

# Biomarker strategies to diagnose NSTEMI



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MEDICINE

# Learning objectives

- Understand physiology of troponin testing using highly sensitive assays
- Describe validated pathways to rule out MI using contemporary troponin assays
- Use biomarkers to risk-stratify acute coronary syndromes



# 48 year old man

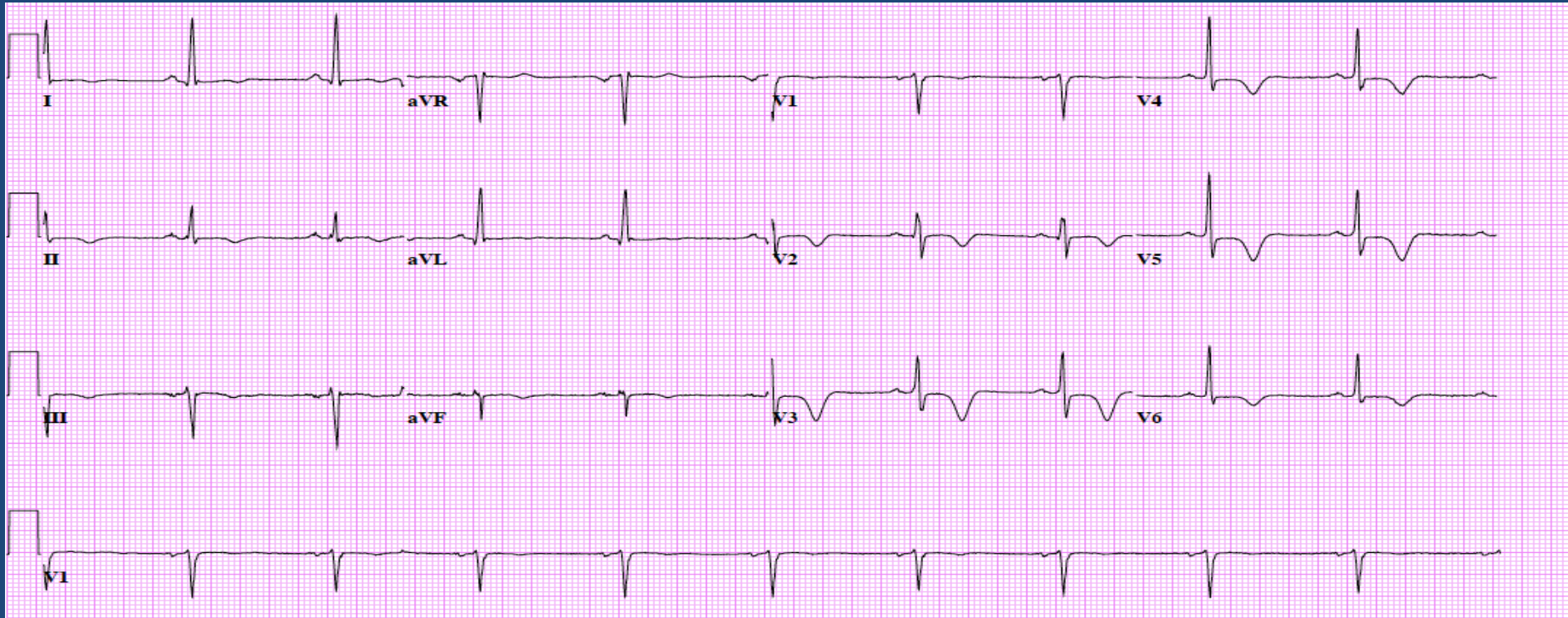
- PMH of dyslipidemia and FH of CAD (dad with MI at age 52)
- While shoveling snow 4 h prior, had 'indigestion' and diaphoresis which abated with rest.
- Symptoms recurred while sitting on the couch prompting ER visit
- Took aspirin and tums
- Symptom free on ED arrival



# Physical exam

- General: comfortable, not distressed
- JVP: 5 cm H<sub>2</sub>O
- Pulses normal, no bruits
- Extremities warm
- Lungs clear
- Cor: regular, S1: 1/6 midpeaking murmur: S2
- Abd: NT





# 48 yo M with unstable and rest angina, TWI on ECG in an ischemic pattern

- How can we use biomarkers in patients with suspected acute MI?



# Guideline recommendations

## 2.3.4. Biomarkers

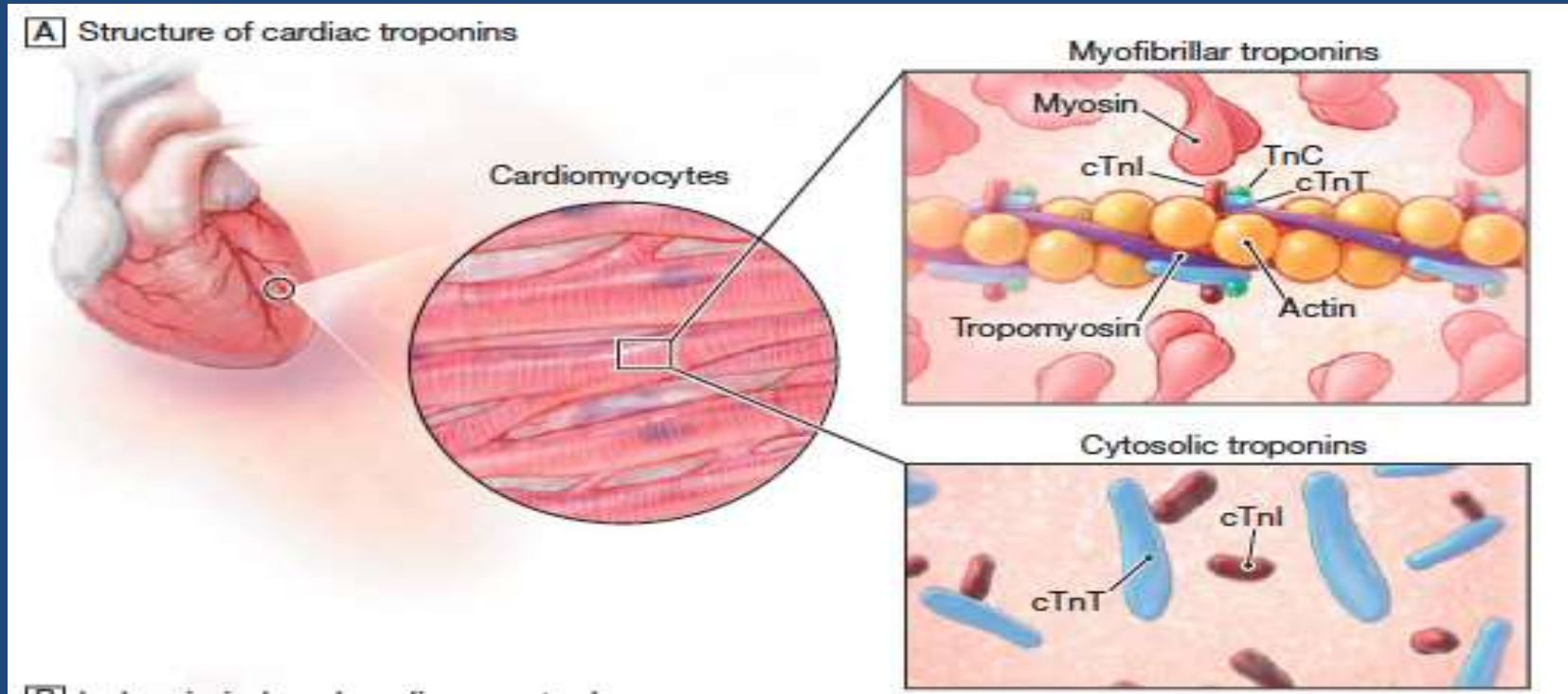
### Recommendations for Biomarkers

Referenced studies that support the recommendations are summarized in [Online Data Supplement 7](#).

COR	LOE	Recommendations
1	B-NR	1. In patients presenting with acute chest pain, serial cTn I or T levels are useful to identify abnormal values and a rising or falling pattern indicative of acute myocardial injury. <sup>1-21</sup>
1	B-NR	2. In patients presenting with acute chest pain, high-sensitivity cTn is the preferred biomarker because it enables more rapid detection or exclusion of myocardial injury and increases diagnostic accuracy. <sup>17,21-25</sup>
1	C-EO	3. Clinicians should be familiar with the analytical performance and the 99th percentile upper reference limit that defines myocardial injury for the cTn assay used at their institution. <sup>23,26</sup>
3: No benefit	B-NR	4. With availability of cTn, creatine kinase myocardial (CK-MB) isoenzyme and myoglobin are not useful for diagnosis of acute myocardial injury. <sup>27-32</sup>



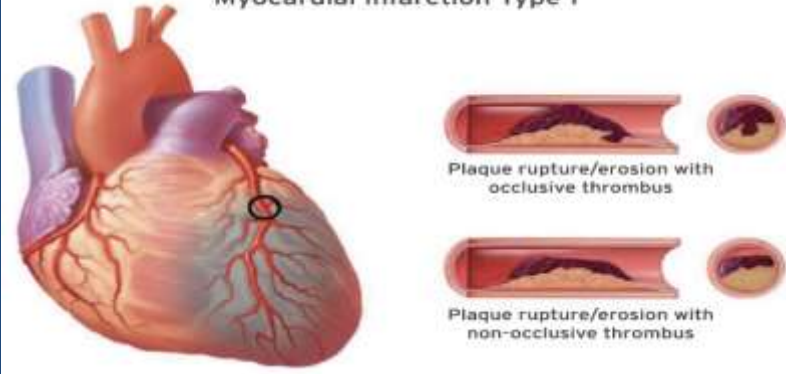
# Troponin- pathobiology



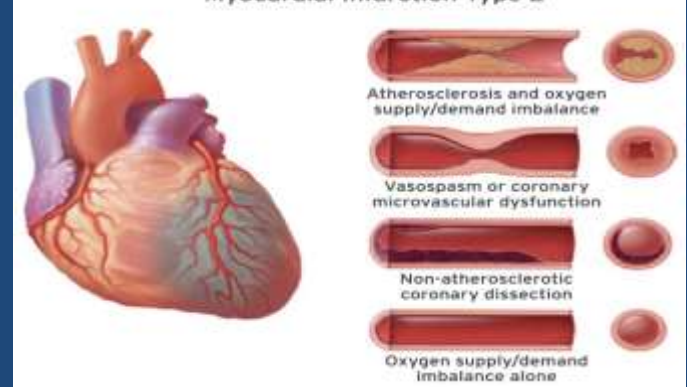


# Pathophysiology

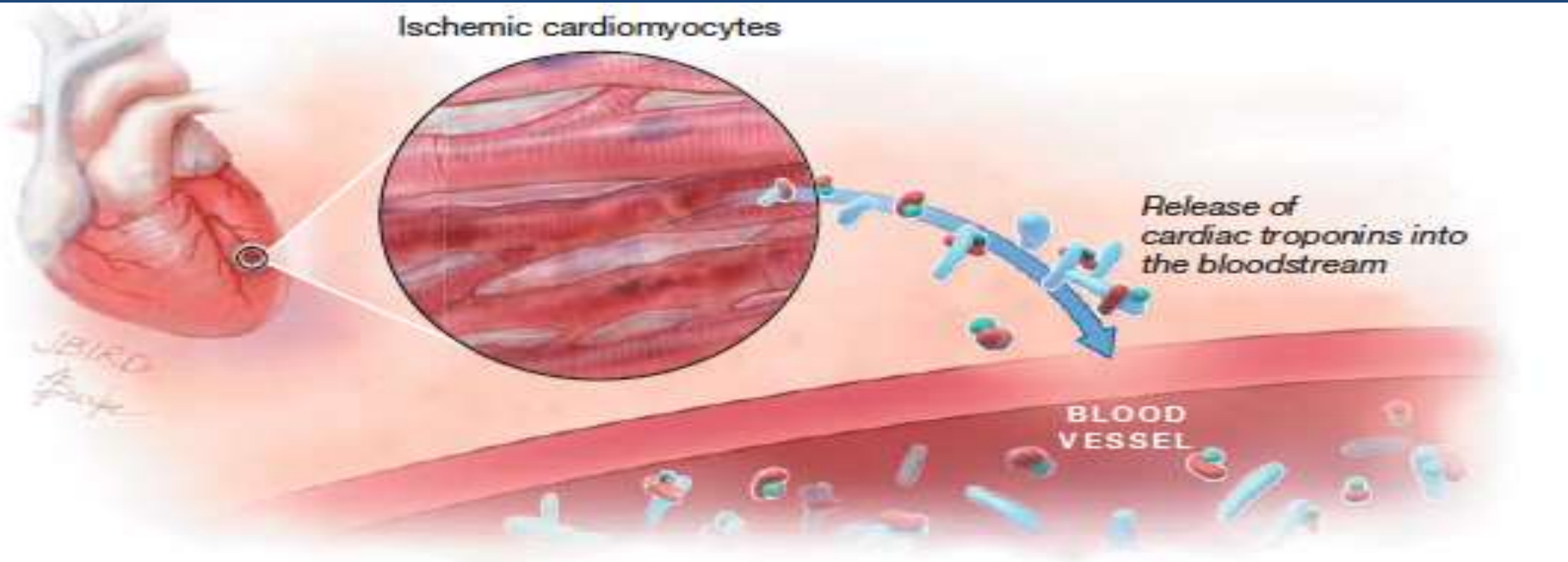
Myocardial Infarction Type 1



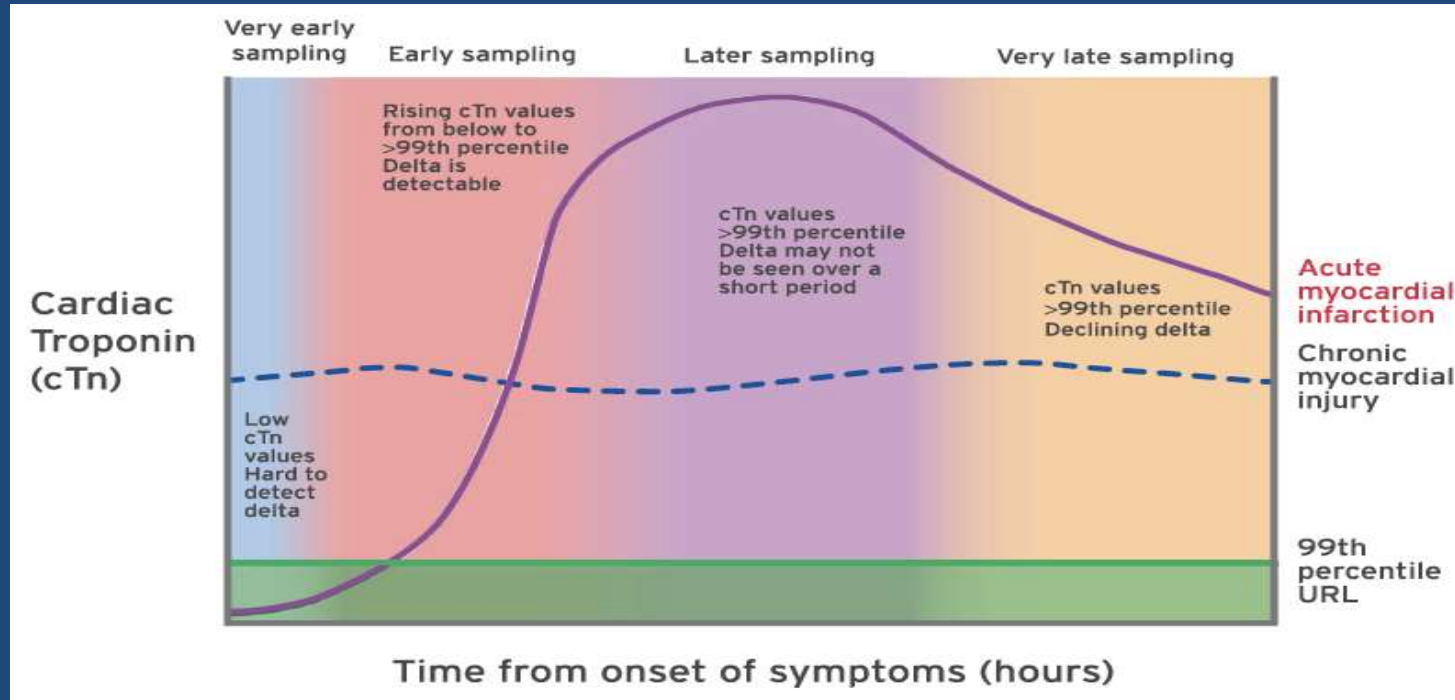
Myocardial Infarction Type 2



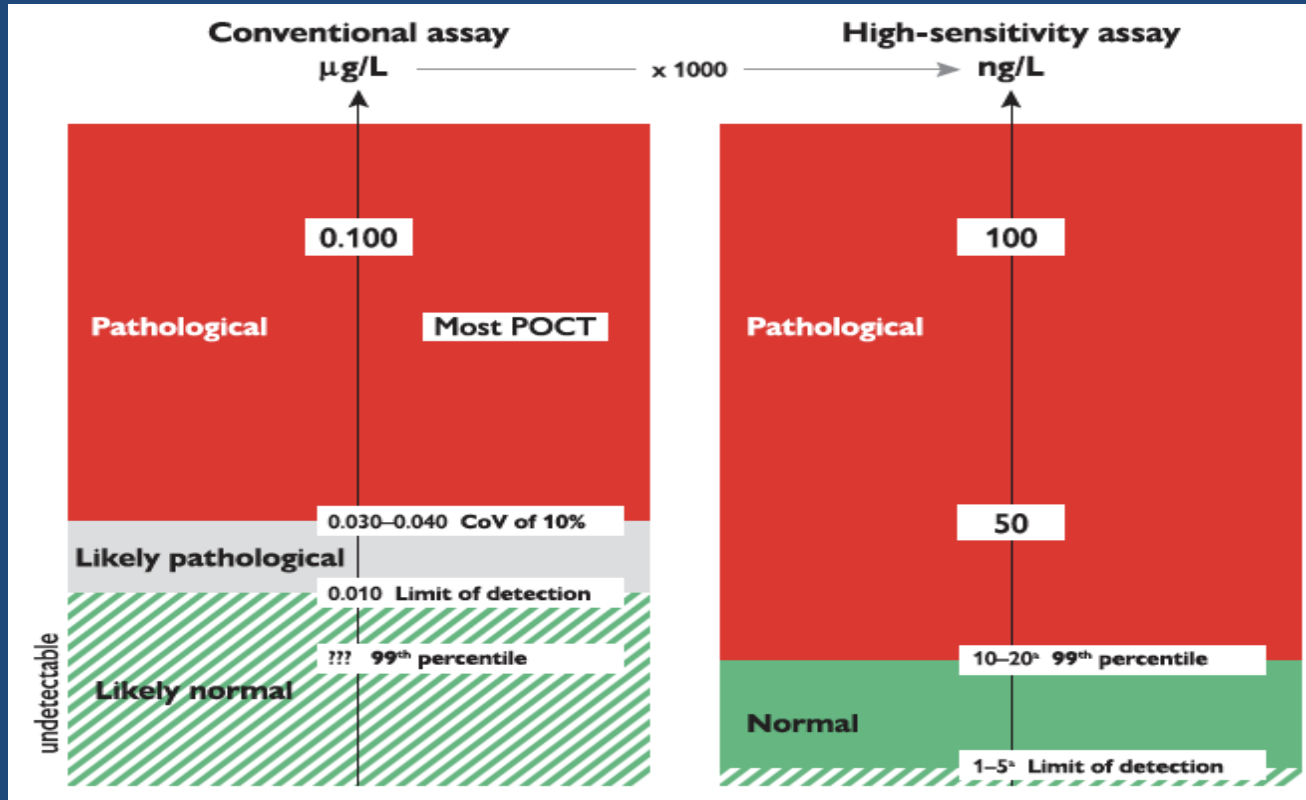
# Troponin- pathobiology



# Serial sampling and kinetics



# Troponin assays: conventional & HS



# Criteria

## Clinical Criteria for MI

The clinical definition of MI denotes the presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia.

## Criteria for Myocardial Injury

Detection of an elevated cTn value above the 99th percentile URL is defined as myocardial injury. The injury is considered acute if there is a rise and/or fall of cTn values.

## Criteria for Type 1 MI

Detection of a rise and/or fall of cTn values with at least 1 value above the 99th percentile URL and with at least 1 of the following:

- Symptoms of acute myocardial ischemia;
- New ischemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology;
- Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.\*

## Criteria for Type 2 MI

Detection of a rise and/or fall of cTn values with at least 1 value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute coronary atherosclerosis, requiring at least 1 of the following:

- Symptoms of acute myocardial ischemia;
- New ischemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology



# Reminder: assay specificity

**Table 5 Assay specific cut-off levels in ng/l within the 0 h/1 h and 0 h/2 h algorithms**

<b>0 h/1 h algorithm</b>	<b>Very low</b>	<b>Low</b>	<b>No 1hΔ</b>	<b>High</b>	<b>1hΔ</b>
hs-cTn T (Elecsys; Roche)	<5	<12	<3	≥52	≥5
hs-cTn I (Architect; Abbott)	<4	<5	<2	≥64	≥6
hs-cTn I (Centaur; Siemens)	<3	<6	<3	≥120	≥12
hs-cTn I (Access; Beckman Coulter)	<4	<5	<4	≥50	≥15
hs-cTn I (Clarity; Singulex)	<1	<2	<1	≥30	≥6
hs-cTn I (Vitros; Clinical Diagnostics)	<1	<2	<1	≥40	≥4
hs-cTn I (Pathfast; LSI Medience)	<3	<4	<3	≥90	≥20
hs-cTn I (TriageTrue; Quidel)	<4	<5	<3	≥60	≥8
<b>0 h/2 h algorithm</b>	<b>Very low</b>	<b>Low</b>	<b>No 2hΔ</b>	<b>High</b>	<b>2hΔ</b>
hs-cTn T (Elecsys; Roche)	<5	<14	<4	≥52	≥10
hs-cTn I (Architect; Abbott)	<4	<6	<2	≥64	≥15
hs-cTn I (Centaur; Siemens)	<3	<8	<7	≥120	≥20
hs-cTn I (Access; Beckman Coulter)	<4	<5	<5	≥50	≥20
hs-cTn I (Clarity; Singulex)	<1	TBD	TBD	≥30	TBD
hs-cTn I (Vitros; Clinical Diagnostics)	<1	TBD	TBD	≥40	TBD
hs-cTn I (Pathfast; LSI Medience)	<3	TBD	TBD	≥90	TBD
hs-cTn I (TriageTrue; Quidel)	<4	TBD	TBD	≥60	TBD

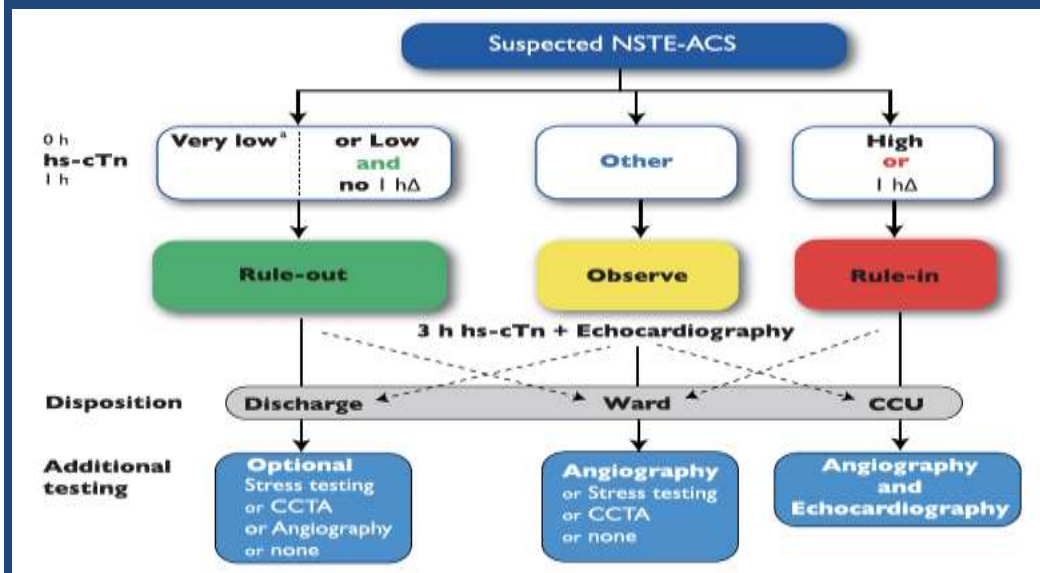
# So far we have...

- Established troponin as the preferred biomarker in AMI
- Established kinetics of trop release in AMI
- Reviewed contemporary HS assays with very low LoD
- Reviewed the fact that clinical presentation, absolute Tn value and delta Tn over time all matter



# Let's build pathways

Low Risk (<1% 30-d Risk for Death or MACE)	
hs-cTn Based	
T-0	T-0 hs-cTn below the assay limit of detection or "very low" threshold if symptoms present for at least 3 h
T-0 and 1- or 2-h Delta	T-0 hs-cTn and 1- or 2-h delta are both below the assay "low" thresholds (>99% NPV for 30-d MACE)
Clinical Decision Pathway Based	
HEART Pathway <sup>20</sup>	HEART score $\leq 3$ , initial and serial cTn/hs-cTn < assay 99th percentile
EDACS <sup>14</sup>	EDACS score $\leq 16$ ; initial and serial cTn/hs-cTn < assay 99th percentile
ADAPT <sup>21</sup>	TIMI score 0, initial and serial cTn/hs-cTn < assay 99th percentile
mADAPT	TIMI score 0/1, initial and serial cTn/hs-cTn < assay 99th percentile
NOTR <sup>10</sup>	0 factors



Caveats: clinical judgement, timing, age, renal function, time of symptoms



**Table 3 Clinical implications of high-sensitivity cardiac troponin assays**

**Compared with standard cardiac troponin assays, hs-cTn assays:**

- Have higher NPV for AMI.
- Reduce the 'troponin-blind' interval leading to earlier detection of AMI.
- Result in ~4% absolute and ~20% relative increases in the detection of type 1 MI and a corresponding decrease in the diagnosis of unstable angina.
- Are associated with a 2-fold increase in the detection of type 2 MI.

**Levels of hs-cTn should be interpreted as quantitative markers of cardiomyocyte damage (i.e. the higher the level, the greater the likelihood of MI):**

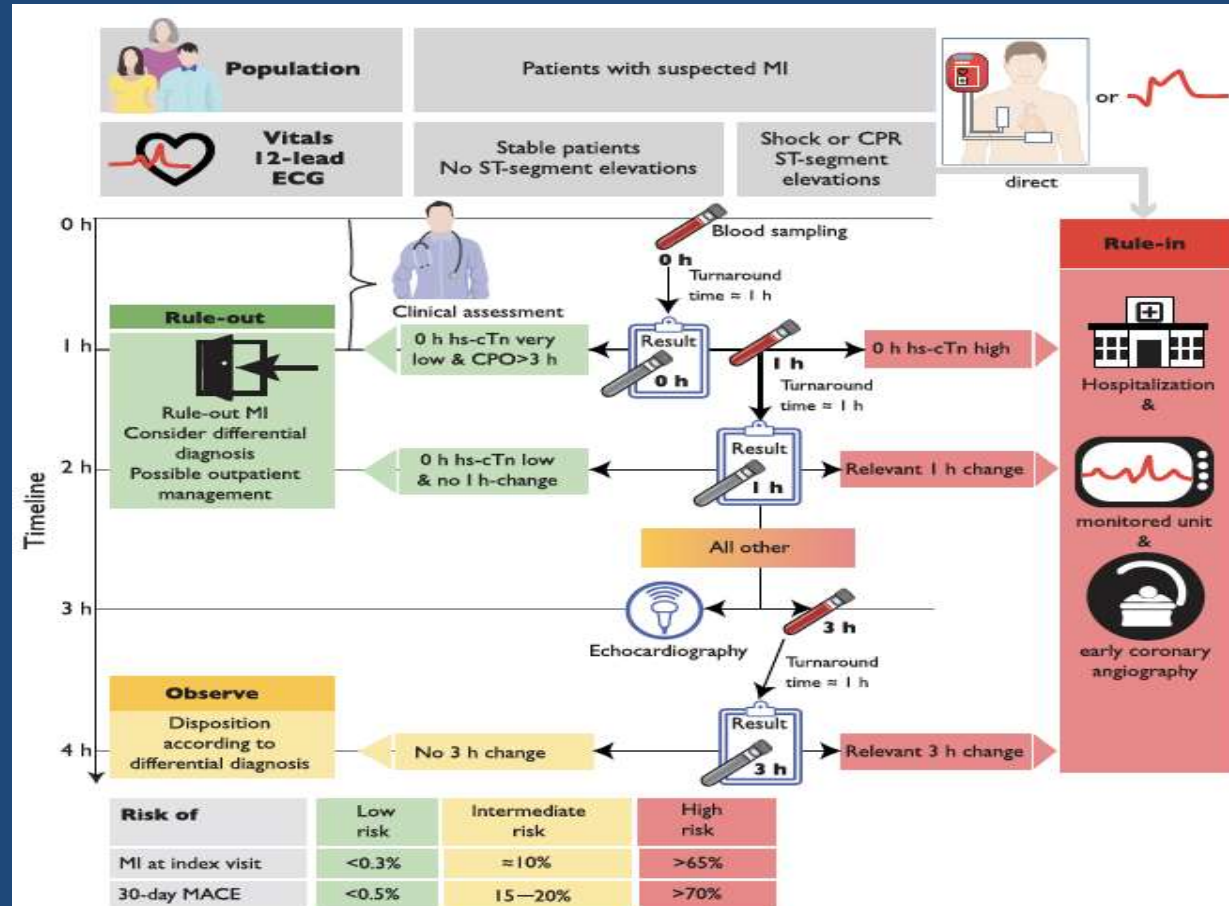
- Elevations beyond 5-fold the upper reference limit have high (>90%) PPV for acute type 1 MI.
- Elevations up to 3-fold the upper reference limit have only limited (50–60%) PPV for AMI and may be associated with a broad spectrum of conditions.
- It is common to detect circulating levels of cardiac troponin in healthy individuals.

**Rising and/or falling cardiac troponin levels differentiate acute (as in MI) from chronic cardiomyocyte damage (the more pronounced the change, the higher the likelihood of AMI).**

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# Put it all together

- 48 yo M with unstable and rest angina stuttering over hours, TWI on ECG in an ischemic pattern



- HsTnT 50 ng/L**

# Case conclusion

- Early cor angio: prox LAD lesion, successful PCI
- Normal LV function
- Discharge HD 2 to cardiac rehab
- Doing well



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# Thanks!

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