- Cardiac death with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.</td>
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<td>- Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values (&gt;5 x 99th percentile URL) in patients with normal baseline values (≤99th percentile URL) or a rise of cTn values &gt;20% if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischaemia or (ii) new ischaemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.</td>
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<tr>
<td>- Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.</td>
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<td>- Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (&gt;10 x 99th percentile URL) in patients with normal baseline cTn values (≤99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.</td>
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<th>Criteria for prior myocardial infarction</th>
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<td>Any one of the following criteria meets the diagnosis for prior MI:</td>
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<td>- Pathological Q waves with or without symptoms in the absence of non-ischaemic causes.</td>
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<td>- Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischaemic cause.</td>
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<td>- Pathological findings of a prior MI.</td>
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To make things simple

• Rise and/or fall of troponin with at least one positive value

  Plus at least one of the following

  - Evidence of Ischaemia
  - ST-T ECG changes
  - Pathological Q waves in ECG
  - Imaging evidence of new loss of viable myocardium and/or RWMA
  - Identification of intracoronary thrombus by angiography or autopsy
## Type 1: Spontaneous myocardial infarction

Spontaneous myocardial infarction related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis. The patient may have underlying severe CAD but on occasion non-obstructive or no CAD.

## Type 2: Myocardial infarction secondary to an ischemic imbalance

In instances of myocardial injury with necrosis where a condition other than CAD contributes to an imbalance between myocardial oxygen supply and/or demand, e.g., coronary endothelial dysfunction, coronary artery spasm, coronary embolism, tachy-/brady-arrhythmias, anemia, respiratory failure, hypotension, and hypertension with or without LVH.

## Type 3: Myocardial infarction resulting in death when biomarker values are unavailable

Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurring before blood samples could be obtained, before cardiac biomarker could rise, or in rare cases cardiac biomarkers were not collected.

## Type 4a: Myocardial infarction related to percutaneous coronary intervention (PCI)

Myocardial infarction associated with PCI is arbitrarily defined by elevation of cTn values > 5×99th percentile URL in patients with normal baseline values (≤ 99th percentile URL) or a rise of cTn values > 20% if the baseline values are elevated and are stable or failing. In addition, either (i) symptoms suggestive of myocardial ischemia, or (ii) new ischemic ECG changes or new LBBB, or (iii) angiographic loss of patency of a major coronary artery or a side branch or persistent slow-or no-flow or embolization, or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.

## Type 4b: Myocardial infarction related to stent thrombosis

Myocardial infarction associated with stent thrombosis is detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarkers values with at least one value above the 99th percentile URL.

## Type 5: Myocardial infarction related to coronary artery bypass grafting (CABG)

Myocardial infarction associated with CABG is arbitrarily defined by elevation of cardiac biomarker values > 10×99th percentile URL in patients with normal baseline cTn values (≤ 99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Diagnostic algorithm for troponin positivity.

Matthew W. Sherwood, and L. Kristin Newby J Am Heart Assoc 2014;3:e000403
Evolution of the cardiac troponin (cTn) assays and their diagnostic cutoffs.

Vinay S. Mahajan, and Petr Jarolim Circulation. 2011;124:2350-2354
Cardiac troponin I (cTnI) levels in a healthy reference population and in an acute coronary syndrome (ACS) population.

Vinay S. Mahajan, and Petr Jarolim Circulation. 2011;124:2350-2354
Troponin kinetics in the index cases.

#1 Myocarditis

#2 CHF

#3 Myocardial infarction

Vinay S. Mahajan, and Petr Jarolim Circulation. 2011;124:2350-2354
Differential Diagnosis

Absolute levels of hs-cTnT (μg/L)

<table>
<thead>
<tr>
<th>Level</th>
<th>Condition</th>
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<tbody>
<tr>
<td>10</td>
<td>Very large AMI, myocarditis</td>
</tr>
<tr>
<td>1</td>
<td>Large AMI, myocarditis, Tako-tsubo, PE, critical illness</td>
</tr>
<tr>
<td>0.100</td>
<td>Small AMI, early large AMI, myocarditis, Tako-tsubo, PE, shock, CHF, SAB, ...</td>
</tr>
<tr>
<td>0.050</td>
<td>Micro AMI, early large AMI, myocarditis, Tako-tsubo, PE, shock, CHF, hypertensive crisis, SAB, stable CAD...</td>
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<tr>
<td>0.014</td>
<td>Stable angina, CHF, LVH, subclinical heart disease, etc</td>
</tr>
<tr>
<td>0.010</td>
<td>Healthy individuals</td>
</tr>
</tbody>
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Hs-cTnT = Quantitative Marker
A 45 years old man came with severe chest pain with diaphoresis. Pain score 10/10 of 1 hour duration
• The doctor in emergency department order hs Troponin T that come back as negative.

• Remembering the 3 hour rule out protocol, the doctor decided to start nitrate infusion and repeat the hsTrop T

• What do you all think happens after 3 hours?
A 76 years old man come with syncopal attacks. He denies any chest pain or failure symptoms
The doctors was worried about the t wave inversion in anterior leads and order hs Troponin T. It come back as positive (26).

Due to the positive troponin, the doctor plan to admit the patient with diagnosis of NSTEMI.
• Severe aortic stenosis with severe LVH
BEWARE LVH IN ECG

• UGLY
• Screw up the ST-T segment

Mimic STEMI
Mimic ischaemic ST depression
Mimic LMS disease
A 52 year old man came with shortness of breath and confusion
The doctor was baffled with the bizarre appearance of the ECG. It seems to him that there is widespread ST depression and ST elevation in aVR.

He immediately think about STEMI due to LMS occlusion. Because of the bizarre appearance he decided to send hsTropT which come back as positive (45) after 1H

Now he decided to activate the cath lab and he was immediately send to the lab

What do you think happens on the way there?
• Hyperkalaemia - The tuberculosis of ECG
Another case

- Patient with history of coronary artery disease, defaulted antiplatelets for 6 months
- Presented with chest pain. The chest pain resolved after a while
- ECG during pain and pain free captured.
ECG on admission
The chest pain now better. What do you think?
The hs troponin T was negative in the emergency department.

The doctor was breathing a sigh of relief when the pain is now better but think that the repeat ECG is a little bit weird.

He decided to do another hs troponin T which again come back negative and he feel reassured.

Should he?
Another case

- Indian Lady presented with severe chest pain.
- She have history of proximal LAD disease- stented in February 2015
- She presented for current episode on the 22\textsuperscript{nd} Sept 2015
Previous ECG
ECG on admission - Chest pain better
Still no chest pain
Now having severe chest pain. What now?
hsTrop T 0.066 to 0.103 to 1.380

• Findings: In stent thrombosis proximal LAD

• Normal ECG – Transient occlusion of LAD that subsequently reperfused (Wellens) – Occlusion of LAD (Pseudonormalisation on the way to ST elevation)
Wellens original image

Fig. 1. ECG patterns in precordial leads of the patients reported. Pattern A was found in four patients; pattern B, in 22 patients. See text.
Wellens criteria

1. Chest pain (not some other atypical symptom) of at least 20 minutes duration
2. Complete resolution of pain at the time of the ECG
3. Presence of normal R-waves in the precordial leads (not Q-waves, not LVH)
4. Pattern A or Pattern B (see bottom of post) T-wave inversions in V2-V3, and also possibly, in decreasing order of prevalence, V3, V4, and V5.
5. Evolution of the pattern [though de Zwaan and Wellens' did not describe evolution (probably because they did not do serial ECGs nearly as often as we do today), in Dr Smith (of Smith-sgarbossa) experience Wellens' always evolves: biphasic T-waves (Pattern A) become deep symmetric (Pattern B) and they also extend out to V4, then V5, then V6.]
47 years old Chinese man presented with severe chest pain of 3 hours duration in Hospital Lahad Datu Sabah. No cath lab facility there.

The initial 3\textsuperscript{rd} generation troponin I come back as negative. However the doctor worried about hyperacute T wave of initial STEMI.

But after 3 hours of chest pain, it should already evolved to full blown ST elevation. She was thinking of treating the patient as unstable angina

ECG sent to me for consult. What do you think?
Severe chest pain 1656h
Repeat ECG at 0241h
What is de Winters T wave?

• More urgent compare to Wellens. Some said that it is STEMI equivalent necessitating emergent trip to cath lab.
• The LAD is occluded or almost entirely occluded with very slight flow distal to the occlusion.
• There is st depression in the anterior leads followed by giant upright T waves
• There is controversy whether there is any role for lytics with some proponent both sides of the divide
The initial paper of de Winter’s waves

- 1890 patients who had LAD occlusion. They found these ‘de Winter’s waves’ in 2% of these patients, and stated they were persistent
- “We have observed this pattern as a static ECG pattern lasting from the time of first medical contact until the recording of the pre-procedural ECG and lasting until angiographic establishment of an occluded LAD artery”

De Winter et al (Heart 2009;95:1701-1706)
• The de Winter ECG pattern was first reported in a 2008 case series by de Winter and Wellens, who observed this ECG pattern in 30 / 1532 patients with acute LAD occlusions (2% of cases).

• Verounden and colleagues replicated this finding in a 2009 case series. They found a de Winter ECG pattern in 35 / 1890 patients requiring PCI to the LAD (2% of cases).

• Patients with the de Winter ECG pattern were younger, more likely to be male and with a higher incidence of hypercholesterolaemia compared to patients with a classic STEMI pattern.
Criteria for de Winters

- Tall, prominent, symmetric T waves in the precordial leads
- Upsloping ST segment depression >1mm at the J-point in the precordial leads
- ST segment elevation (0.5mm-1mm) in aVR

![ECG waveform](image)
65 years old man, premorbid hypertension referred for ongoing chest pain
Patient was referred to me few days ago when I was on call for primary PCI. She was worried about LMS occlusion but I disagree.

When he reach IJN emergency department he was still in pain. Because I don’t think that this is STEMI, I decided to send hsTroponin T.

Am I doing the right thing?
Some interesting information......

• In his publish book from 1992 "The ECG in Emergency Decision Making", Dr. "Hein" Wellens (Wellens Syndrome) and Mary Conover write in chapter 2 "ECG Identification of High-Risk Patients With Unstable Angina" on page 34: ECG recognition

• If there is St segment elevation in V1 and aVR plus ST segment depression in eight or more leads in a patient with unstable angina, the chance of having severe left-mainstem or three-vessel disease is very high (71%).

In a study involving 125 patients with left mainstem disease, of the eight leads with St depression, the most frequently involved leads were V3 to V5. Lead V4 showed the greatest amount of St depression (67% of patients).(1988)

Note: 25% of patients with as much as 91-99% occlusion of the left main coronary artery have a normal ECG when they are pain-free! It's therefore important to record the ECG during chest pain.
• There are many publications stating that ST elevation in lead aVR, with diffuse ST depression elsewhere, is due to left main (LM) occlusion.

• *This is even stated in the lastest 2013 ACC/AHA STEMI guidelines* (O’Gara PT et al. JACC 61(4):e83; January 29, 2013).

• However, the guidelines use as evidence [an article by Jong et al.](http://www.intohj.com/article/S0142-2860(05)00884-3/fulltext) (Int Ht J 2006; 47(1):13-20). That article misleadingly defines "occlusion" as any stenosis greater than 50%, when it should rather be defined as 100%, or nearly so. All of the articles that claim ST elevation in aVR is a sign of LM occlusion confuse LM occlusion with LM insufficiency.
In reality, ischemic ST elevation in aVR occurs in two broad categories:

1) in patients with recognized STEMI (due to coronary occlusion, usually of the LAD) and is associated with higher mortality than in patients without STE in aVR and

2) in patients without ischemic ST elevation (except for V1), in which case there is always diffuse ST depression of subendocardial ischemia (which can be due to supply-demand mismatch or due to ACS). If due to ACS, this STE in aVR is associated not only with acute LM insufficiency, but alternatively with 3 vessel disease, or with LAD insufficiency.
Below is the ECG of a patient who collapsed in v fib, underwent prolonged resuscitation and had return of spontaneous circulation, but was in cardiogenic shock:
• There is diffuse ST depression, with ST elevation in aVR. This is diffuse subendocardial ischemia. The ST elevation in aVR is reciprocal to the ST depression vector that is directed anterior, lateral, and inferior (towards leads II and V5). STE in aVR is thus reciprocal ST Elevation!
• The hsTrop T came back as positive. As we know CPR can also elevate the troponin, but in this case the ECG again gave us the diagnosis.
• **Left Main occlusion** results in an ECG with **overlapping syndromes of proximal LAD occlusion** (STE in V1-V6, I, aVL) and **circumflex occlusion** (lateral STE and posterior STEMI, which has ST depression in V1-V4, which may diminish the ST elevation of the anterior STEMI.)
A 32 year old male presented with a 4 day history of dyspnea, cough, palpitations, and chest pain. He had an ECG done immediately.
• Again, patient is 32 years old. The t inversion is extensive. Again hsTrop T is elevated.
• The doctor diagnosed patient with NSTEMI. What do you think?
This showed anterior T wave inversions, a QTc of 431, and also T inversion in lead III. There is sinus tachycardia and an S1Q3T3. This is all highly suspicious for pulmonary embolism.

Kosuge et al. (Am J Cardiol 2007;99:817-821) compared patients with ACS and PE who had precordial T wave inversions in V1-V4. They found that in this select population, negative T waves in lead III were observed in only 15% of patient with ACS, compared with 88% of patients with Acute PE.
An elderly woman presented with 6 hours of arm, back, jaw pain, diaphoresis, and dyspnea (no chest pain!). There was an unclear history of CAD as previous care was at another hospital.
• The hsTrop T come back elevated. However the doctor remember someone told her that myocardial infarction cannot be diagnosed in patient with pacemaker.

• Is she right?
In right ventricular pacing, which was formerly by far the most common, the pacing lead was usually in the apex of the RV and, therefore, the depolarization vector was usually away from the apex, resulting in a negative QRS in all of V1-V6. **Here, the QRS is positive in V1**, which suggests left to right ventricular activation, at least of the septum.

Biventricular pacing (especially "cardiac resynchronization therapy") is common now because it has been shown to improve cardiac function in patients with heart failure who also have QRS duration more than 120ms. A biventricular pacer has a lead in the RV and a lead that goes through the coronary sinus (the large vein that drains myocardial blood supply into the right atrium) and then into a branch vein on the epicardium of the LV. Its location can be somewhat variable. Thus, the QRS morphology is variable.
Previous ECG 5 years prior
A 52 years old diabetics patient came with 3 hours of central chest pain. Patient have underlying CKD and haemodynamically stable.
• Previous ECG 5 years ago was normal.
• So this is new onset LBBB. The 1st hsTroponin T was elevated at 32pg/ml however this was attributed to the CKD
• The decision was taken to treat as unstable angina. Repeat troponin 3 hours after shows increase in reading to 68pg/ml
There is sinus rhythm and Left Bundle Branch Block. There is not a lot of ST elevation, nowhere near 5 mm. Lead V5 possibly has some concordant STE, but there is a wandering baseline and it certainly does not come to 1 mm. However, the ST/S ratio in V2 is high in spite of only 3 mm of STE, and it thus meets the Smith-modified Sgarbossa criteria.
• It is important to remember that the latest (2013) ACC/AHA STEMI guidelines removed New Left Bundle Branch Block (LBBB) as an indication for emergent reperfusion because there are too many false positives

• Proportionally excessive discordant ST elevation (as in V2) was far more specific than less than 1 mm of concordant ST elevation
ACS vs. Non-ACS Presentations

ACS vs. Non-ACS Presentations

4 factors decreased LR for rule-in for ACS

- Pain described as pleuritic
- Pain described as sharp
- Pain described as reproducible
- Pain described as positional

- Note that decrease ≠ rule out!
ACS vs. Non-ACS Presentations

4 factors increased LR for rule-in for ACS

- Pain that radiates
  - Bilateral > right >> left
- Pain with diaphoresis
  - Observed >> reported
- Pain with exertion
- Pain with vomiting (not nausea!)
Troponin testing

- In isolation it is non specific
- Determine pre-test likelihood of myocardial infarction before ordering the test. If PTL low and troponin positive often need serial testing.
- Troponin usually most helpful when negative- even then need to interpret with caution
Take home points

• Unfortunately we still need physician
• Troponin in the right clinical circumstances do help immensely in patient management- But clinical context is important
• Know your ECG, it is a lifetime learning but it save lives
• If in doubt, repeat ECG- it is just ink and paper
• Remember the Universal definition of myocardial infarction does not depend on a single measurement of troponin
Remember: ACS is a dynamic process. Occlusion can closed and opened by itself at anytime so that negative troponin does not rule out unstable angina, and unstable angina can be deadly.