High Sensitivity Troponin
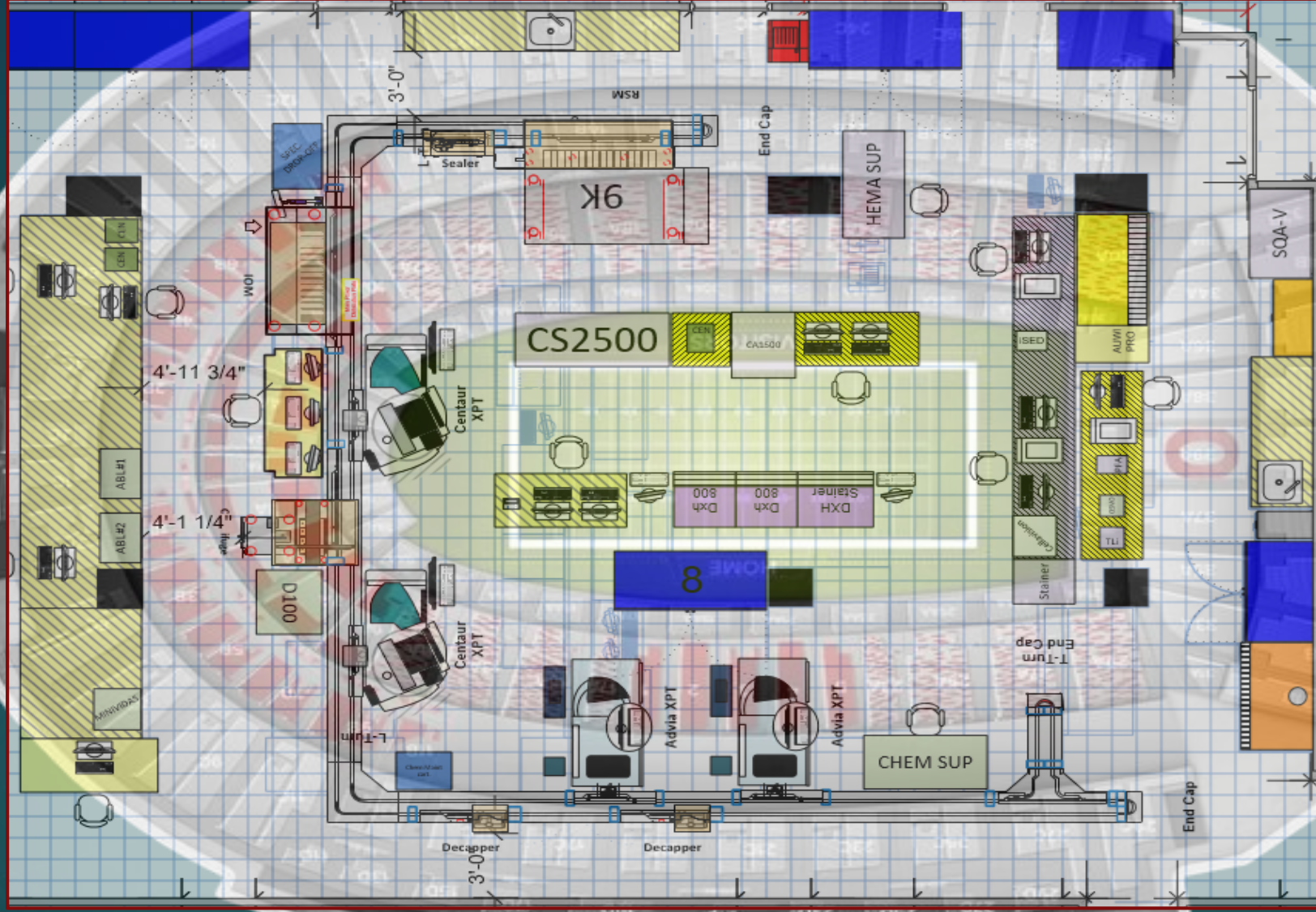
Lori J. Elwood, M.D. with expert consultation from Debra Heldman, M.D.

Can you name this site?

Can you name this site?

A. Progressive field , Cleveland, Ohio

B. Memorial stadium, Lincoln, Nebraska

C. First Energy stadium, Cleveland, Ohio

D. The "Shoe", Columbus, Ohio

ADVIA Centaur® XP Immunoassay System
ADVIA Centaur® XPT Immunoassay System

SIEMENS
Healthineers

Siemens Healthcare Diagnostics Inc.

Customer Bulletin
July 2018

Introducing the New High-Sensitivity Troponin I (TNIH) Assay (U.S.)

11316483, Rev. A

Introduction

Siemens Healthineers is pleased to announce the availability of the new High-Sensitivity Troponin I (TNIH) assay on the ADVIA Centaur® XP and ADVIA Centaur® XPT Immunoassay Systems. Refer to Table 1 for ordering information.

Table 1. **Product Ordering Information**

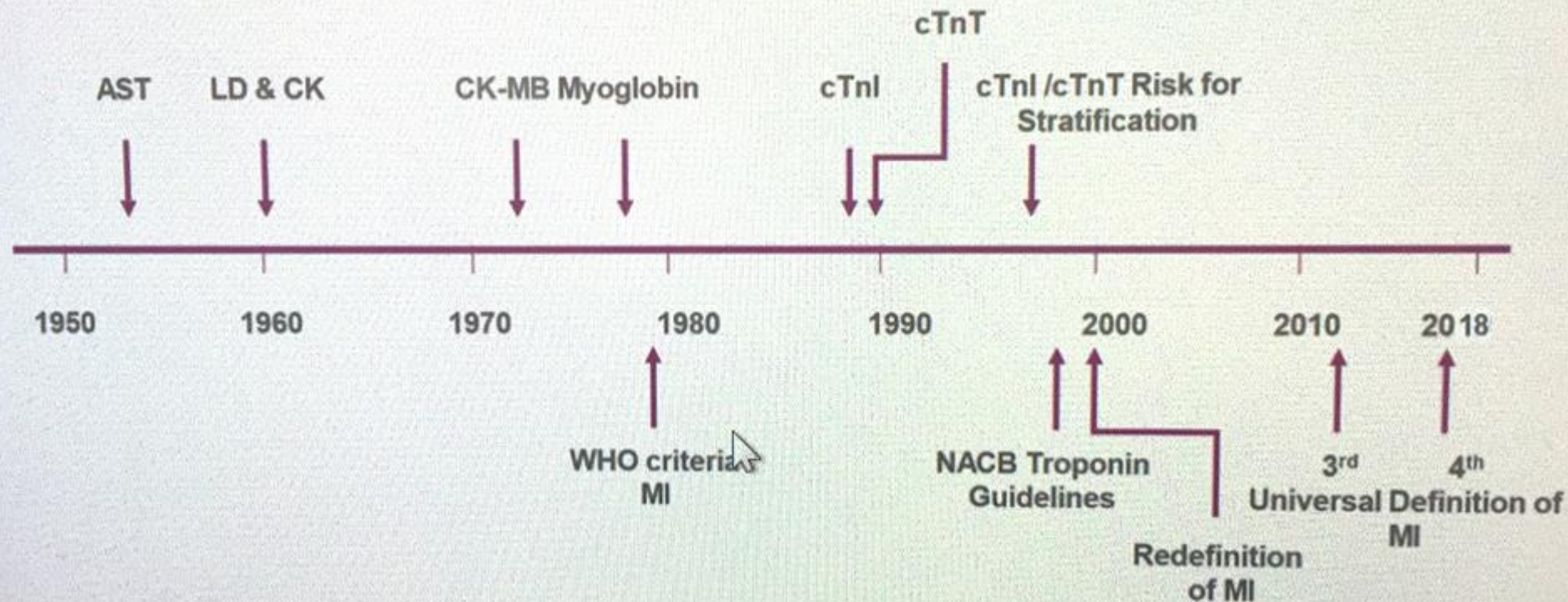| Product Name	Product Description	Siemens Material Number (SMN)/REF
ADVIA Centaur High-Sensitivity Troponin I (TNIH) Assay	100 tests Calibrators included	10994774
ADVIA Centaur High-Sensitivity Troponin I (TNIH) Assay	500 tests Calibrators included	10994775
ADVIA Centaur Multi-Diluent 11	2 ReadyPack® ancillary reagent packs, 5.0 mL per pack	05699280/117228

History of diagnostic testing in Acute MI

- ► **1912: Development of the electrocardiogram (nobel prize to William Einthoven 1924)**

- ► **1933: Early laboratory testing with recognition that WBC and ESR often elevated in the setting of myocardial infarction.**

- ► **1950: Quest for biomarkers based on concept that tissue damage results in release of enzymes that could be measured in serum.**

- ► **Development of biomarkers progressed from SGOT (AST), LDH, LDH isoenzymes, CPK, CPK isoenzymes, CK-MB, myoglobin and finally to troponin.**
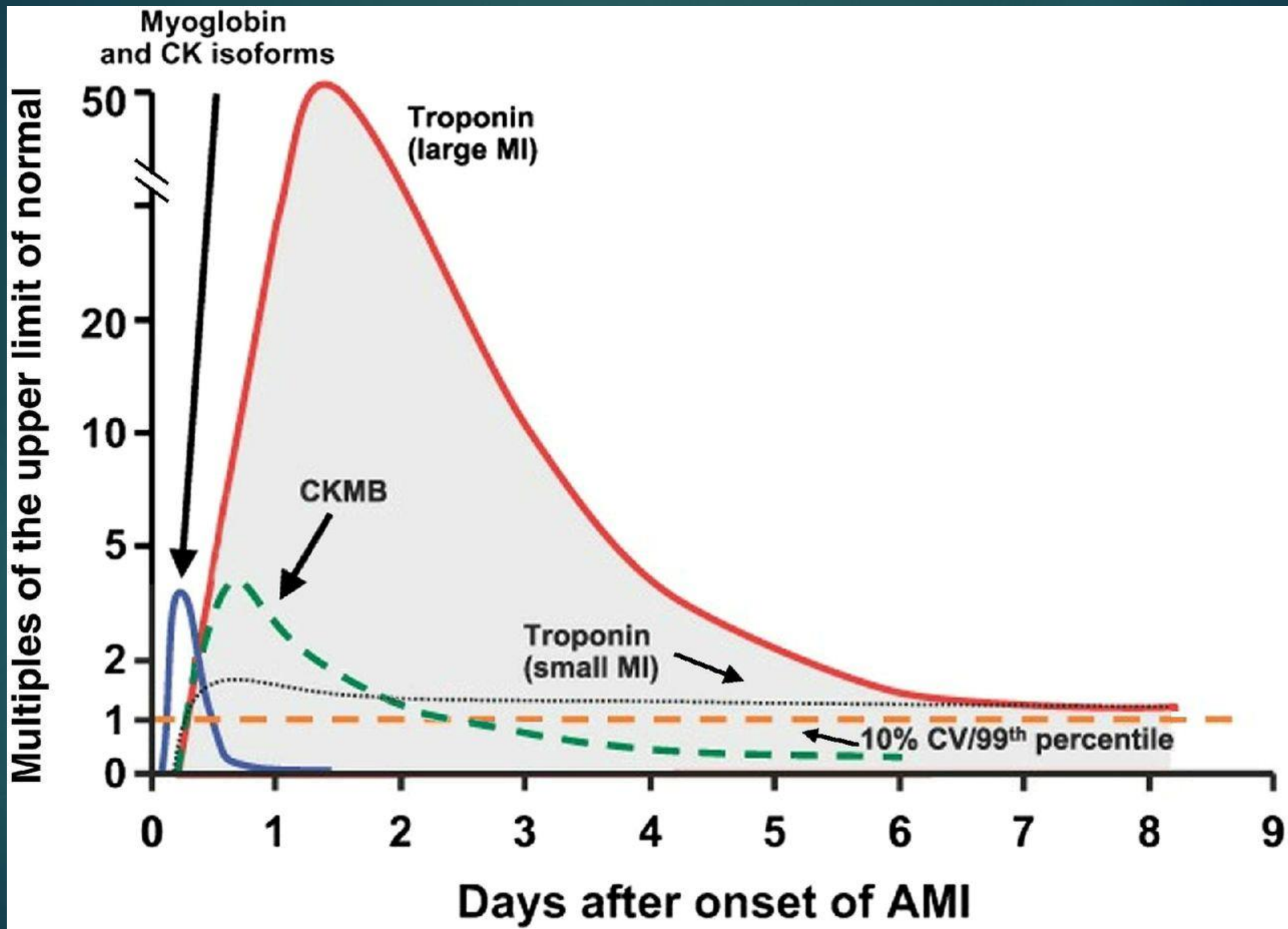
Clinical definition of MI

- **1979 WHO definition of MI – at least 2 of three criteria:**
  - **Positive clinical history of chest pain.**
  - **Unequivocal ECG changes.**
  - **Abnormal serial cardiac enzyme measurements.**
- **2000 First Global Task Force – New definition of MI placing cardiac troponin measurements central to the diagnosis.**
- **2007 Universal definition of myocardial infarction.**
- **2012 and 2018 Third and Fourth Universal definitions of MI**

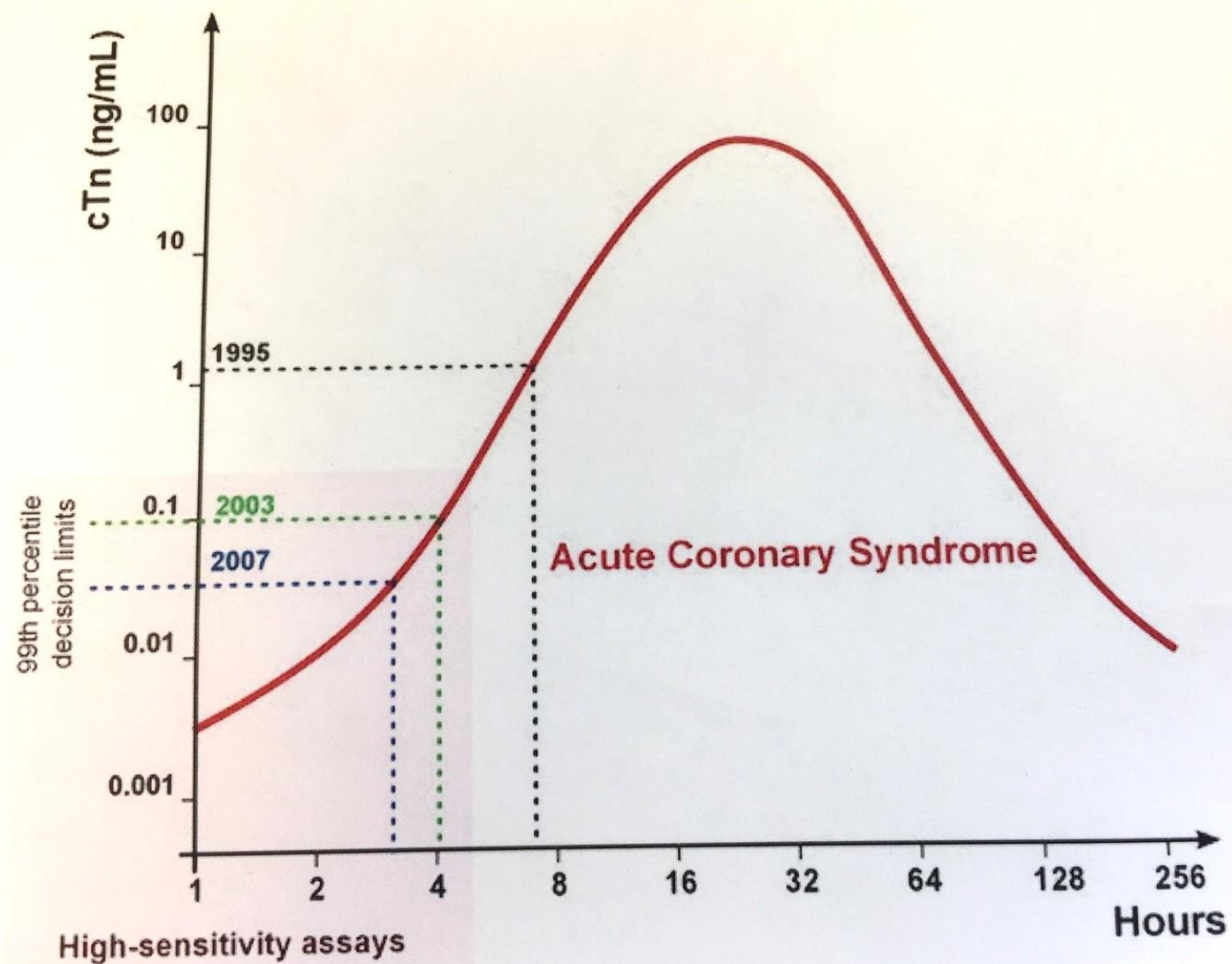# Evolution of clinical guidelines and cardiac biomarker testing[2]

Troponins

- Troponin complex is associated with the contractile apparatus of striated muscle. It consists of three separate proteins, TnI, TnT, TnC.

- There are different isoforms of each associated with cardiac and skeletal muscle.

- Cardiac troponin I and troponin T assays are commercially available.

- Assays are heart specific (although some cross-reactivity reported with troponin T).

- Troponin I (used at LMH) is totally heart specific.

Evolution of troponin assays

▶ First commercial assays were more specific but less sensitive for the diagnosis of MI.

▶ Successive generations have become more sensitive at the cost of specificity.

▶ New generations of assays have been termed "high sensitivity".

▶ Only the most recent generation of assays are, by definition, high sensitivity.

▶ Fourth universal definition of myocardial infarction states that high sensitivity assays "are recommended for routine use".

Fourth universal definition of myocardial infarction (2018)

- **Myocardial injury:** Detection of an elevated cTn value above the 99th percentile URL.

- **Myocardial infarction:** Presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia.

- **Type I MI:** Detection of rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following:

  - Symptoms of acute myocardial ischemia

  - New ischemic EKG changes

  - Development of pathologic Q waves

  - Imaging evidence of loss of myocardium.

  - Identification of a coronary thrombus by angiography or autopsy.

Fourth universal definition of myocardial infarction, cont.

- Criteria for type 2 MI: Detection of rise and/or fall of cTn values with at least one value above the 99th URL and evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute coronary athero-thrombosis, requiring at least one of the following:
  - Symptoms of acute myocardial ischemia
  - New ischemic EKG changes;
  - Development of pathological Q waves;
  - Imaging evidence of new loss of viable myocardium with an ischemic etiology.
- Acute myocardial injury: Troponin above 99th URL without acute ischemia (may detect a rise or fall in value), eg acute heart failure or myocarditis.
- Chronic myocardial injury: Troponin above 99th URL with stable elevation, eg chronic heart failure, cardiomyopathy, renal failure, chemotherapy

Issues with interpretation of cardiac troponin

- Time from onset of symptoms.

- Values from different assays are not interchangeable.

- 99th percentile URL for normal population is designated the decision level for presence of myocardial injury.

- Troponin may not be detectable in patients who present early, i.e. <2 hours after onset of chest discomfort.

- Definitions of significant change in troponin value, defined as rise or fall of >20% for values above the 99th percentile.

- Troponin is not a one and done test! Looking for rise/fall.

High sensitivity cardiac troponin

- Guideline acceptable with CV <10% at the 99th percentile URL.

- Should measure cTn above the limit of detection in >50% of the healthy patients used to determine the 99th percentile.

- Results should be reported in pg/mL instead of ug/L giving results in whole values instead of decimals.

- 99th percentile URL for our assay is 47 pg/mL.

- Our assay has 10% CV at troponin level of 6.0 pg/mL.

- Because our assay has such minimal imprecision, we can detect significant changes in troponin levels over a short period of time. We can exclude MI in 2 hours with the same degree of confidence that it took us 6-8 hours in our previous assay.

March 13, 2019

Blood test to diagnose heart attacks is flawed, warn researchers

by British Medical Journal

The blood test used to diagnose a heart attack (acute myocardial infarction) in patients admitted to hospital can be misleading, warn researchers in a study published by *The BMJ* today.

Of 20,000 consecutive patients undergoing blood tests at University Hospital Southampton, one in 20 had levels of troponin (a protein released into the bloodstream during a heart attack) greater than the manufacturer's recommended upper limit. But in most of these patients were being seen for other conditions and so there were no clinical signs or symptoms of a heart attack.

Troponin levels also differed according to several factors such as age, sex and whether inpatient or outpatient.

The researchers, led by cardiologist Professor Nick Curzen, say these results highlight the need for medical staff to interpret troponin levels carefully in order to avoid misdiagnosis of a heart attack and inappropriate treatment.

Current guidelines recommend troponin tests to help exclude or diagnose a heart attack. Manufacturers of troponin tests provide a recommended level (known as the 99th centile) based on values from a few hundred healthy individuals.
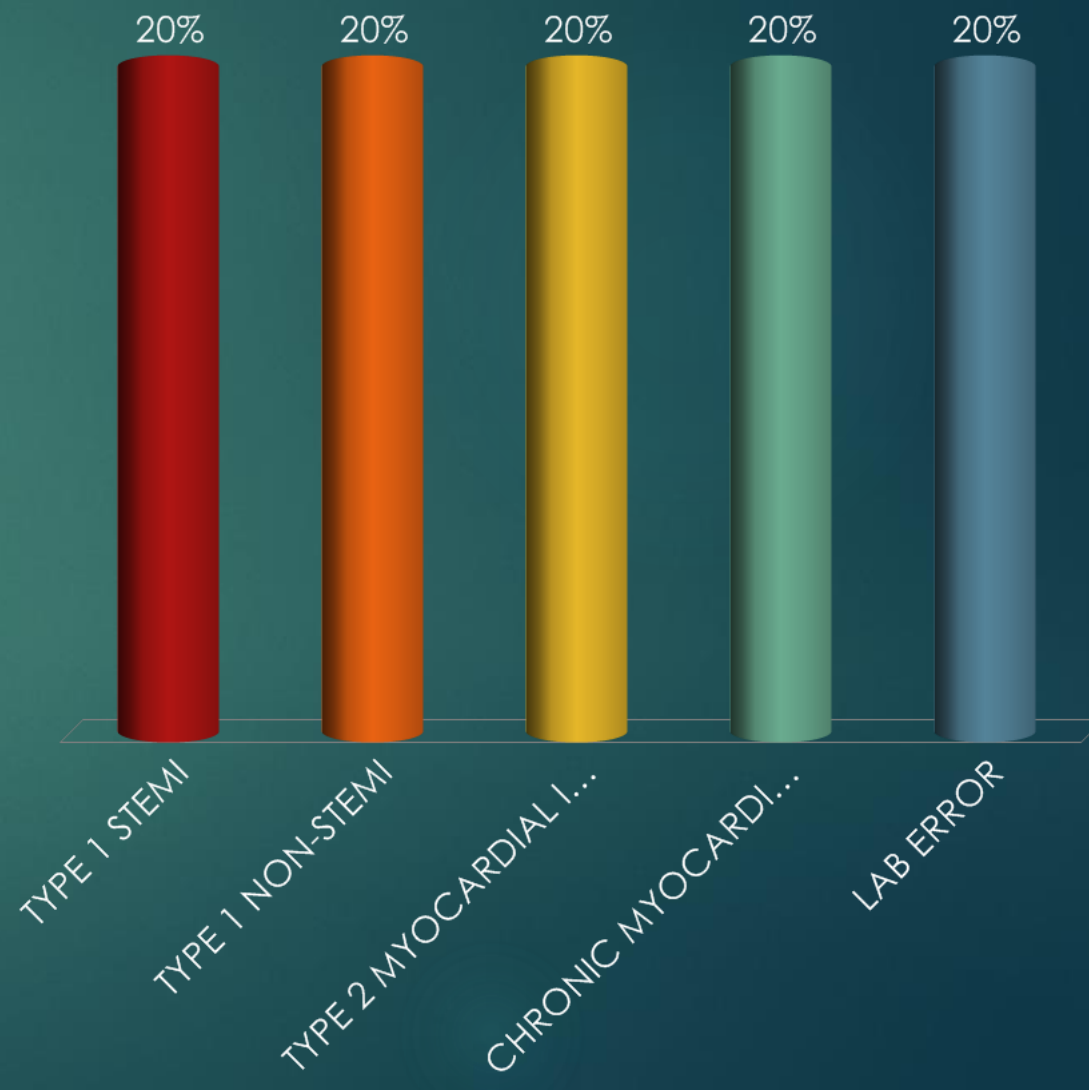
Future considerations

- ▶ **Use of change in absolute value of troponin vs percentage change.**
- ▶ **Early rule out protocols: studies are underway.**

Case #1

- 50 year old white male
- History of hypertension, GE reflux.
- Chief Complaint: Chest pain "left sided discomfort" with radiation to jaw, diaphoresis, nausea.
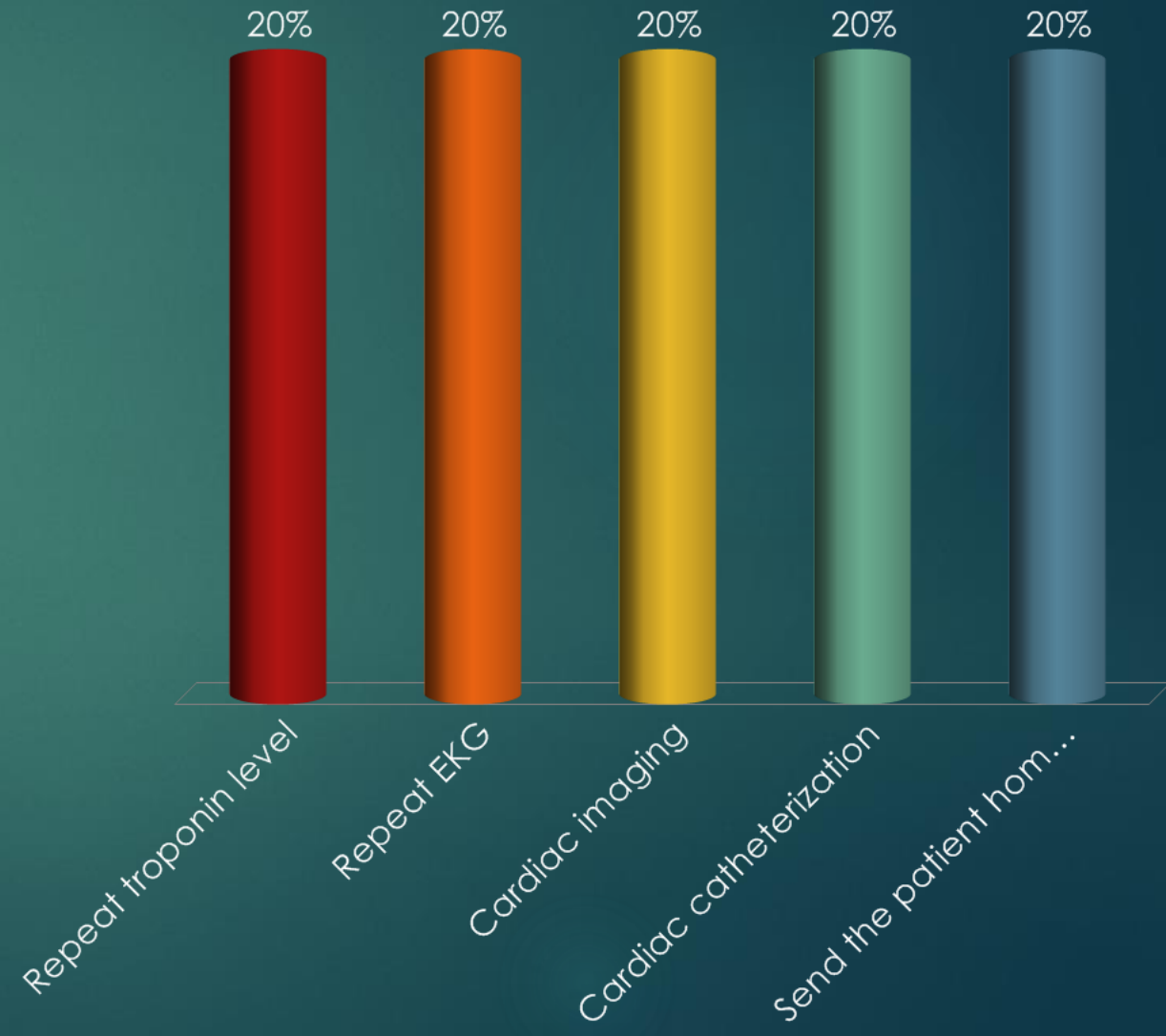- EKG: No acute ischemic ST changes.
- Troponins 192, 252, 367

What is your preliminary diagnosis?

A. **TYPE 1 STEMI**

B. **TYPE 1 NON-STEMI**

C. **TYPE 2 MYOCARDIAL INFARCTION**

D. **CHRONIC MYOCARDIAL INJURY PATTERN WITHOUT INFARCTION.**

E. **LAB ERROR**

20%	20%	20%	20%	20%
TYPE 1 STEMI	TYPE 1 NON-STEMI	TYPE 2 MYOCARDIAL I...	CHRONIC MYOCARDI...	LAB ERROR

Cardiac Catheterization

► **Anomaly of circumflex artery with origin from right coronary artery**

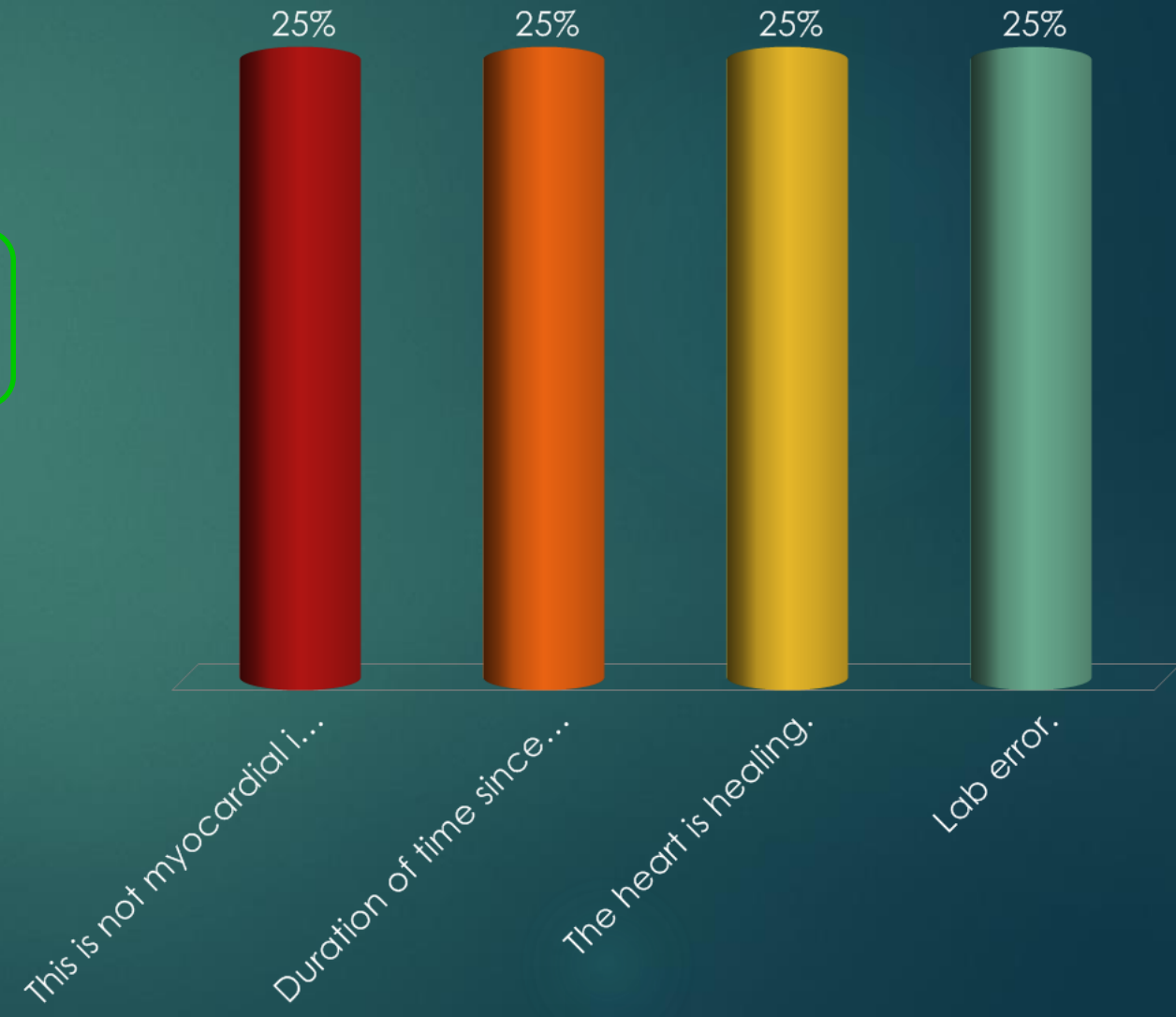► **No evidence of obstructive coronary artery disease**

Diagnosis

- **Type 2 myocardial infarction.**
- **Etiology indeterminate**
  - Coronary artery spasm or resolved clot?
  - Acute ischemia related to the anomaly unlikely.

Case #2

- **80 year old male**
- **History of multi-vessel coronary artery disease, multiple MI, PCI and diffuse LAD disease with severe distal stenosis not amenable to intervention. Aortic stenosis.**
- **Presented with worsening SOB, cough, wheezing for 1 week and an episode of chest pain responding to NTG.**
- **EKG: Sinus in 90's, LVH with secondary repolarization abnormality.**
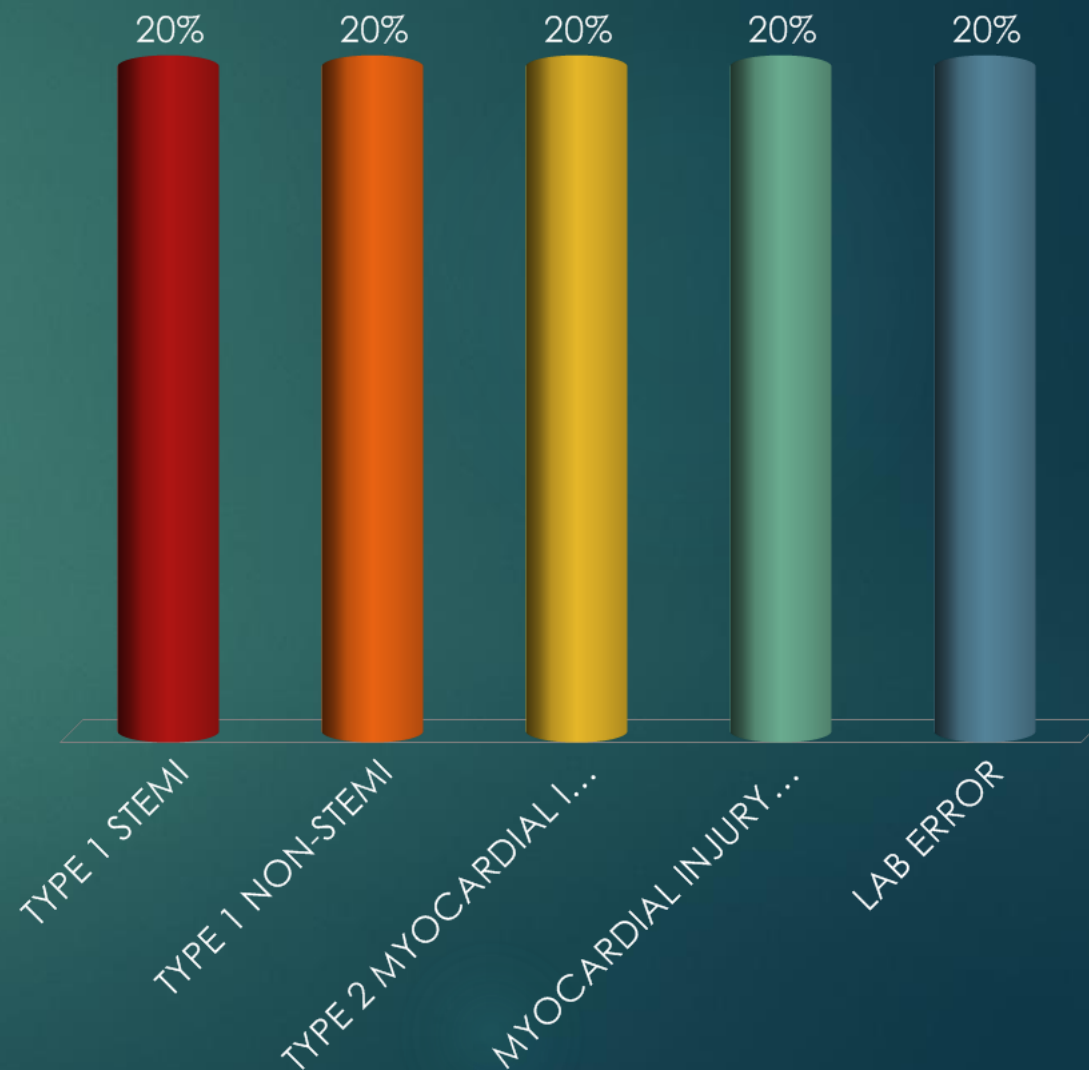- **CXR: New right basilar infiltrate.**
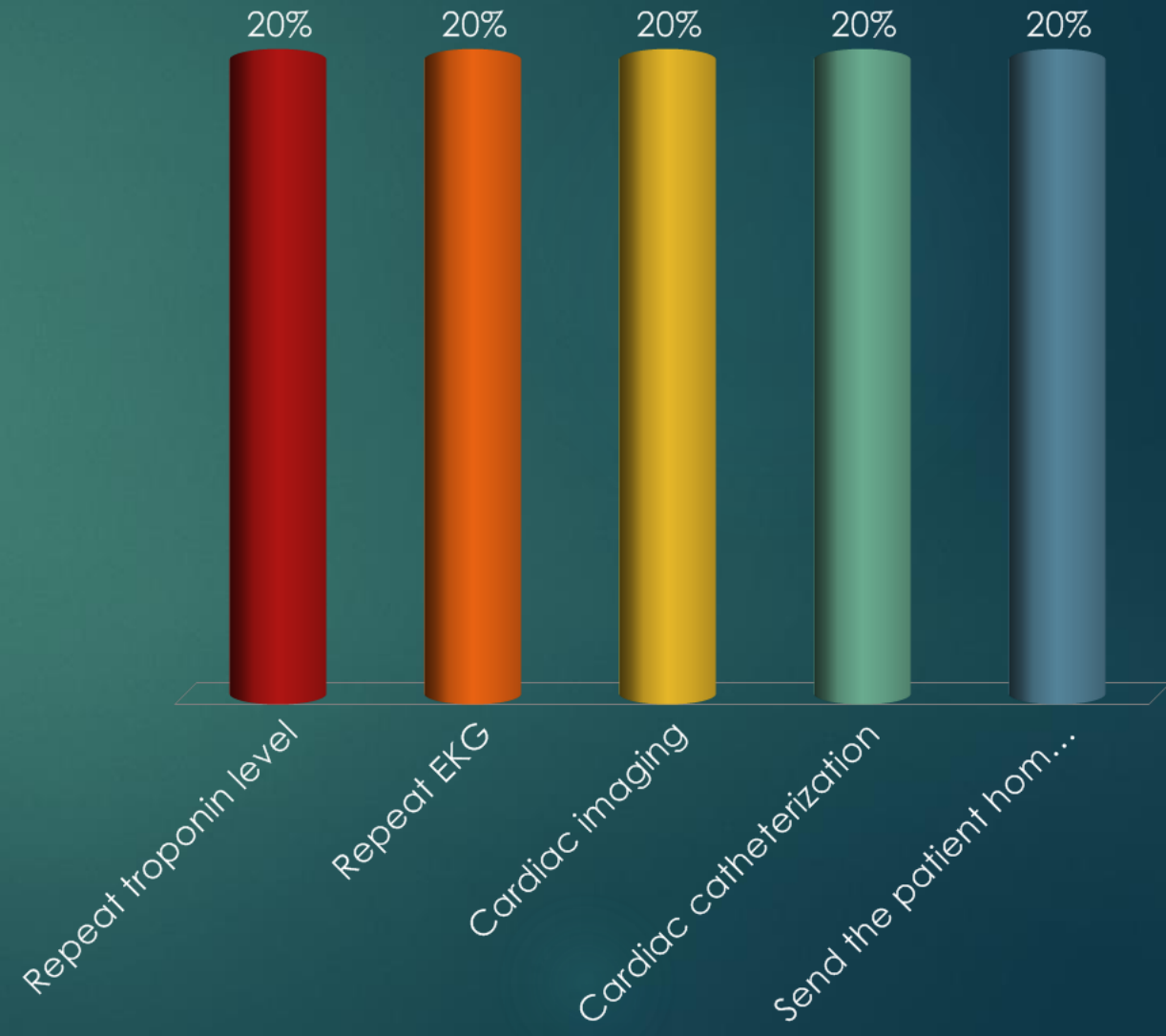- **Troponins: 1222, 974, 889**

What is your preliminary diagnosis?

A. **TYPE 1 STEMI**

B. **TYPE 1 NON-STEMI**

C. **TYPE 2 MYOCARDIAL INFARCTION**

D. **MYOCARDIAL INJURY PATTERN WITHOUT INFARCTION.**

E. **LAB ERROR**

20%	20%	20%	20%	20%
TYPE 1 STEMI	TYPE 1 NON-STEMI	TYPE 2 MYOCARDIAL I...	MYOCARDIAL INJURY ...	LAB ERROR

What is your next diagnostic step?

A. Repeat troponin level
B. Repeat EKG
C. Cardiac imaging
D. Cardiac catheterization
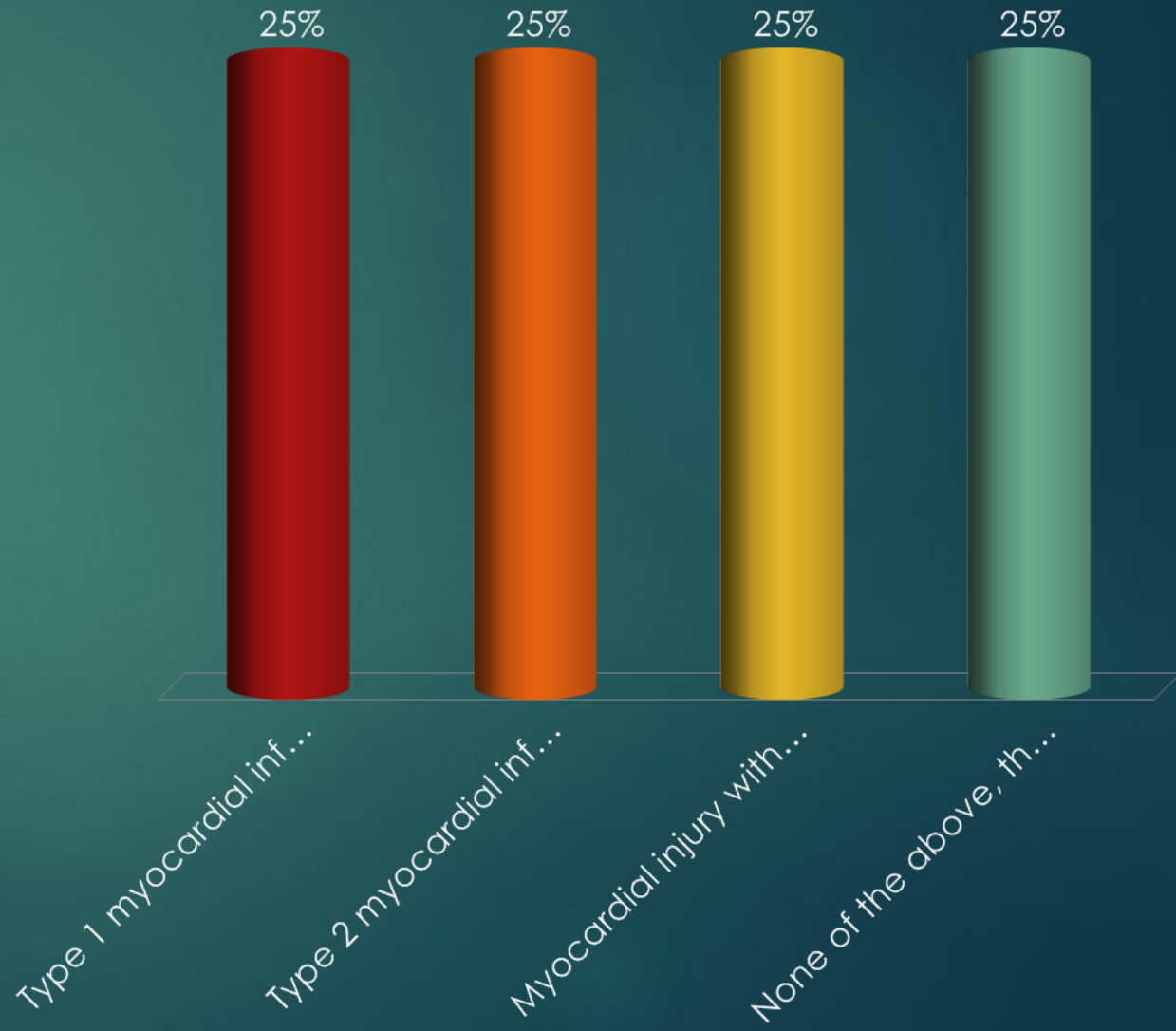E. Send the patient home and schedule outpatient cardiology visit.

Hospital Course

- ▶ Type II due to pneumonia vs type I non-STEMI.
- ▶ Cardiac catheterization not performed since the patient's disease was known.
- ▶ Treated with 48 hours of heparin, aspirin and Plavix.
- ▶ Continued on statin, beta blocker, Imdur, and calcium channel blocker.
- ▶ Treatment for pneumonia/COPD exacerbation.
- ▶ Had 2-D echo to evaluate aortic stenosis.
- ▶ Clinically improved and discharged for outpatient follow-up.

Case #3

▶ **79 year old female presenting with confusion and poor sugar control. Denies fever, chest pain and shortness of breath.**

▶ **Admitted for diabetic ketoacidosis, acute renal failure, hyponatremia and hyperkalemia. Also history of hypertension.**

▶ **EKG: Sinus tachycardia, possible left atrial enlargement, RBBB.**

▶ **Troponins on admission: 39, 50, 44.**

What is your diagnosis?

A. **Type 1 myocardial infarction**

B. **Type 2 myocardial infarction.**

C. **Myocardial injury without infarction.**

D. **None of the above, there was no clear indication to do the test**

25%   25%   25%   25%

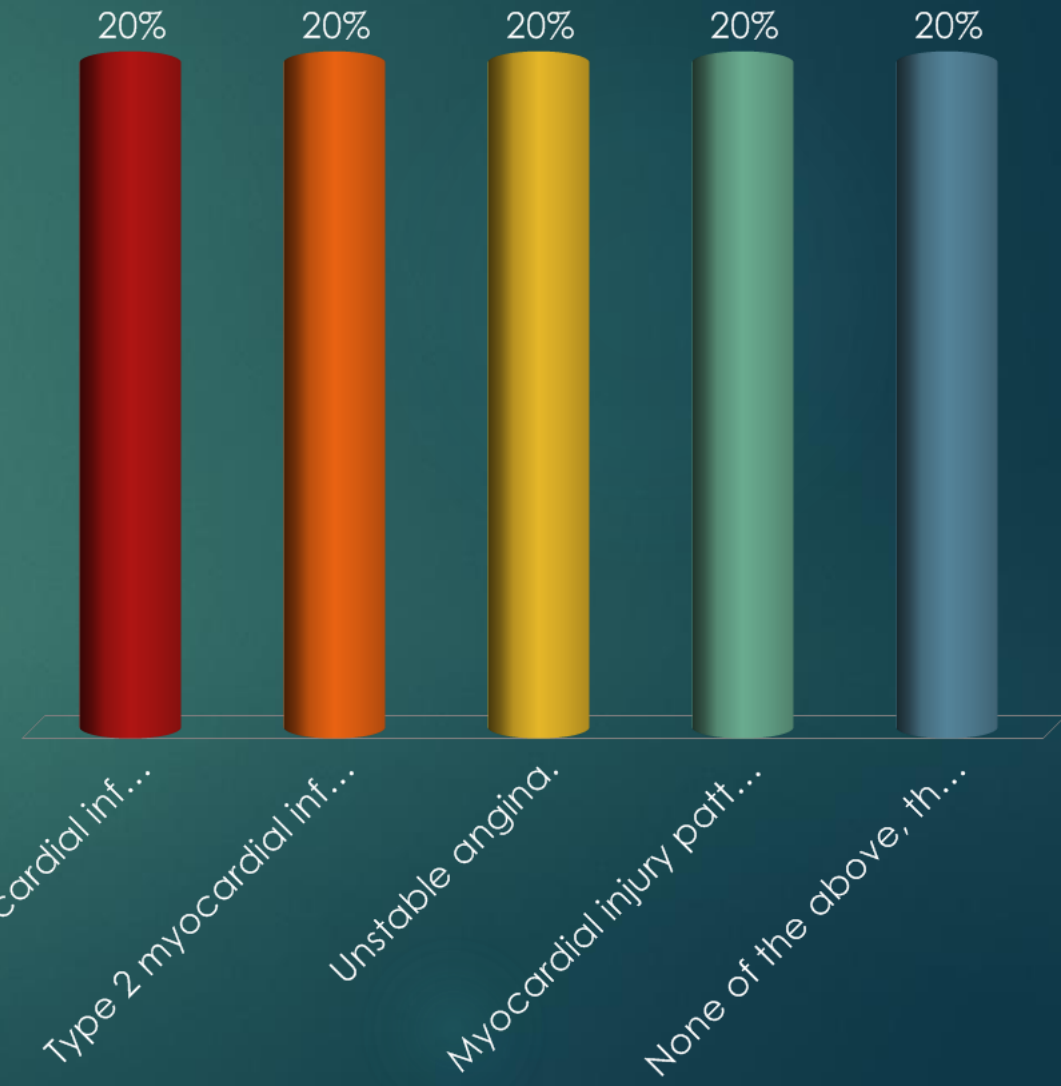Type 1 myocardial inf…   Type 2 myocardial inf…   Myocardial injury with…   None of the above, th…

Case #4

- 88 year old male presenting with increasing SOB over 1 month, abdominal distension, leg swelling, cough, wheezing and 10# weight gain. Denied chest pain or tightness.

- History of hypertension, hyperlipidemia, CRF (Cr 2.1), diabetes.

- EKG: Normal sinus rhythm, anterior infarct age undetermined.

- Repeat EKG: Sinus rhythm with premature atrial and junction beats rate 73, normal axis, low voltage QRS, septal infarct age undetermined.

- Troponins 2580, 2200, 2348

- BNP in the 300s

What is your diagnosis?

A. Type 1 myocardial infarction.

B. Type 2 myocardial infarction.

C. Unstable angina.

D. Myocardial injury pattern without infarction.

E. None of the above, there was no clear indication to do the test.

Case #4, continued
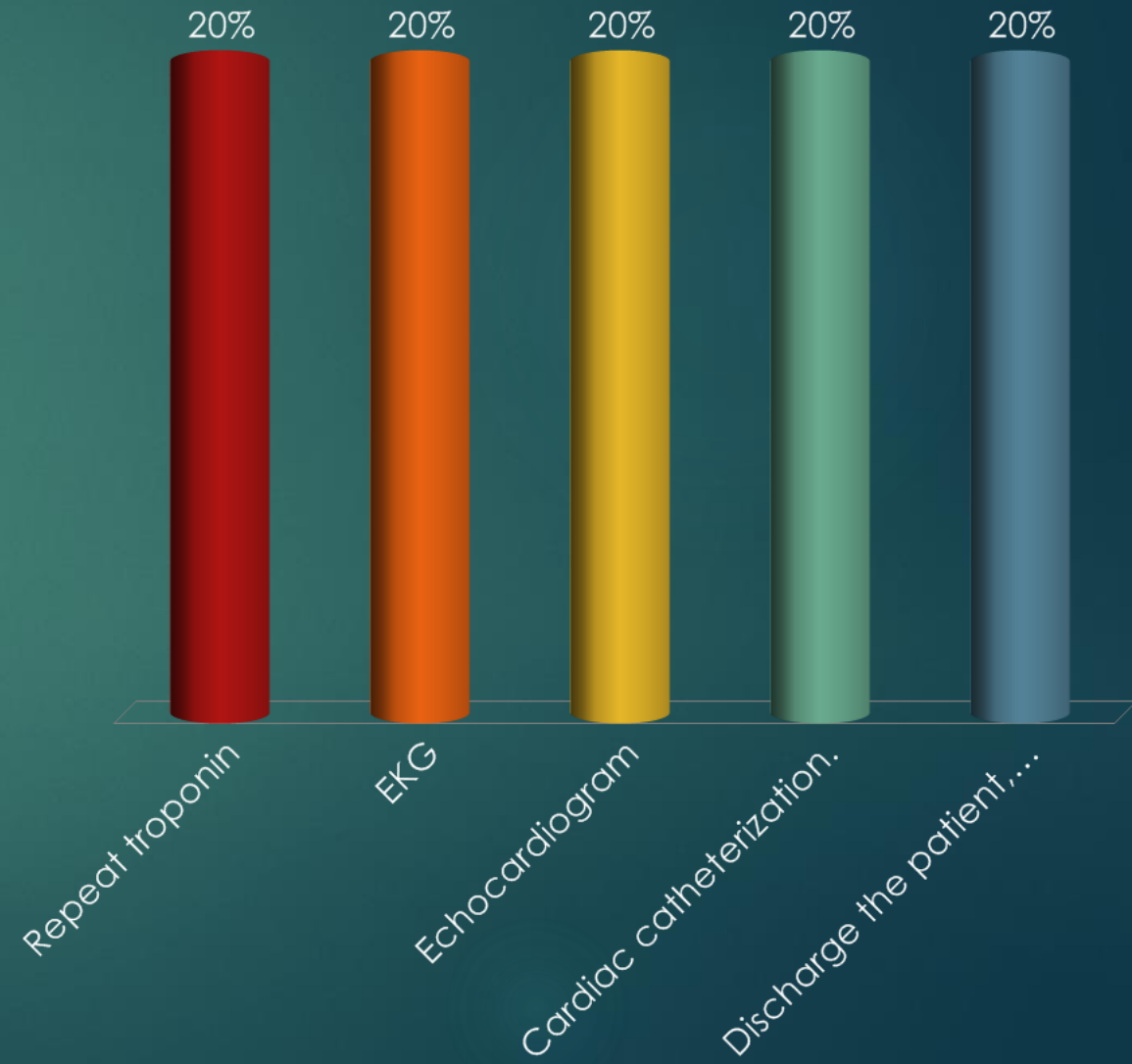
- **Echocardiogram:**
  - **Normal size left ventricle**
  - **Mildly reduced systolic LV function.**
  - **Ejection fraction 45%**
  - **Grade 1 diastolic dysfunction.**
  - **Mild aortic regurgitation**
  - **Mild mitral valve regurgitation.**

Case #5

- 86 year old male with history of atrial fibrillation s/p ablation with pacemaker on Coumadin.

- BCC of ear s/p radiation and immunotherapy.

- Esophagitis secondary to immunotherapy with malnutrition and dehydration secondary to esophagitis, treated with steroids.

- Presents to ED 12/28/18 with weakness and hypotension.

- Denies chest pain and syncope
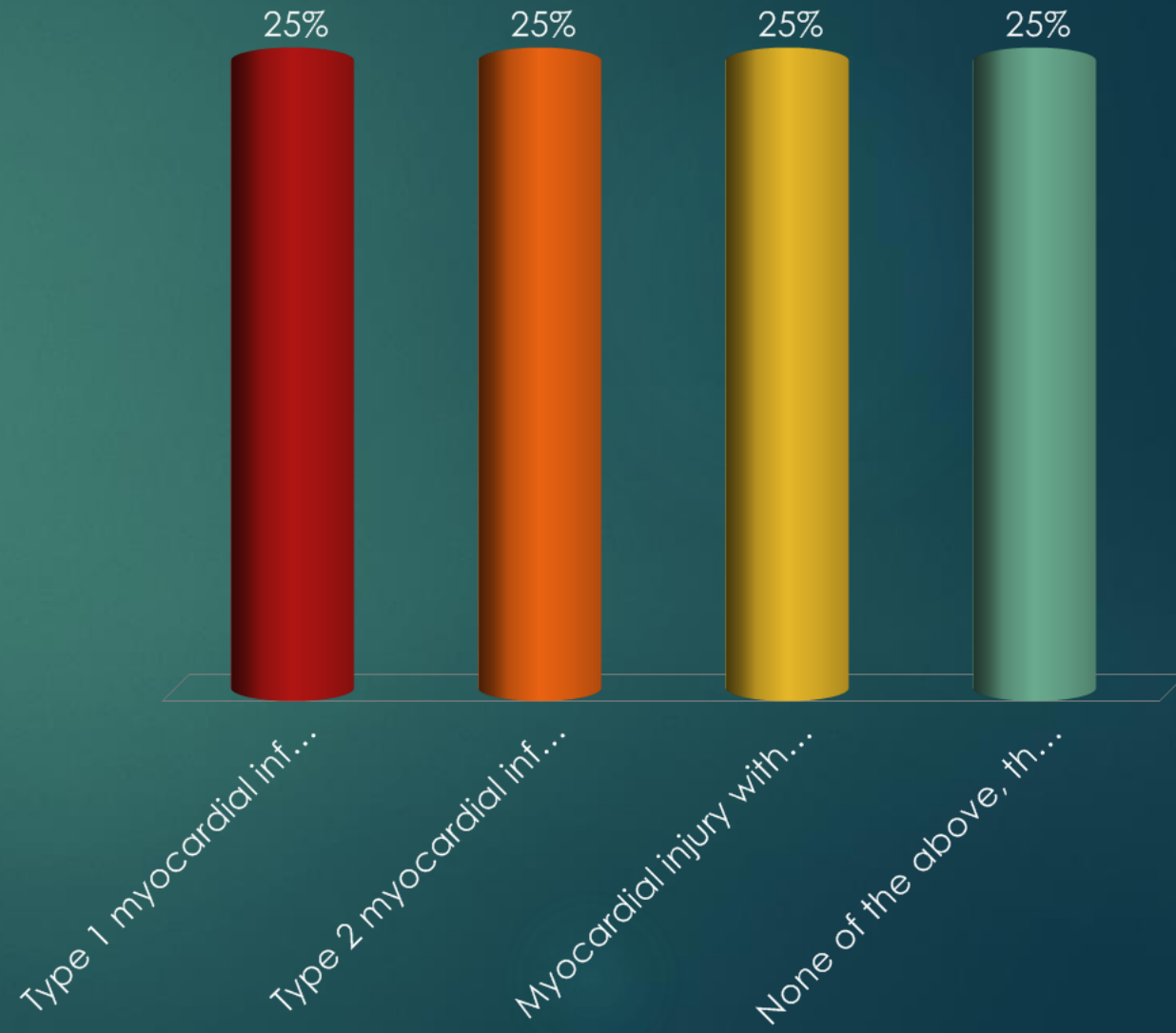
- Troponins 145, 133, 139

What test should you do next?

A. **Repeat troponin**
B. **EKG**
C. **Echocardiogram**
D. **Cardiac catheterization.**
E. **Discharge the patient, he doesn't need any more tests.**

20% — Repeat troponin
20% — EKG
20% — Echocardiogram
20% — Cardiac catheterization.
20% — Discharge the patient…

What is your diagnosis?

A. Type 1 myocardial infarction.

B. Type 2 myocardial infarction.

C. Myocardial injury without infarction.

D. None of the above, there was no clear indication to do the test

25%   25%   25%   25%

Type 1 myocardial inf...   Type 2 myocardial inf...   Myocardial injury with...   None of the above, th...

Case #5, continued
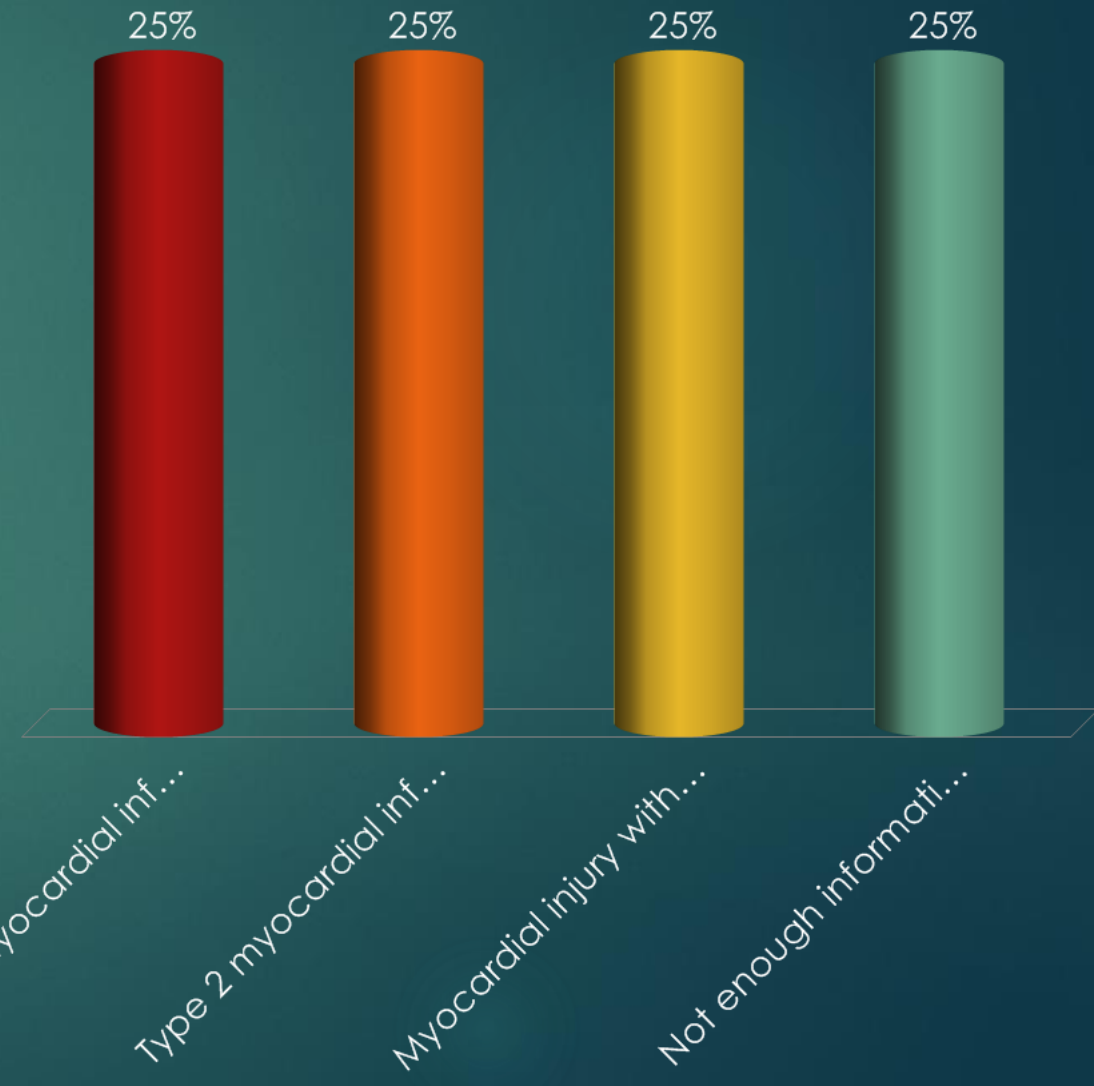
- Readmitted 1/10/19 with acute CHF and malnutrition.
- Echocardiogram (1/11/19):
    - Lower limits of normal systolic LV function.
    - Ejection fraction, measured in 2D mode, is 50%.
    - Mildly dilated right ventricle.
    - Left atrium moderately dilated.
    - Mild mitral valve regurgitation.
    - Mild aortic valve regurgitation.
    - Mild tricuspid regurgitation.

Case #5, continued

► **Treated for congestive heart failure and discharged to rehabilitation.**

► **Discharged from rehabilitation to home 1/30/19.**

► **2/1/2019 called EMS for SOB. PO2 95%. Wheezing reported by EMS, relieved by respiratory treatment en route to ED. No chest pain.**

► **Asymptomatic on arrival.**

► **EKG shows paced rhythm. No mention of ischemic changes.**

► **Troponins 98, 103, 127.**

What is your diagnosis?

A. **Type 1 myocardial infarction.**

B. **Type 2 myocardial infarction.**

C. **Myocardial injury without infarction.**

D. **Not enough information to determine a diagnosis.**

25%   25%   25%   25%

Type 1 myocardial inf...

Type 2 myocardial inf...

Myocardial injury with...
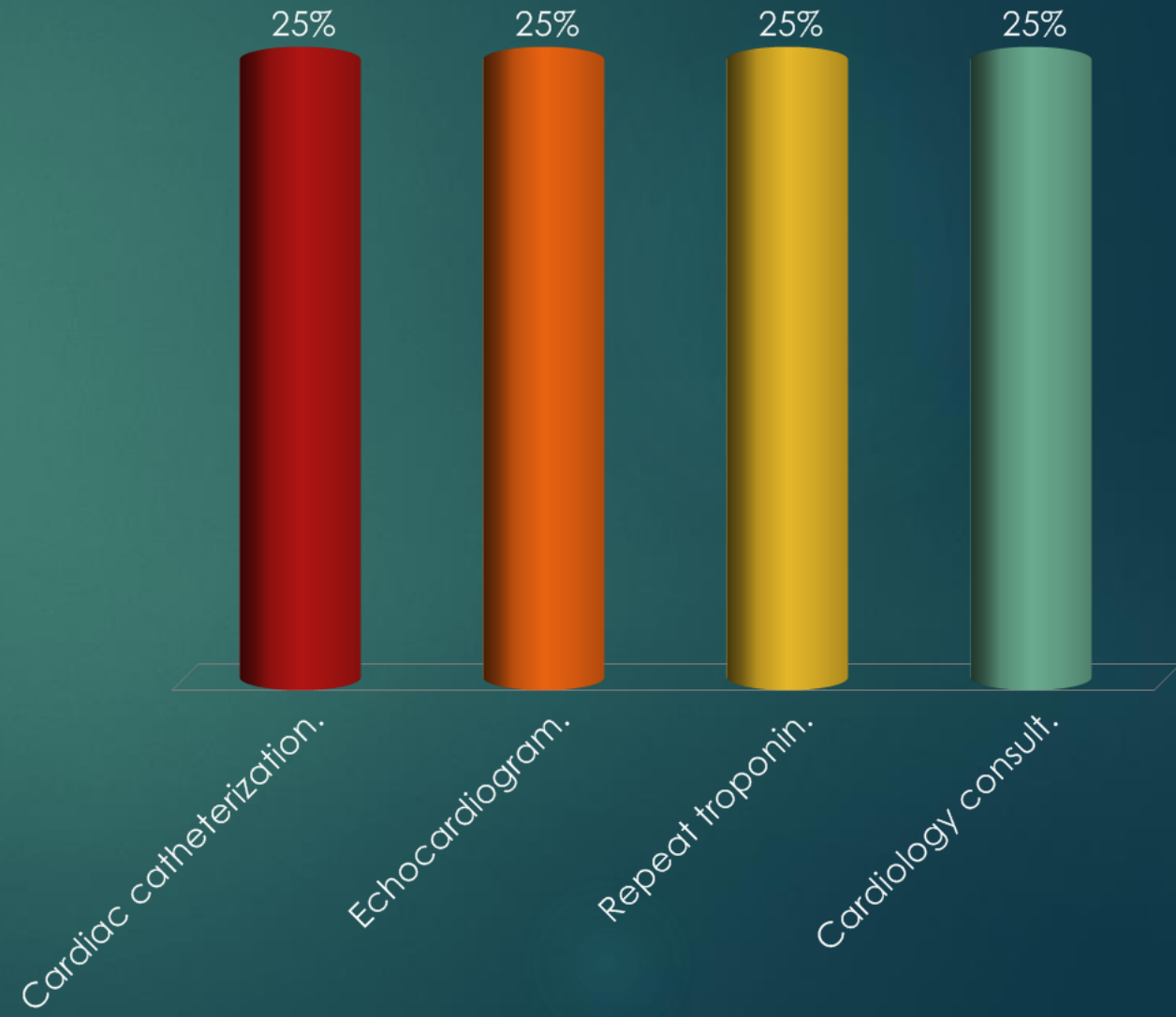
Not enough informati...

Teaching points

- Note the increasing troponin.

  - **You can always keep a patient in the ED an additional hour for another troponin!**

- Positive predictive value of a test is increased when used in a population with a high prevalence of the disease you are testing for.

  - Example: flu testing is most valuable during flu season.

  - Troponin will be most useful when used in a population likely to have ischemia. Clinical story, EKG changes.

  - **Do not use troponin as a general screening test. You will sometimes get results difficult to interpret!**

Case #6

- 64 year old female poor historian with MRDD, multiple admissions for pneumonia, suspected COPD on chronic oxygen, DM, CKD. Brought to ED by caregivers for SOB.

- Admits to difficult breathing and cough.

- Denied chest pain.

- CXR with possible congestion.

- CTA (positive D-dimer) shows airspace disease, no PE.

- Troponins 3, 40, 62.

- EKG normal sinus rhythm.

What is your next step?

A. **Cardiac catheterization.**

B. **Echocardiogram.**

C. **Repeat troponin.**

D. **Cardiology consult.**

25%   25%   25%   25%

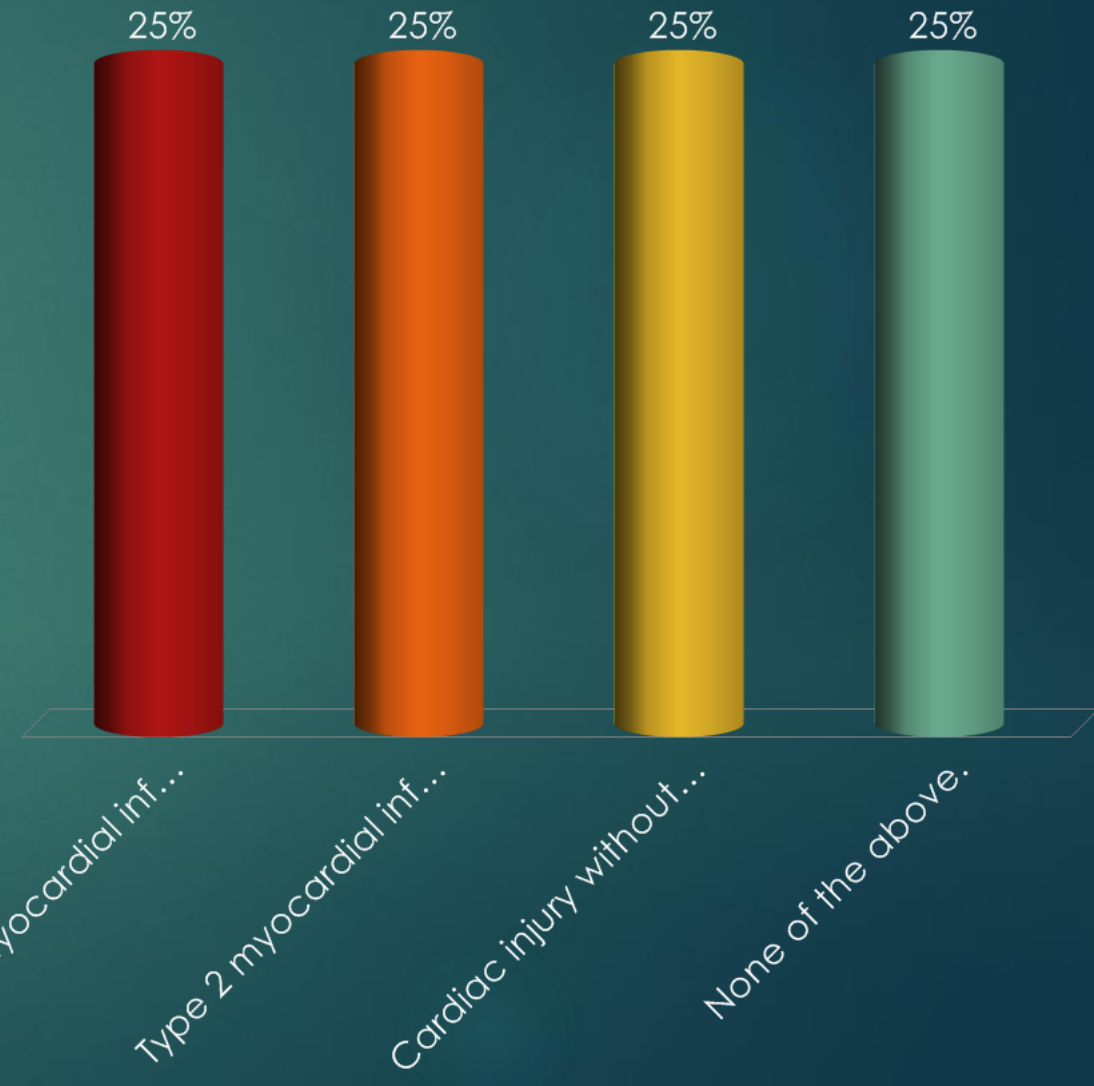Cardiac catheterization.   Echocardiogram.   Repeat troponin.   Cardiology consult.

Case #6, continued

- Repeat troponin, 3 hours after the third troponin of 62, was 68.

- Recent Cardiolite stress test was negative.

- Echocardiogram showed ejection fraction of 71% with no wall motion abnormalities.

What is the most likely diagnosis?

A. Type 1 myocardial infarction.
B. Type 2 myocardial infarction.
C. Cardiac injury without infarction.
D. None of the above.

25%   25%   25%   25%

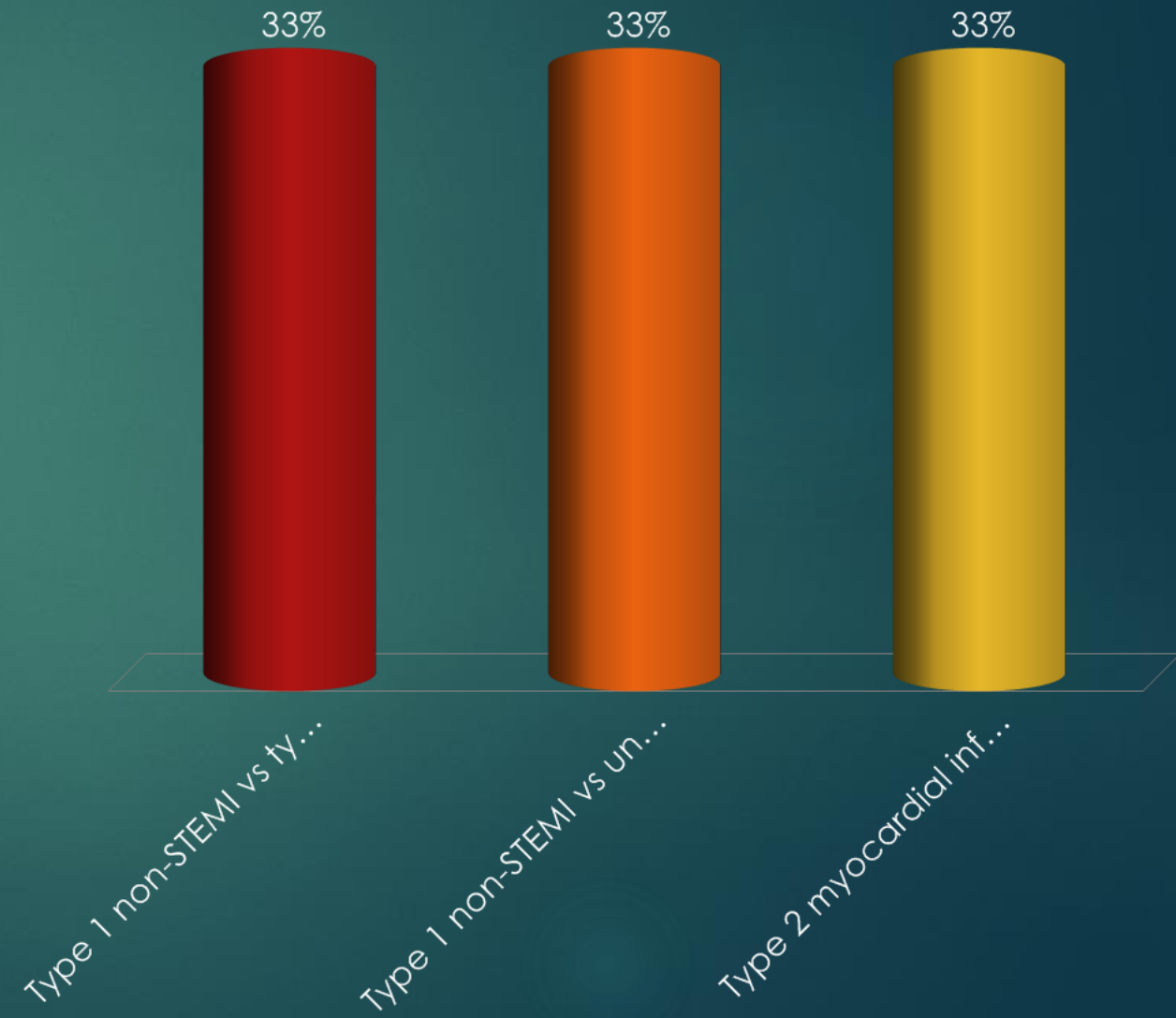Type 1 myocardial inf...   Type 2 myocardial inf...   Cardiac injury without...   None of the above.

Case #7

- 77 year old female with history of hypertension, hypothyroidism, dyslipidemia and mitral valve prolapse.

- Presented to ED with chest pain starting the previous day. The pain was described as pressure across her chest, intermittent, and of moderate intensity. Radiates to back and shoulders. Exacerbated on the day of presentation by walking in the mall.

- There was a visit to urgent care for cough and congestion 2 days prior to presentation. Diagnosed with bronchitis and treated with prednisone and antibiotic. No fever or chills.

- EKG showed lateral ST depression.
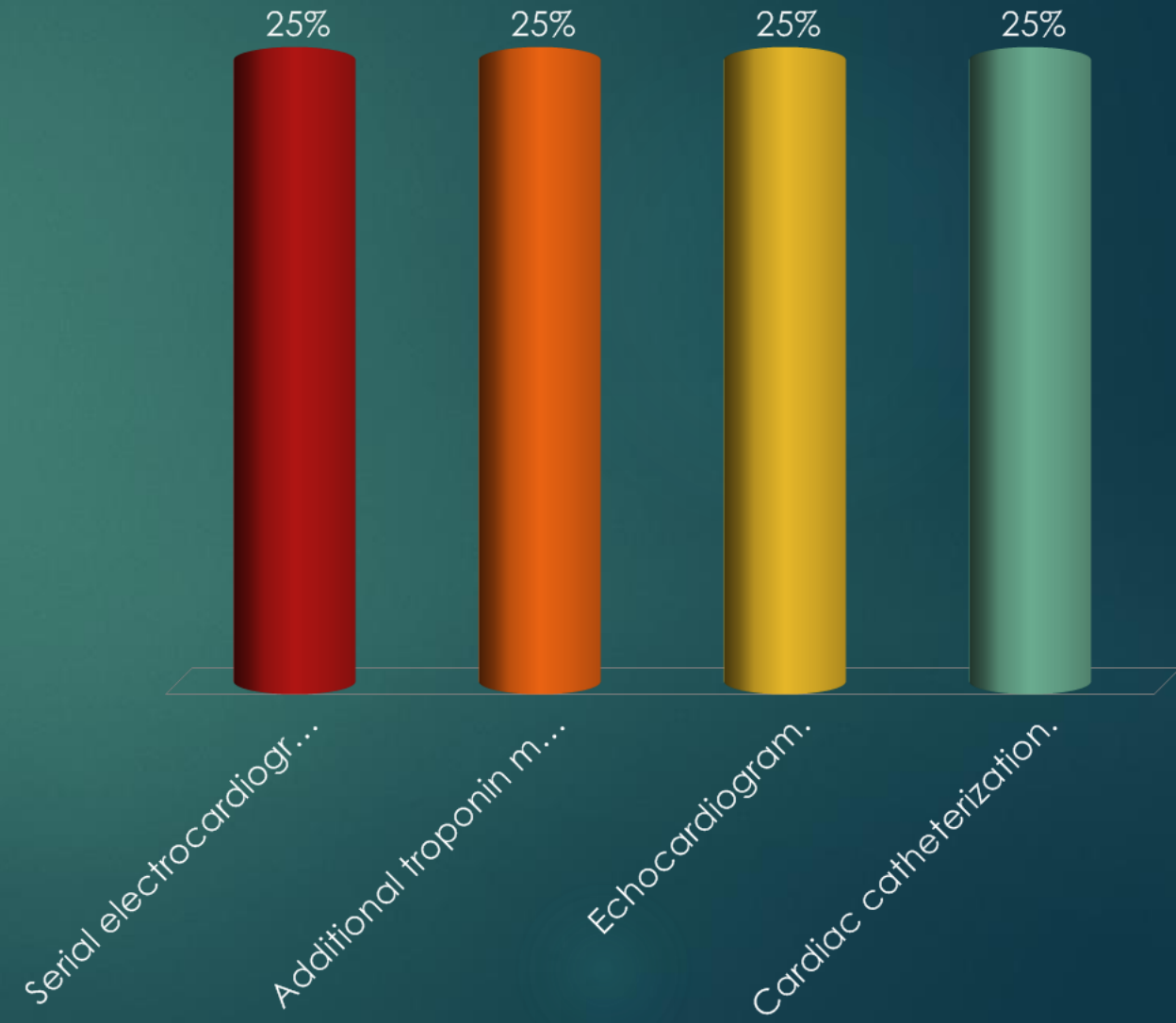
- Troponin 10, 52, 111. Blood pressure 210 systolic.

What is your differential diagnosis?

A. **Type 1 non-STEMI vs type 2 MI.**

B. **Type 1 non-STEMI vs unstable angina.**

C. **Type 2 myocardial infarction due to hypertensive emergency vs cardiac injury without infarction.**

What diagnostic tool would you recommend?

A. Serial electrocardiograms.
B. Additional troponin measurement.
C. Echocardiogram.
D. Cardiac catheterization.

Case #7, continued

- **Cardiac catheterization**
  - ▶ **Ejection fraction: 60%**
  - ▶ **Right dominant coronary circulation.**
  - ▶ **LAD 30% stenosis.**
  - ▶ **Proximal circumflex 30% stenosis.**
  - ▶ **Distal right coronary artery 99% stenosis.**
    - ▶ **Balloon and drug eluting stent intervention.**
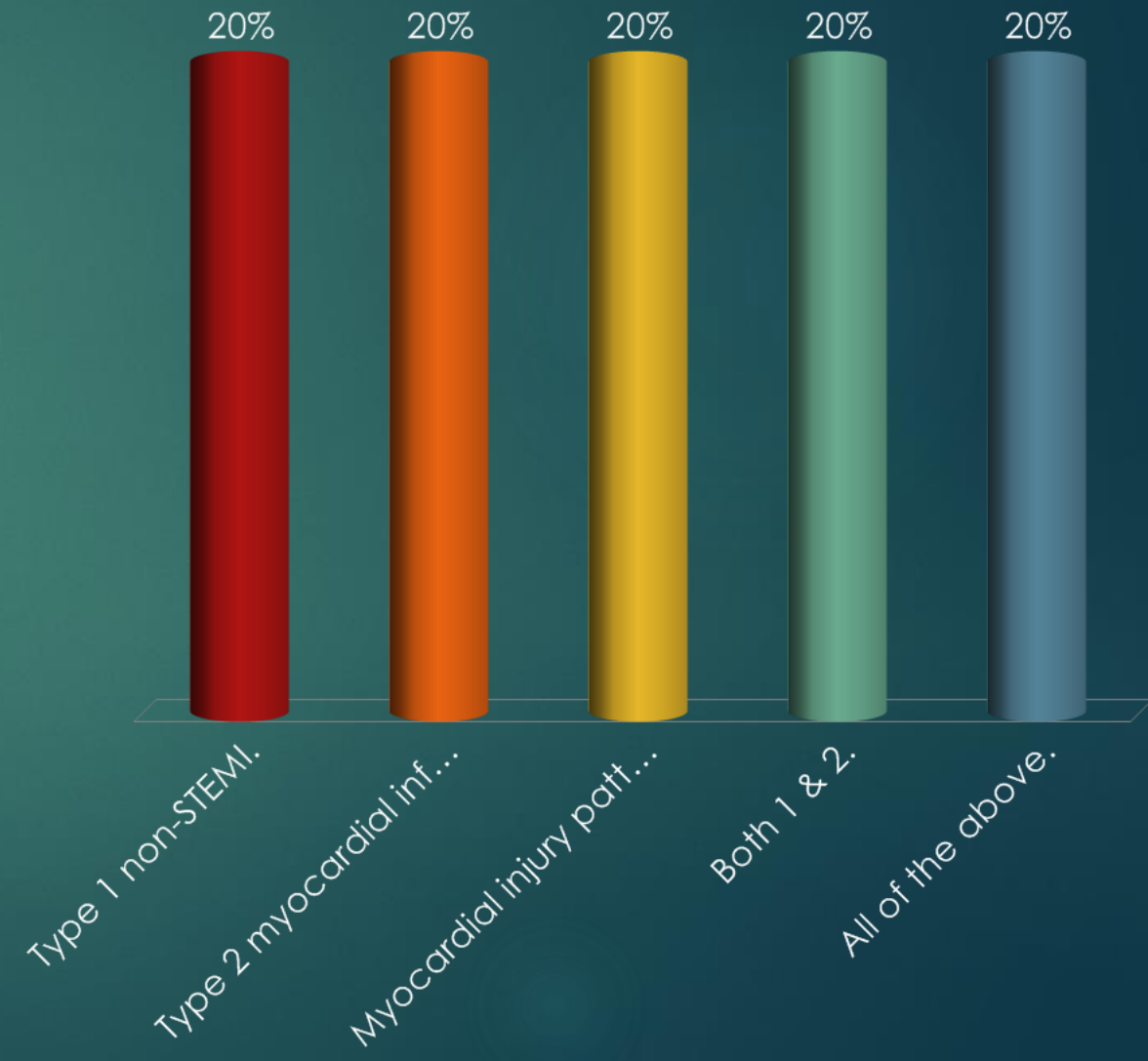
Case #7 continued

- **Final diagnosis: Type 1 non-STEMI**
  - **Placed on aspirin, Plavix, beta blocker, and statins.**
  - **Aggressive risk factor modifications.**

Case #8

▶ 73 year old male has history of hypertension, hyperlipidemia, alcohol abuse and former smoking.

▶ Admitted for acute SOB after episode of severe cough (which is chronic). No fever. Denied chest pain.

▶ O2 sat 86% on room air, 92% on 2L.

▶ EKG showed marked ST abnormality in the inferior leads.

▶ Troponin 64, 184, 239 in ED.

▶ CXR showed cardiomegaly

What is your differential diagnosis?

A. **Type 1 non-STEMI.**

B. **Type 2 myocardial infarction.**

C. **Myocardial injury pattern.**

D. **Both 1 & 2.**

E. **All of the above.**

20%	20%	20%	20%	20%

Type 1 non-STEMI. Type 2 myocardial inf... Myocardial injury patt... Both 1 & 2. All of the above.

Case #8, continued.

▶ EKG 10 hours after 1ˢᵗ EKG shows prolonged QT with resolution of the other ST-T abnormalities.

▶ Troponin 18 hours after third troponin is 88.

▶ Echocardiogram shows normal global systolic LV function with no regional wall abnormality. Ejection fraction 65%.

▶ Cardiac catheterization shows:

   ▶ Right dominant coronary circulation.

   ▶ Left main CA with no angiographically detectable disease.

   ▶ Left anterior descending with minor abnormalities.

Now what is your diagnosis?

A. **Type 1 non-STEMI.**
B. **Type 2 myocardial infarction.**
C. **Myocardial injury pattern.**
D. **I don't know.**