Acute Coronary Syndrome

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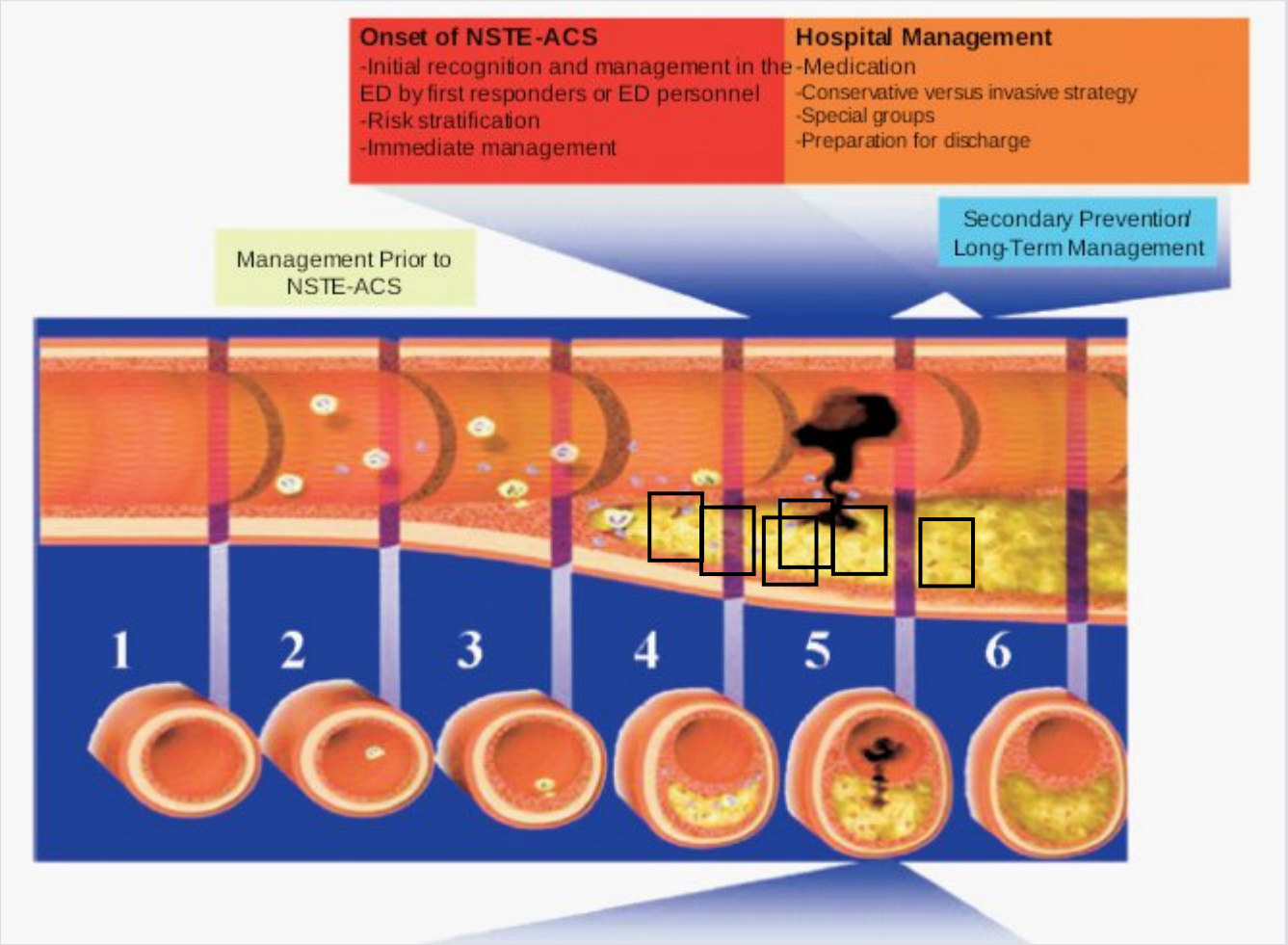
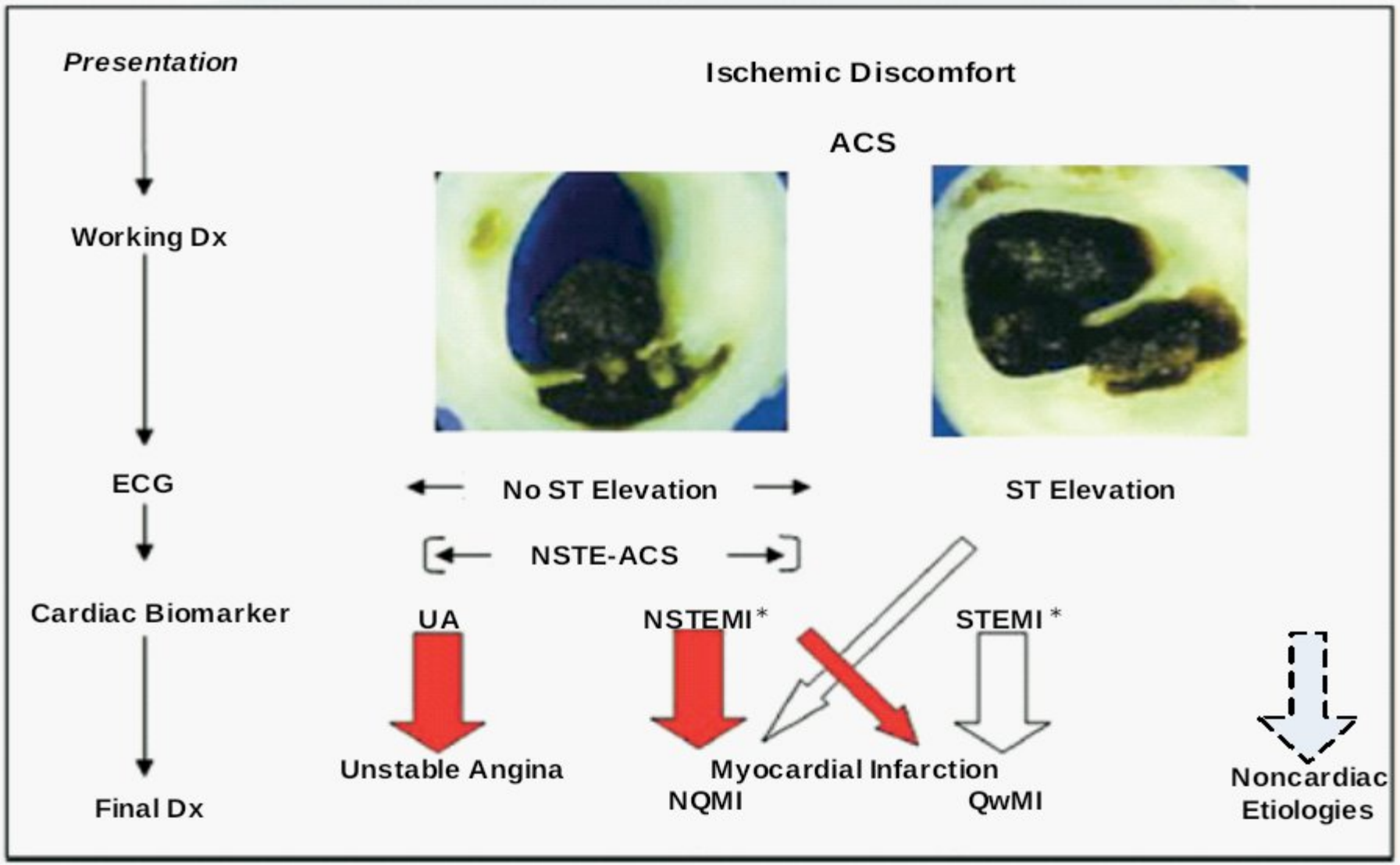
Overview of ACS

- STEMI (Q wave MI)
  - ST-segment elevation or new LBBB
  - Positive cardiac biomarkers of necrosis (Troponin)
- NSTE-ACS
  - NSTEMI
    - Positive cardiac biomarkers
    - ± depression, transient ST elevation, prominent T wave inversions
  - UA
    - Negative cardiac biomarkers
    - ± depression, transient ST elevation, prominent T wave inversions

Pathogenesis of ACS

1. Normal artery
2. Extracellular lipid in subintima
3. Fibrofatty stage
4. Procoagulant expression and weakening of fibrous cap
5. Disruption of fibrous cap, stimulating thrombogenesis
6. Thrombus resorption, may be followed by collagen accumulation and smooth muscle growth



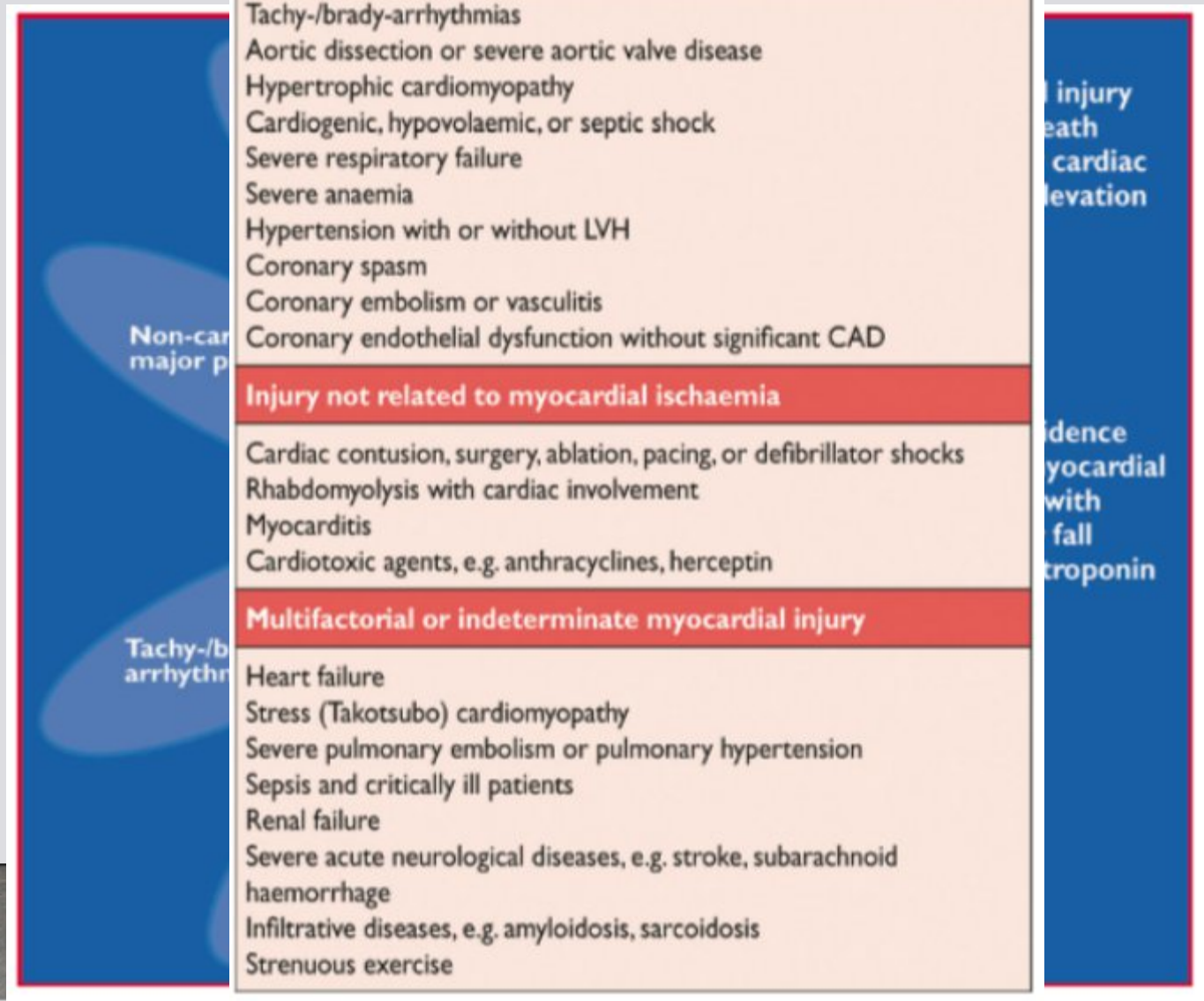

Presentation
Working Dx
ECG
Cardiac Biomarker
Final Dx
Ischemic Discomfort
ACS
No ST Elevation
ST Elevation
NSTE-ACS
UA
NSTEMI*
STEMI*
Unstable Angina
Myocardial Infarction
NQMI
QwMI
Noncardiac Etiologies

Basics of coronary artery perfusion

Supply and Demand

- What can decrease supply?
- What can increase demand?

Third Universal Definition of MI



Injury related to primary myocardial ischaemia

Plaque rupture
Intraluminal coronary artery thrombus formation

Injury related to supply/demand imbalance of myocardial ischaemia

Tachy-/brady-arrhythmias
Aortic dissection or severe aortic valve disease
Hypertrophic cardiomyopathy
Cardiogenic, hypovolaemic, or septic shock
Severe respiratory failure
Severe anaemia
Hypertension with or without LVH
Coronary spasm
Coronary embolism or vasculitis
Coronary endothelial dysfunction without significant CAD

Injury not related to myocardial ischaemia

Cardiac contusion, surgery, ablation, pacing, or defibrillator shocks
Rhabdomyolysis with cardiac involvement
Myocarditis
Cardiotoxic agents, e.g. anthracyclines, herceptin

Multifactorial or indeterminate myocardial injury

Heart failure
Stress (Takotsubo) cardiomyopathy
Severe pulmonary embolism or pulmonary hypertension
Sepsis and critically ill patients
Renal failure
Severe acute neurological diseases, e.g. stroke, subarachnoid haemorrhage
Infiltrative diseases, e.g. amyloidosis, sarcoidosis
Strenuous exercise

Definition of myocardial infarction

Criteria for acute myocardial infarction

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:

Rise and/or fall of cardiac biomarker values with at least one value >99th percentile with at least one of the following:

1. Symptoms of ischemia
2. New or presumed new significant ST segment or T wave changes or new LBBB
3. Development of pathological Q waves
4. Imaging evidence of new loss of viable myocardium or new regional WMA
5. Identification of IC thrombus by angiography or autopsy

- Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (>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.

Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior MI:

- Pathological Q waves with or without symptoms in the absence of non-ischaemic causes.
- 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.
- Pathological findings of a prior MI.

Classification of Acute MI

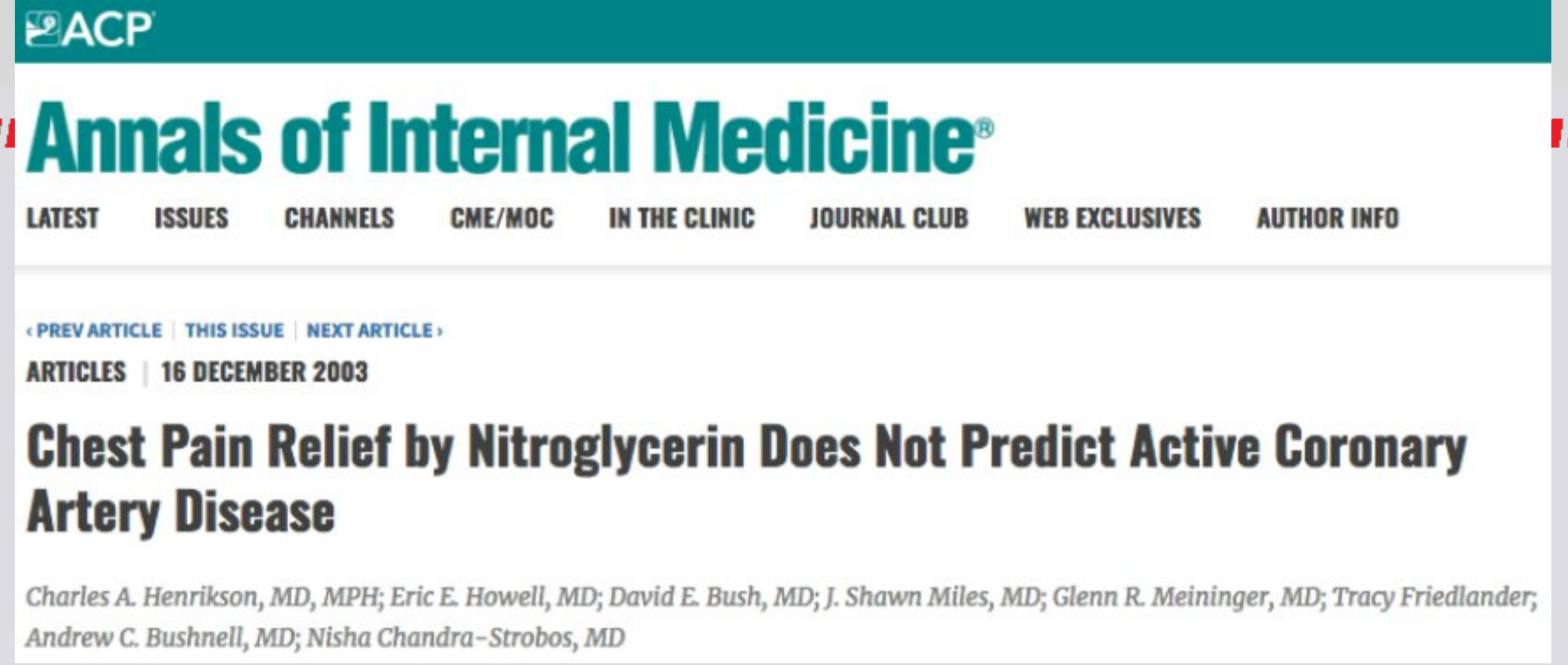
- Type 1:
  - Spontaneous MI related to ischemia due to primary coronary event such as plaque rupture
- Type 2:
  - MI secondary to ischemia due to either increased oxygen demand or decreased supply
- Type 3:
  - Sudden unexpected cardiac death with coronary event prior to troponin evaluation
- Type 4a:
  - MI associated with PCI
- Type 4b:
  - MI associated with stent thrombosis
- Type 5:
  - MI associated with CABG

Diagnosis

- Clinical story
- Physical exam
- Risk factors / Risk scores
- Cardiac biomarkers
- ECG
- Imaging (Echo)

Diagnosis – Clinical Story

- Anginal chest pain
  1. Substernal
  2. Brought on by exertion or emotional stress
  3. Relieved by rest or nitroglycerin*



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ARTICLES | 16 DECEMBER 2003

Chest Pain Relief by Nitroglycerin Does Not Predict Active Coronary Artery Disease

Charles A. Henrikson, MD, MPH; Eric E. Howell, MD; David E. Bush, MD; J. Shawn Miles, MD; Glenn R. Meininger, MD; Tracy Friedlander; Andrew C. Bushnell, MD; Nisha Chandra-Strobos, MD

Results:

- Nitroglycerin relieved chest pain in 39% of patients (181/459) admitted through the ED who received nitro from EMS or ER staff
- 35% had chest pain relief with nitro in patients with active coronary artery disease as cause of chest pain
- 41% had chest pain relief with nitro in patients without active coronary artery disease as cause of chest pain

Conclusion: In a general population admitted for chest pain, relief of pain after nitro treatment does not predict active coronary artery disease and should not be used to guide diagnosis.

Diagnosis – Clinical Story

- Anginal chest pain
  1. Substernal
  2. Brought on by exertion or emotional stress
  3. Relieved by rest or nitroglycerin*
- Typical Anginal – meets all 3 criteria
- Atypical Angina – meets 2 of 3 criteria
- Non-anginal CP – meets 0-1 of 3 criteria

Comparing pretest likelihood of CAD in low-risk symptomatic patients with high-risk symptomatic patients (Duke Database)

Age (year)	Nonanginal chest pain		Atypical angina		Typical angina	
	Men	Women	Men	Women	Men	Women
35	3-35	1-19	8-59	2-39	30-88	10-78
45	9-47	2-22	21-70	5-43	51-92	20-79
55	23-59	4-21	45-79	10-47	80-95	38-82
65	49-69	9-29	71-86	20-51	93-97	56-84

Each value represents the percentage with significant CAD. The lowest (first) value of each range is the likelihood of CAD for a low-risk patient without diabetes mellitus, smoking, or hyperlipidemia. The highest (second) value of each range is the likelihood of CAD for a high-risk patient of the same age with diabetes mellitus, smoking, and hyperlipidemia. Both high- and low-risk patients have normal resting ECGs. If ST-T-wave changes or Q waves had been present, the likelihood of CAD would be higher in each entry of the table. This information was included in the 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease.[1]

Physical Exam

- CAN BE NORMAL
- VS: BP in both arms (dissection, tamponade)
- Signs of LV dysfunction: Rales, S3 gallop
- S4, Murmur, Rub
- Chest wall tenderness

Risk Factors

- Hypertension
- Diabetes Mellitus
- Hyperlipidemia
- Tobacco abuse
- Obesity
- Family Hx premature CAD
- Personal Hx CAD
- Age

Risk Scores

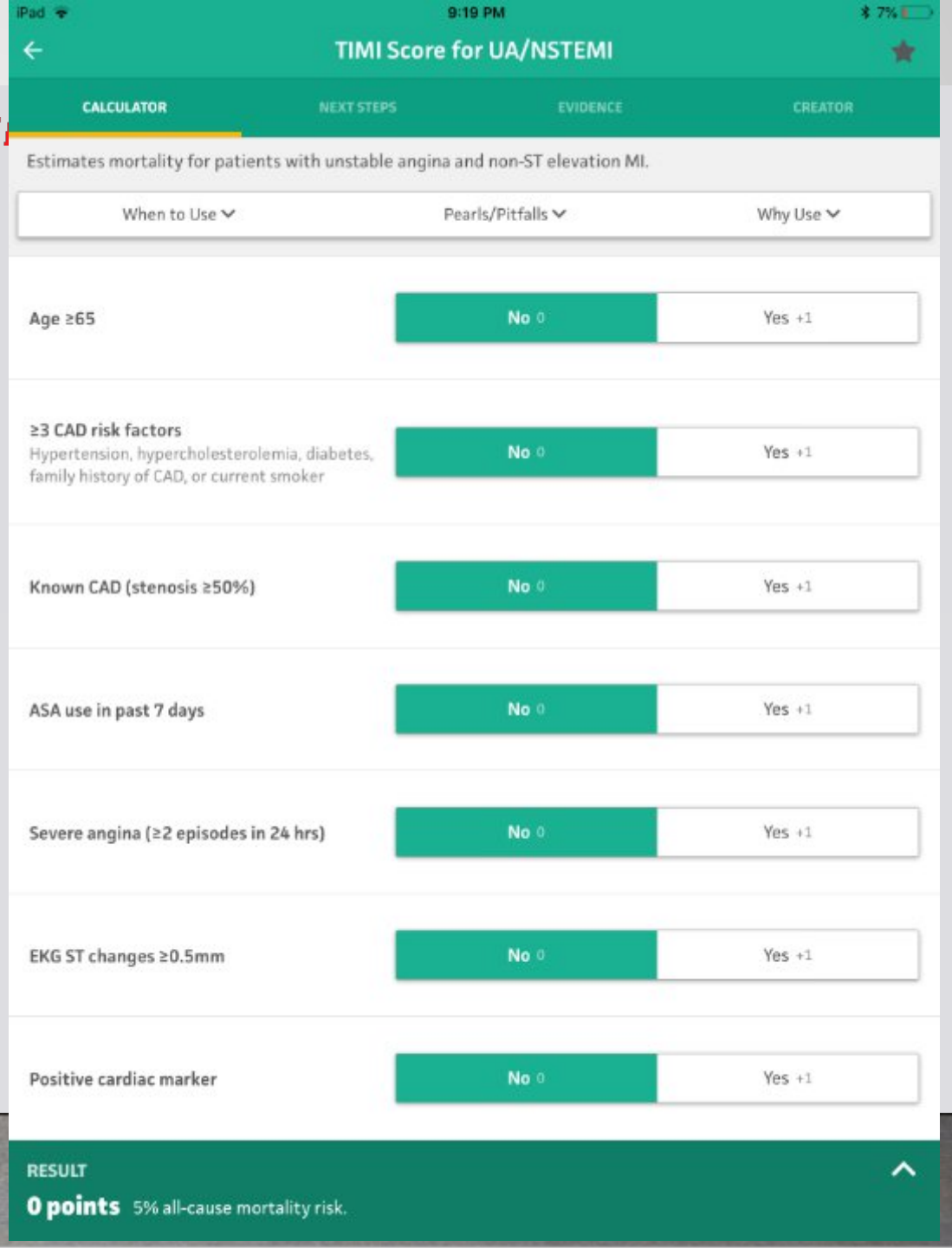
Must be applied to correct patient – Do not use on patient without ACS

Used to predict adverse events based on observational data

- TIMI
- GRACE
- HEART

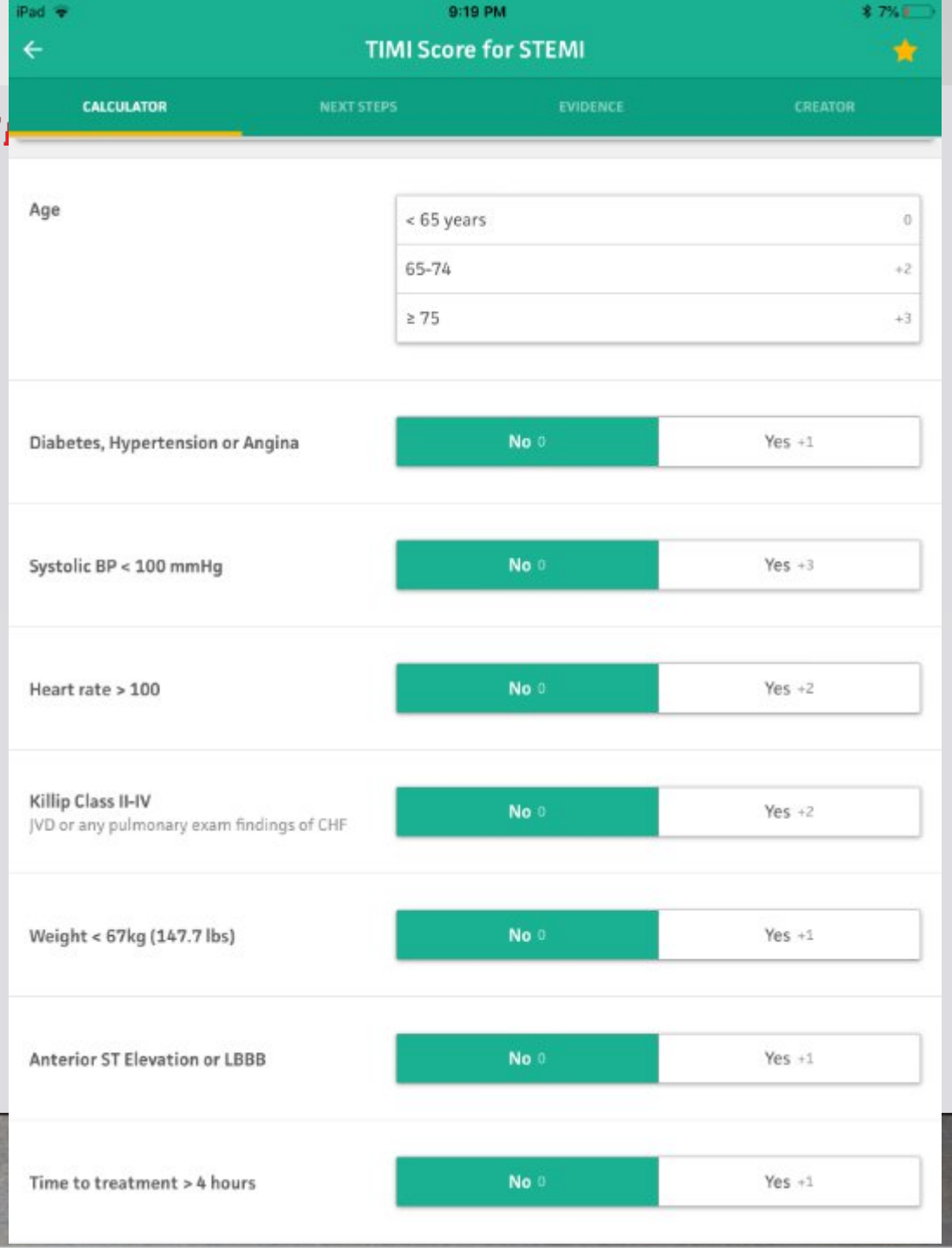
Risk Score – NSTEMI/UA TIMI

TIMI Risk Score	All-Cause Mortality, New or Recurrent MI, or Severe Recurrent Ischemia Requiring Urgent Revascularization Through 14 d After Randomization, %
0–1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6–7	40.9



Risk Score – STEMI TIMI

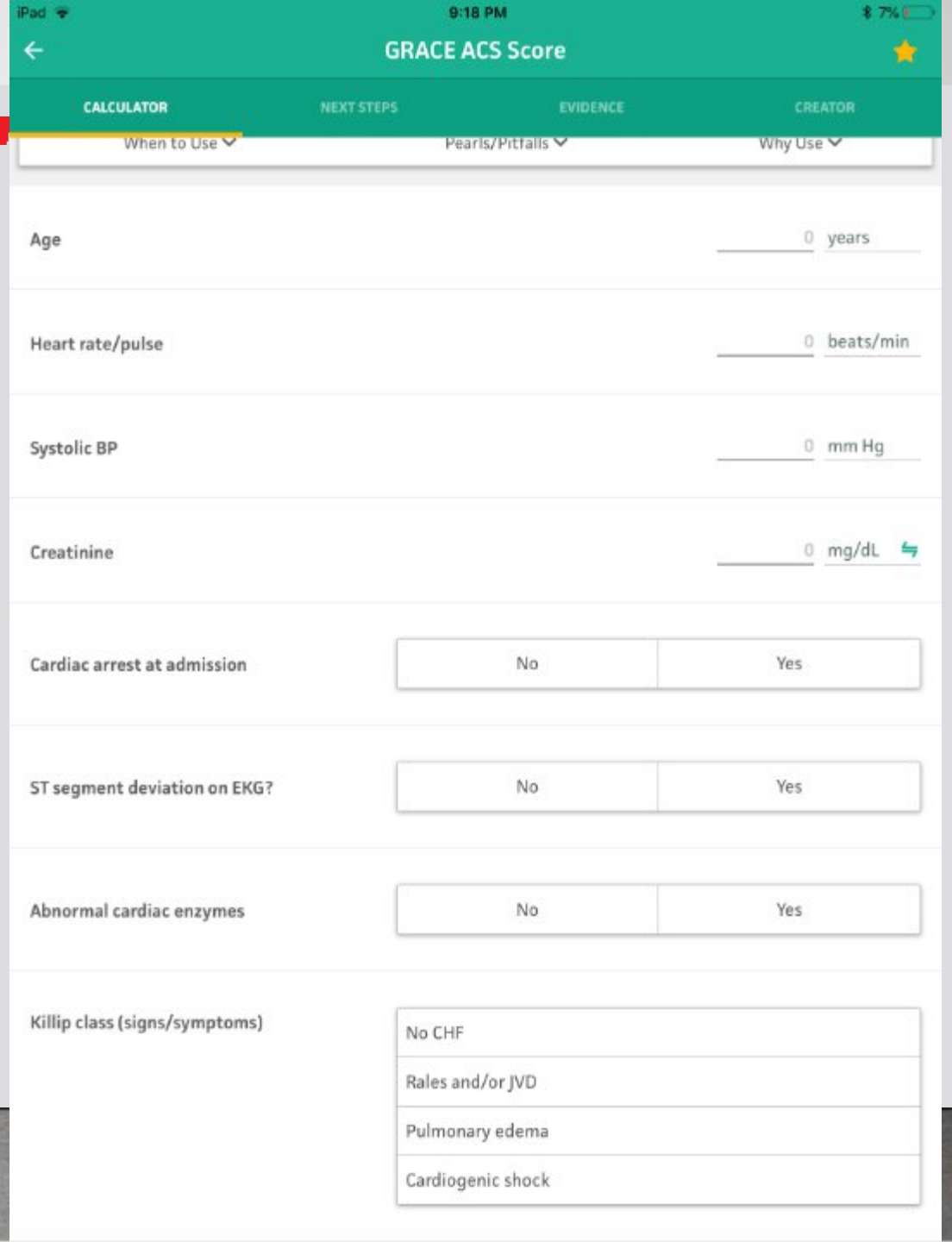
TIMI Risk Score	30 Day Mortality After MI, %
0	0.8
1	1.6
2	2.2
3	4.4
4	7.3
5	12
6	16
7	23
8	27
9-14	36



Risk Score - GRACE

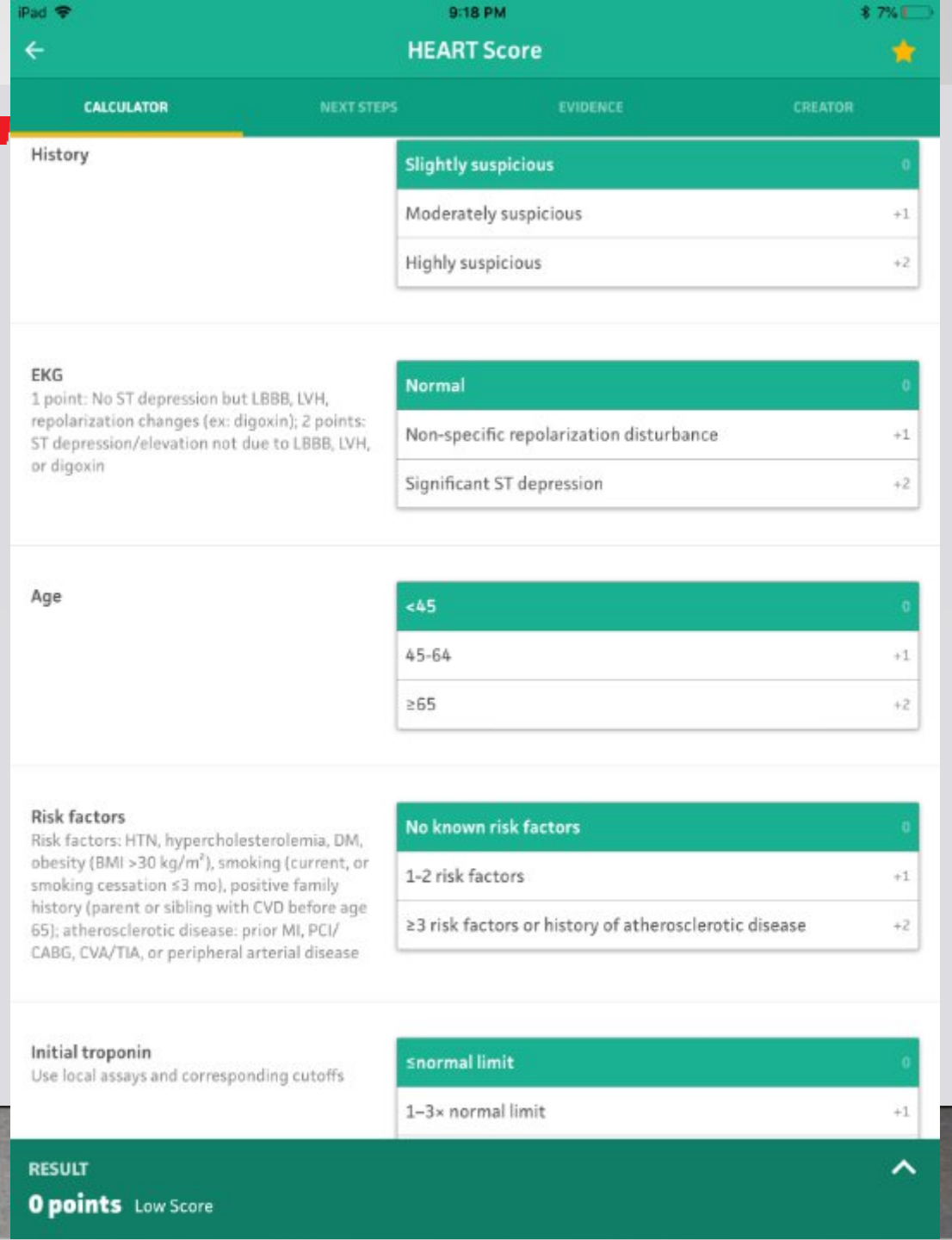
In-hospital, 6 month, 1 year and 3 year risk of death/MI

Risk Category	GRACE risk score	In-hospital death %
Low	<108	<1
Intermediate	109-140	1-3
High	>140	>3
Risk Category	**GRACE risk score**	**Post DC to 6 month death %**
Low	<88	<3
Intermediate	89-118	3-8
High	>118	>8



Risk Score - HEART

HEART Risk Score	Risk of adverse cardiac event defined as all-cause mortality, MI or coronary revascularization in 6 weeks %
0–3	0.9 – 1.7
4-6	12 – 16.6
□7	50-65



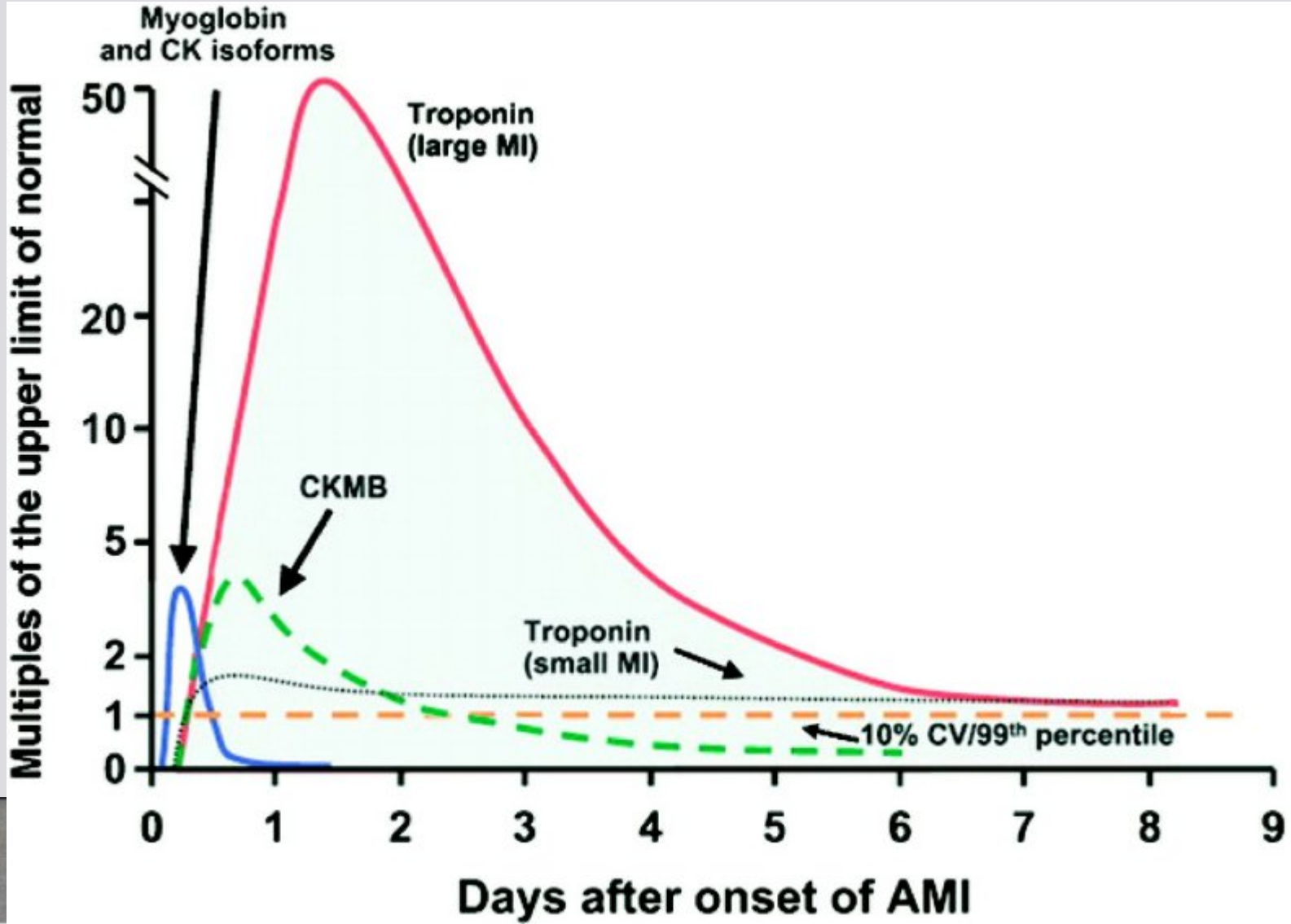
Killip Class

Classification that categorizes patients with an acute MI based upon presence of absence of physical exam findings that suggest LV dysfunction and heart failure.

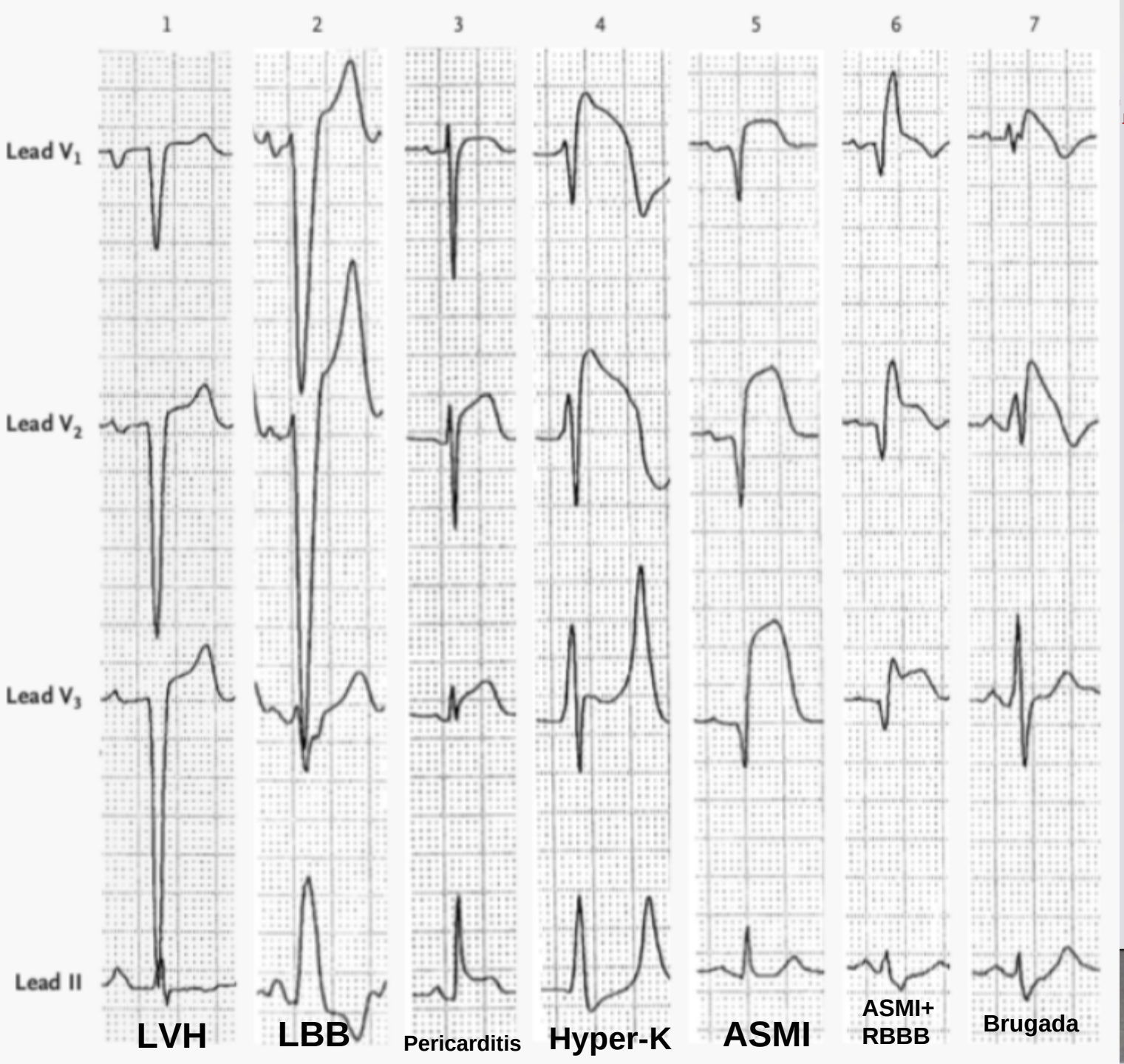
Class I	No evidence of heart failure
Class II	Findings consistent with mild to moderate HF
Class III	Overt pulmonary edema
Class IV	Cardiogenic shock

Cardiac Biomarkers

- Troponin
- CK-MB
- Myoglobin
- High Sensitivity Troponin*



ECG


1
2
3
4
5
6
7
Lead V1
Lead V2
Lead V3
Lead II
LVH
LBB
Pericarditis
Hyper-K
ASMI
ASMI+
RBBB
Brugada

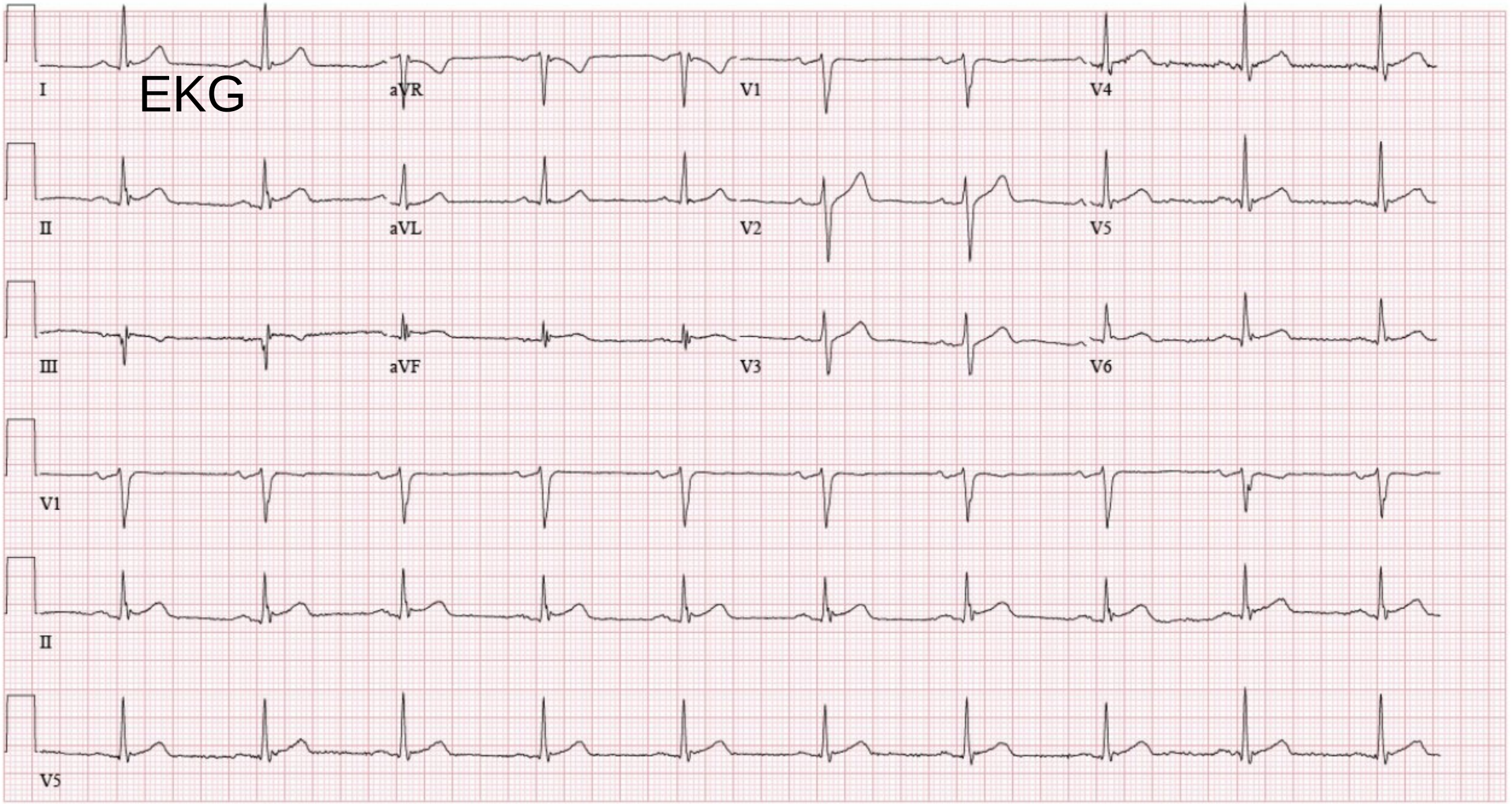
Case #1

55 yo male veteran with PMHx HTN, HLP and hx Tobacco abuse who presented 90 minutes after onset of chest pain. 8/10 substernal chest heaviness with radiation to neck during intercourse with his wife. Symptoms spontaneously resolved with rest. Associated dizziness, nausea and diaphoresis. Chest pain free in ER.

VS: BP 144/88, HR 57, 97% RA

EKG: to follow

Labs: Troponin < 0.10, BNP <10, Cr 1.12, Hb15.3, Plts 209, INR 1.0


EKG
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5

What now?

1. ACS protocol – This represents NSTEMI
2. ACS protocol – This represents UA
3. STEMI – Initiate cath lab
4. No ACS protocol – Chest pain free, troponin negative, EKG nonspecific
5. Turn pager off and hide

TIMI: 2 | GRACE : 64 points

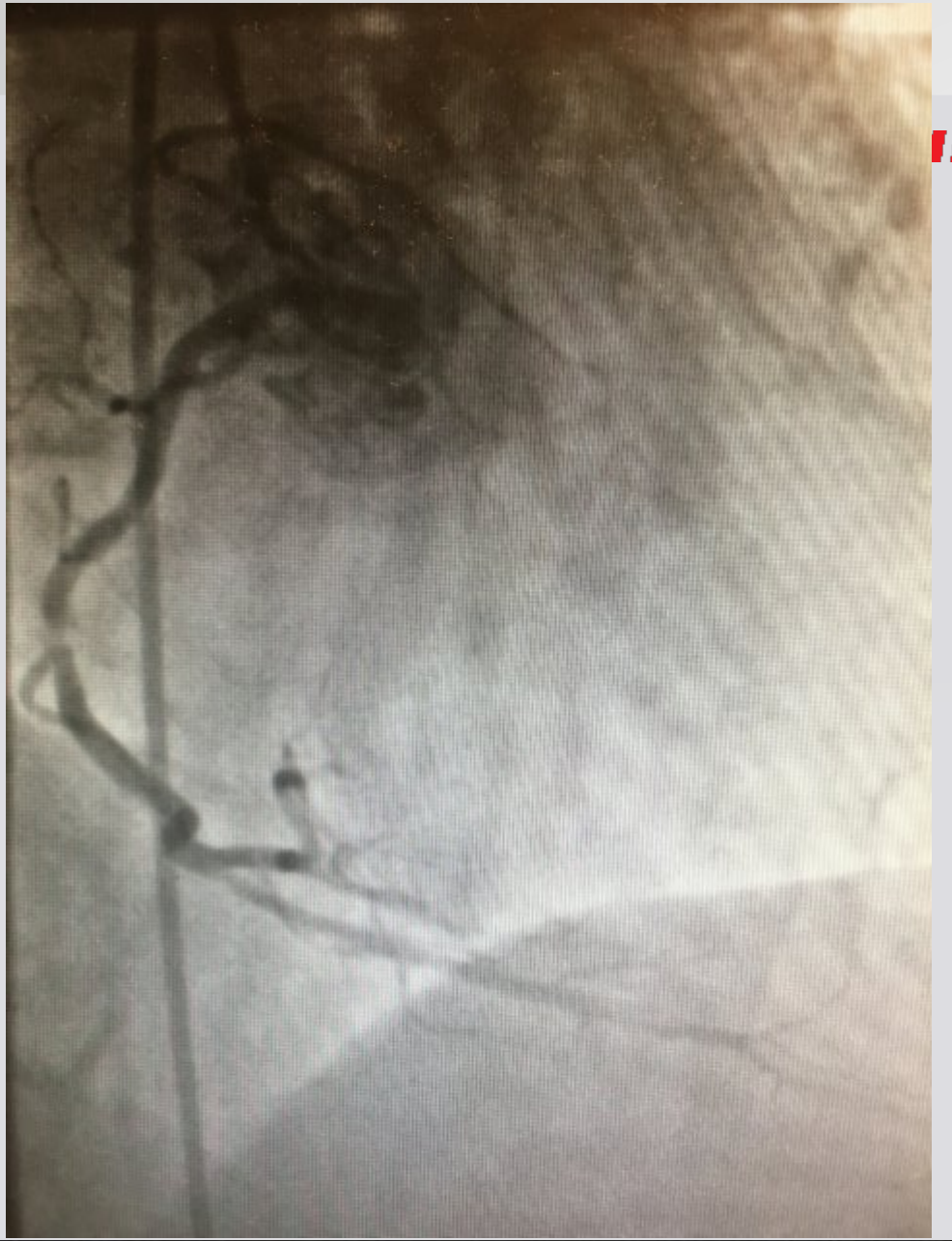
What now?

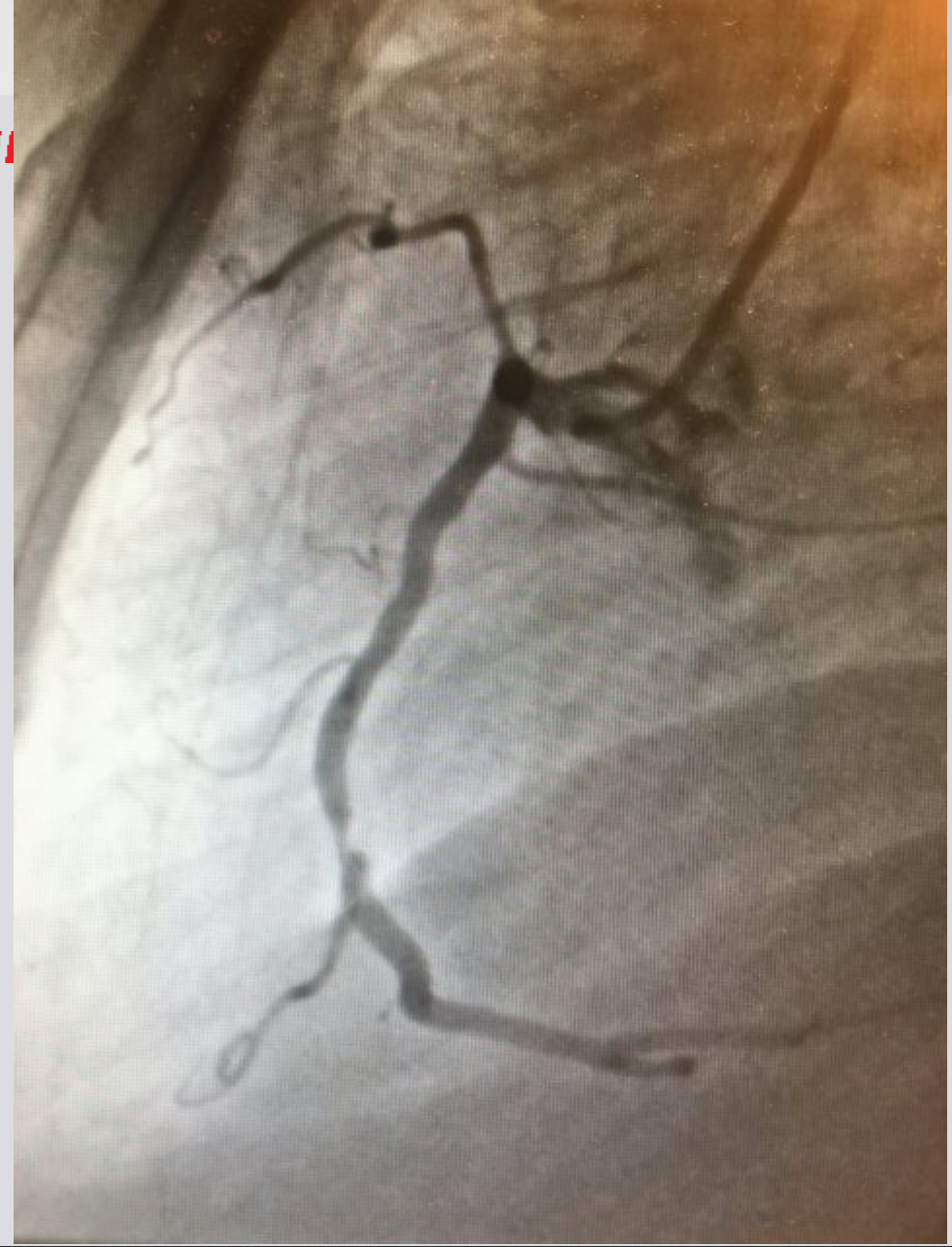
1. ACS protocol – This represents NSTEMI
2. **ACS protocol – This represents UA**
3. STEMI – Initiate cath lab
4. No ACS protocol – Chest pain free, troponin negative, EKG nonspecific
5. Turn pager off and hide

TIMI: 1 | GRACE : 64 points

Next day: Troponin 0.79 (02:00) -> 4.27 (06:00)

TIMI: 3 | GRACE: 77 points





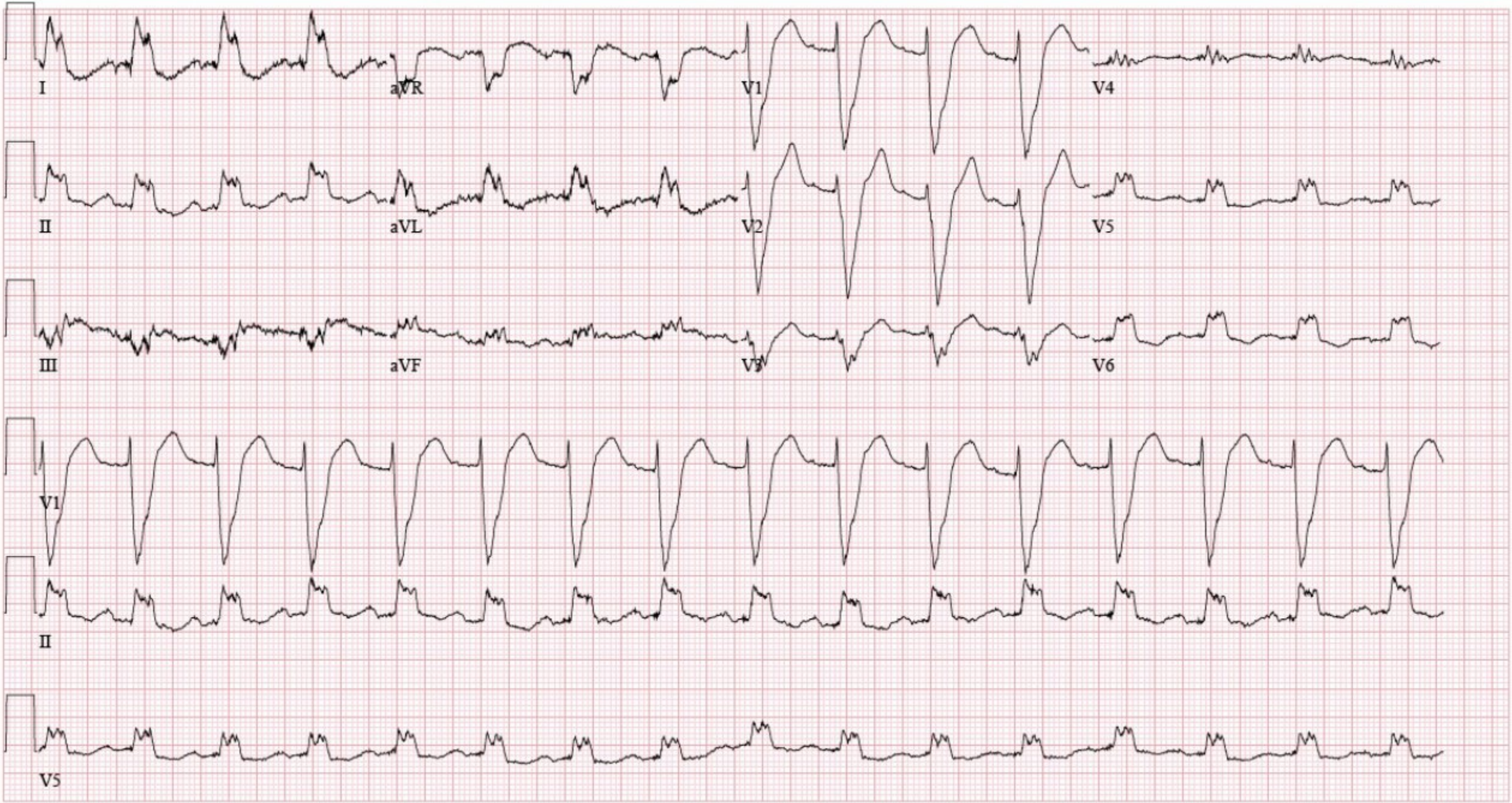
Case #2

77 yo female with PMHx DM2, HTN and previous tobacco abuse presents with 2-3 day history of hot flashes, malaise with increasing exertional dyspnea. Admits to substernal chest pressure associated with dyspnea. No history of CAD.

VS: BP 108/88, HR 85, 94% RA

EKG: to follow

Labs: Troponin 5.2, BNP 340, Cr 1.12, Hb 14.8, Plts 300, INR 1.1

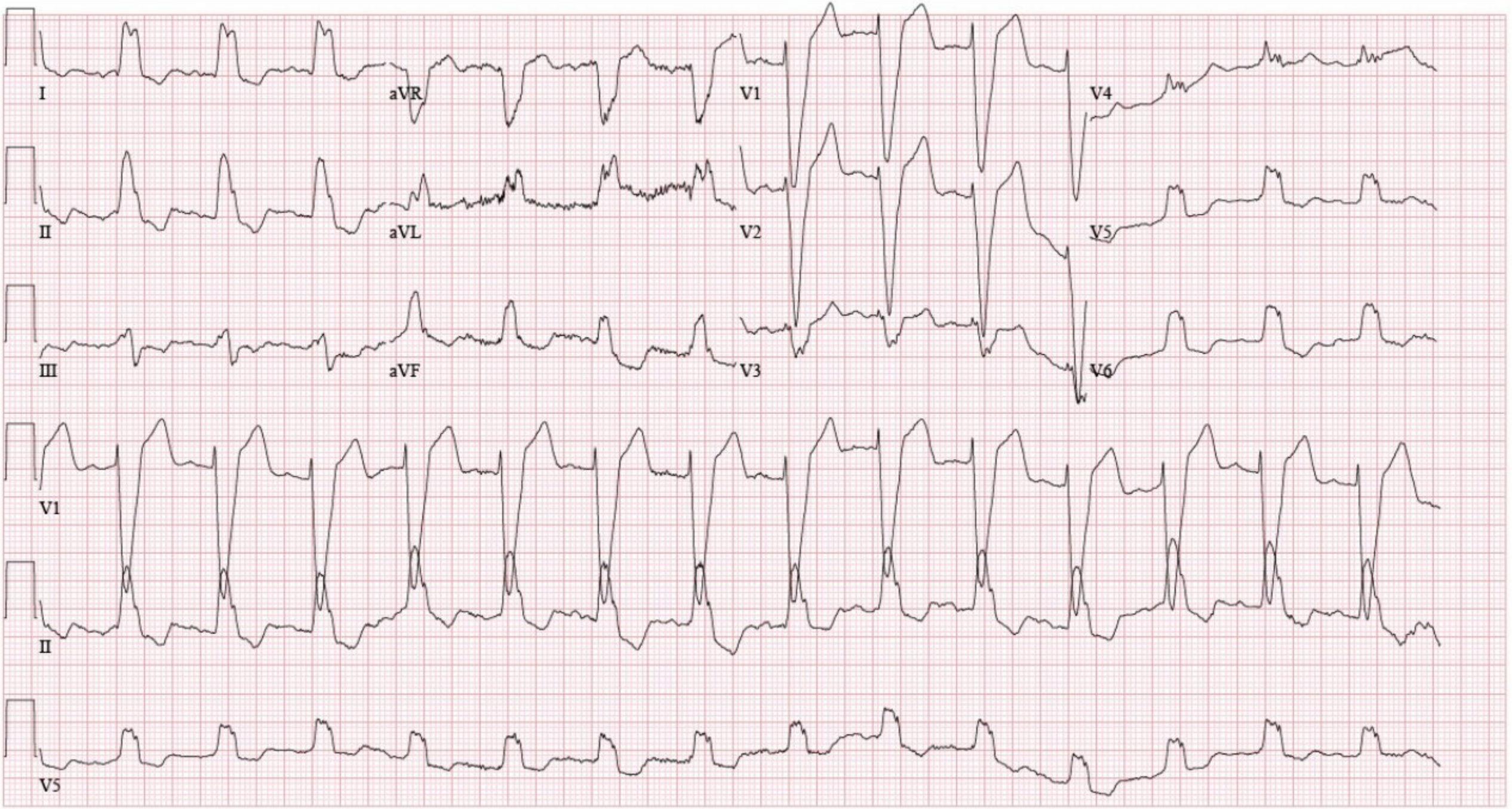

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5

What now?

1. ACS protocol – This represents NSTEMI
2. ACS protocol – This represents UA
3. New LBBB (STEMI)– Initiate cath lab
4. Find an old EKG
5. Turn pager off and hide

What now?

1. ACS protocol – This represents NSTEMI
2. ACS protocol – This represents UA
3. New LBBB (STEMI)– Initiate cath lab
4. **Find an old EKG**
5. Turn pager off and hide


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5

What now?

1. ACS protocol – This represents NSTEMI
2. ACS protocol – This represents UA
3. New LBBB (STEMI) – Initiate cath lab
4. Turn pager off and hide

TIMI: 4 | GRACE: 148

What now?

1. **ACS protocol – This represents NSTEMI**
2. ACS protocol – This represents UA
3. New LBBB (STEMI) – Initiate cath lab
4. Turn pager off and hide

TIMI: 4 | GRACE: 148

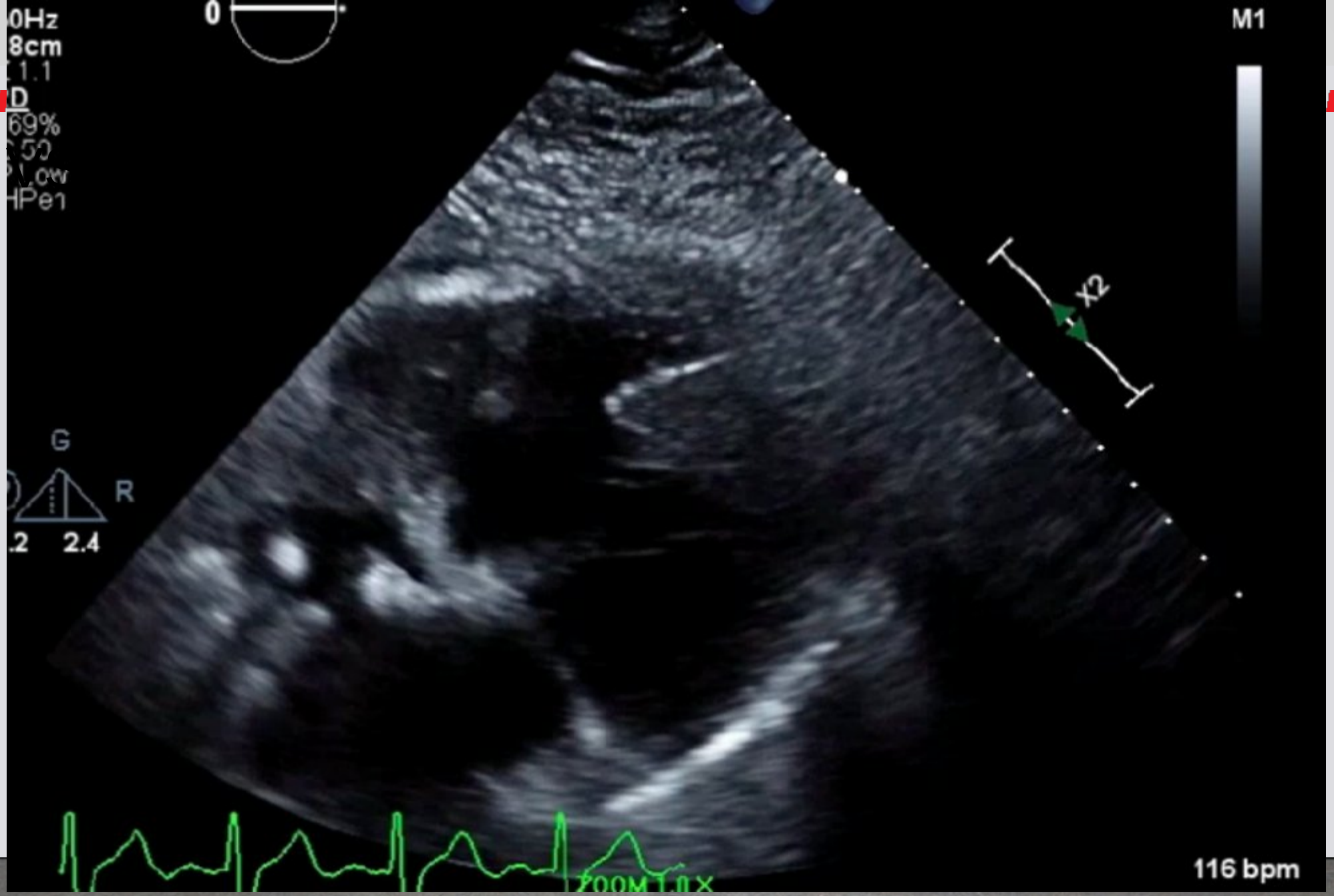
Case #3

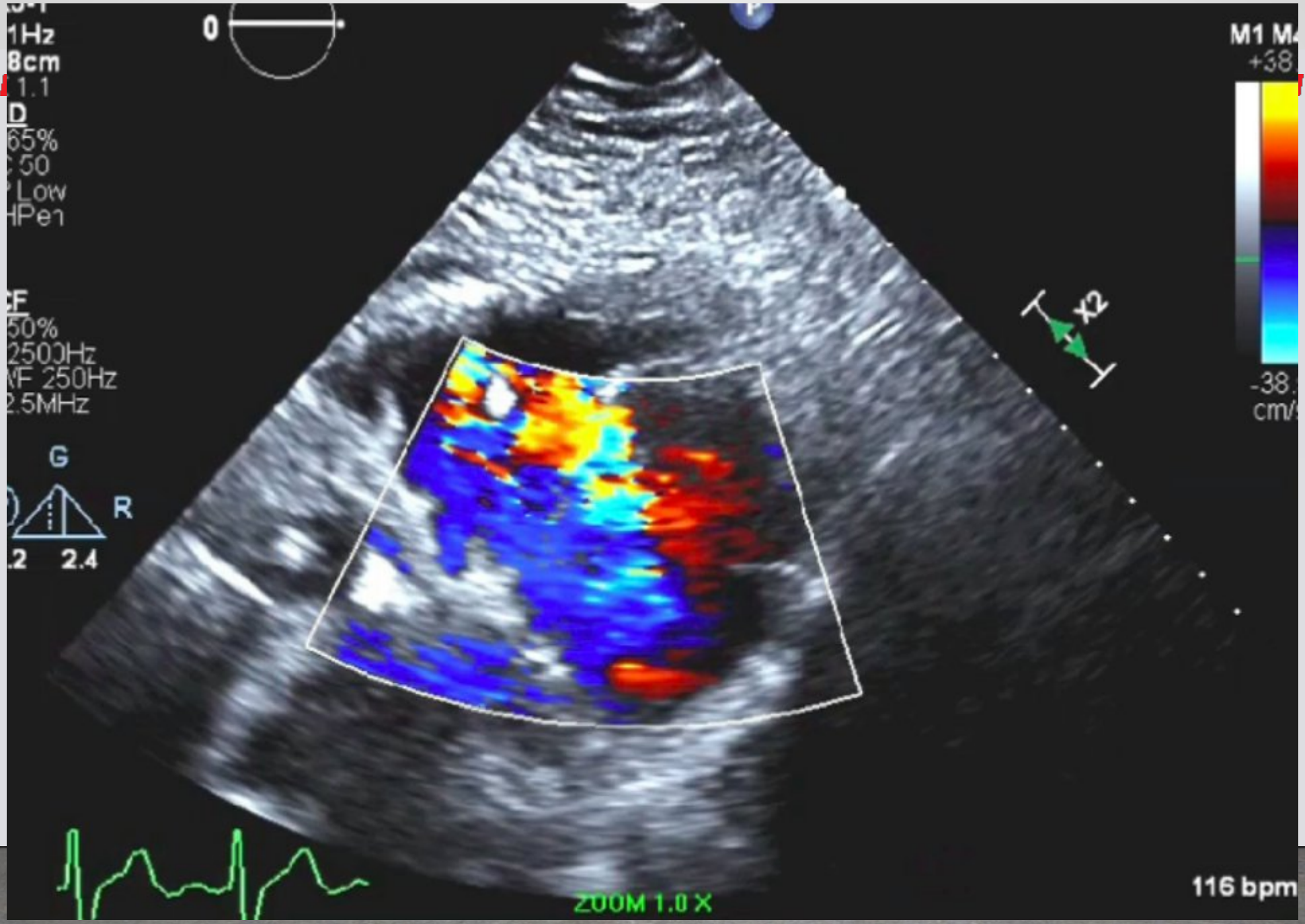
59 yo male with PMHx DM2 and HTN presented to OSH with 2 day history of fatigue and jaw pain. Found to have NSTEMI with multivessel CAD including severe LAD disease, mild LCx disease with proximal CTO of nondominant RCA. Several hours post angiogram, patient developed respiratory failure and cardiogenic shock. Emergently transferred to BUMC-P for higher level of care and ECMO.

PE: Left lower sternal border holosystolic murmur

Differential diagnosis for mechanical complications post MI with cardiogenic shock?

- LV free wall rupture: 5 -14 days
  - Incidence 3-6% post-MI patients with 10% mortality after AMI
  - DOA or Any effusion on post MI patient with hemodynamic collapse
- Interventricular septum rupture (apical vs basal): 2-5 days (early as 16hrs)
  - Incidence 4% in SHOCK registry (lytics), 0.2% GUSTO I trial (PCI)
  - Mortality: 100% without surgery, 87% with surgery
  - Tx: Supportive care (vasodilators, inotropes, mechanical support) until surgery
- Acute mitral regurgitation: 2-5 days
  - Pap muscle rupture or pap muscle tethering due to hypokinesis
  - Incidence 7% in SHOCK registry
  - No murmur/gradient, no left atrial enlargement
  - Tx: Same as VSD


M1
X2
G
R
2.4
116 bpm


1Hz
8cm
1.1
D
65%
50
Low
HPe1
CF
50%
2500Hz
F 250Hz
2.5MHz
G
R
2.2
2.4
0
M1 M4
+38
-38.
cm/s
X2
116 bpm
200M 1.0 X

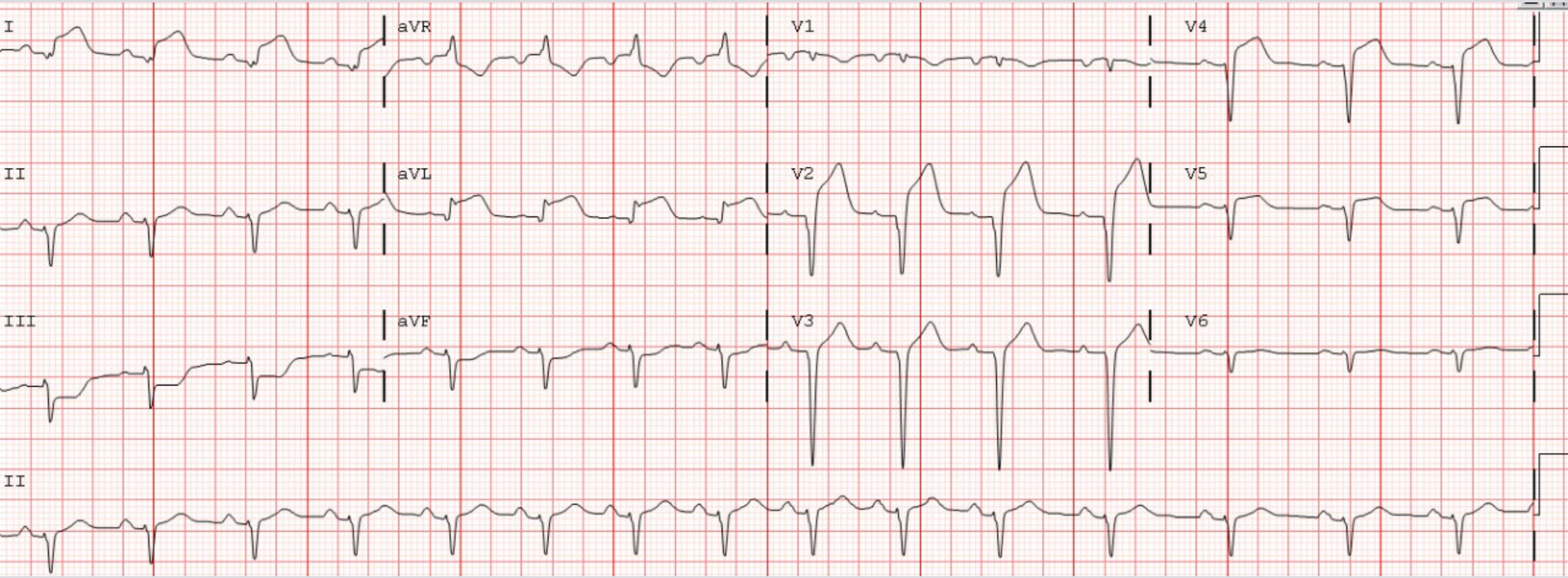
Case #4

19 yo male with PMHx tobacco abuse and IDDM with multiple admissions for DKA presents to ER after waking up with stuttering, nonspecific, substernal chest pain. Denies radiation of pain or associated dyspnea, palpitations, nausea or diaphoresis. Waited in triage before EKG.

VS: BP133/83, HR 74, 98% RA

EKG to follow

Troponin pending


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

What now?

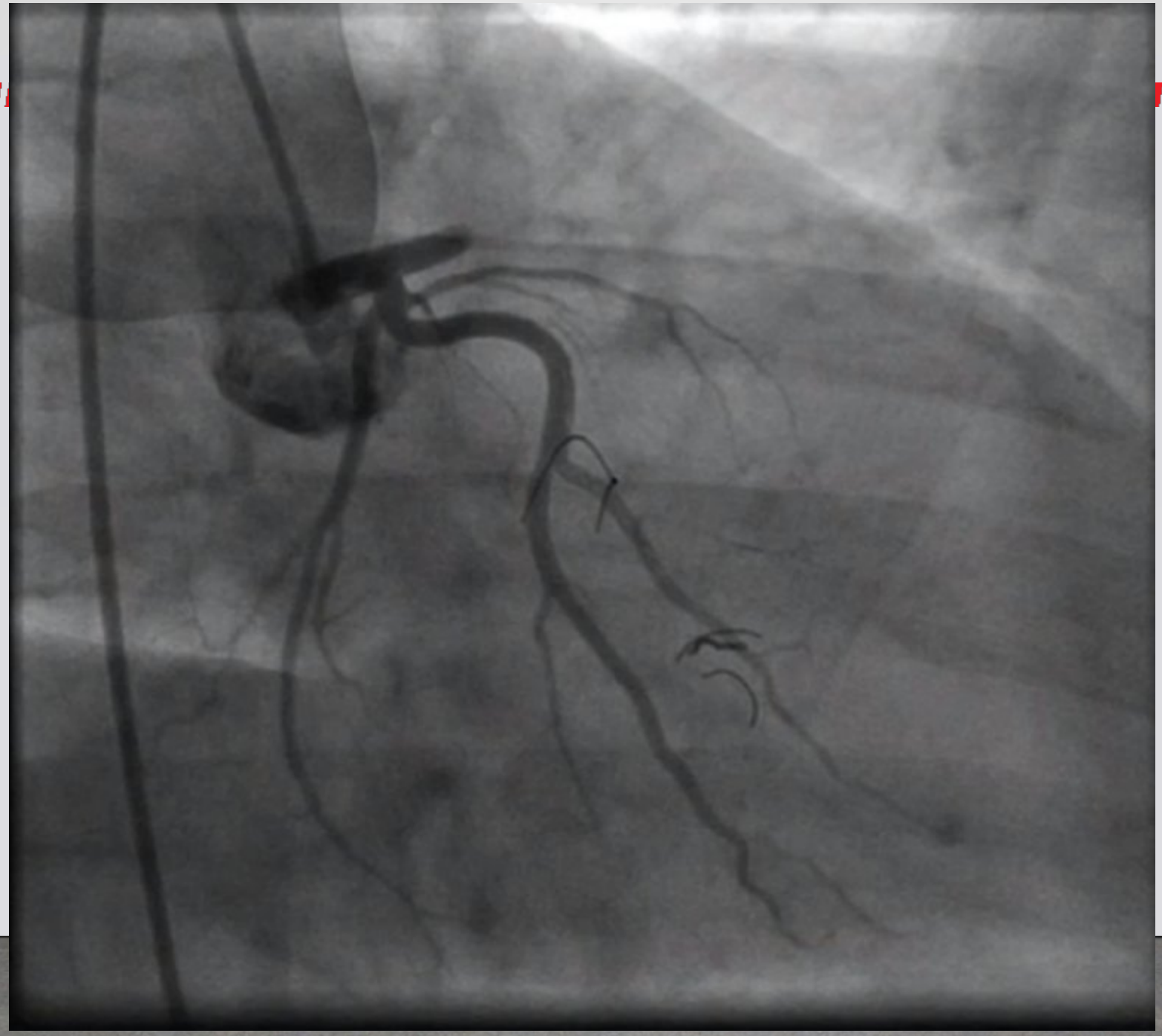
1. ACS protocol – This represents NSTEMI
2. ACS protocol – This represents UA
3. STEMI – Initiate cath lab
4. No ACS protocol
5. Turn pager off and hide

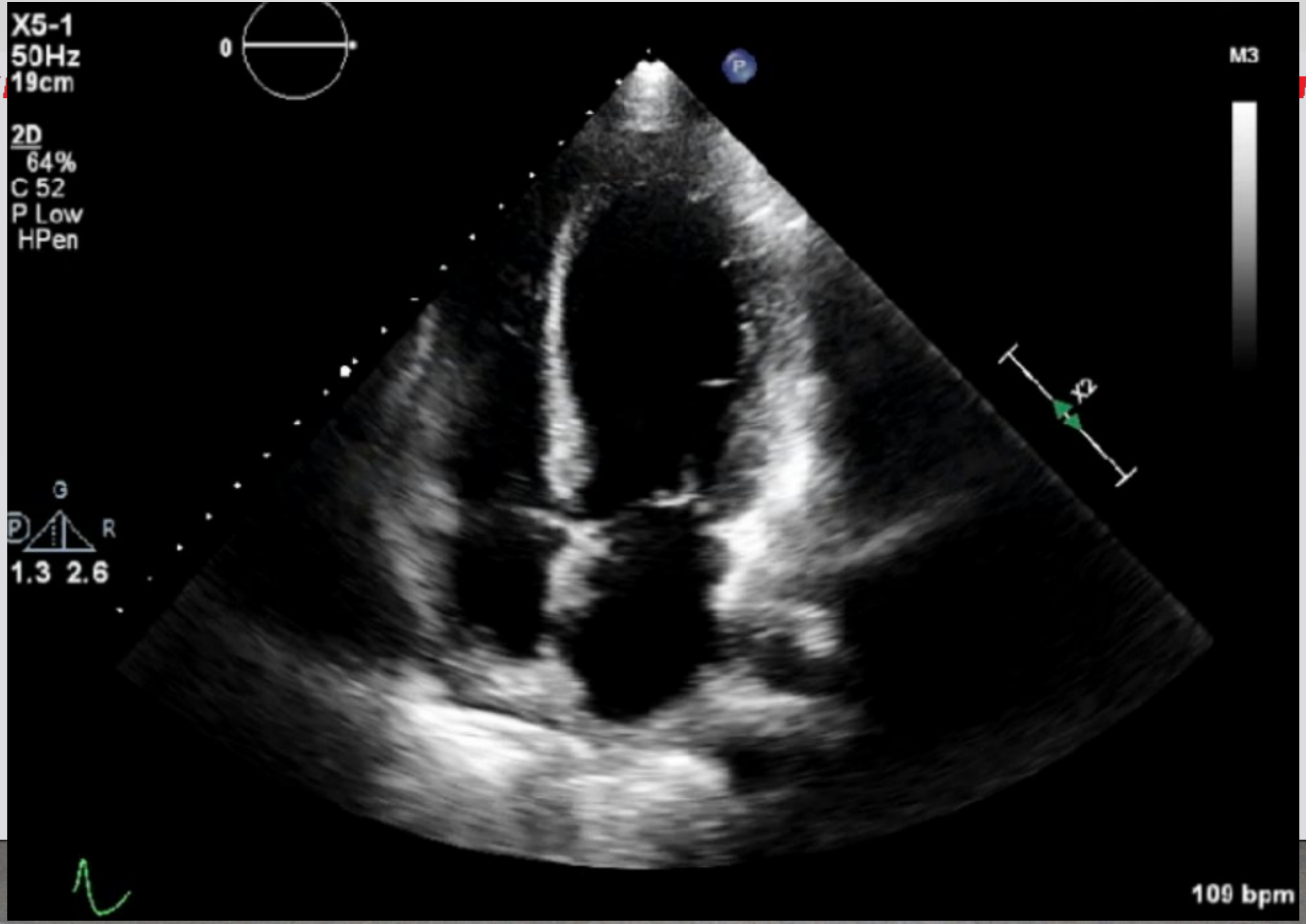
Troponin: 161 ng/ml

What now?

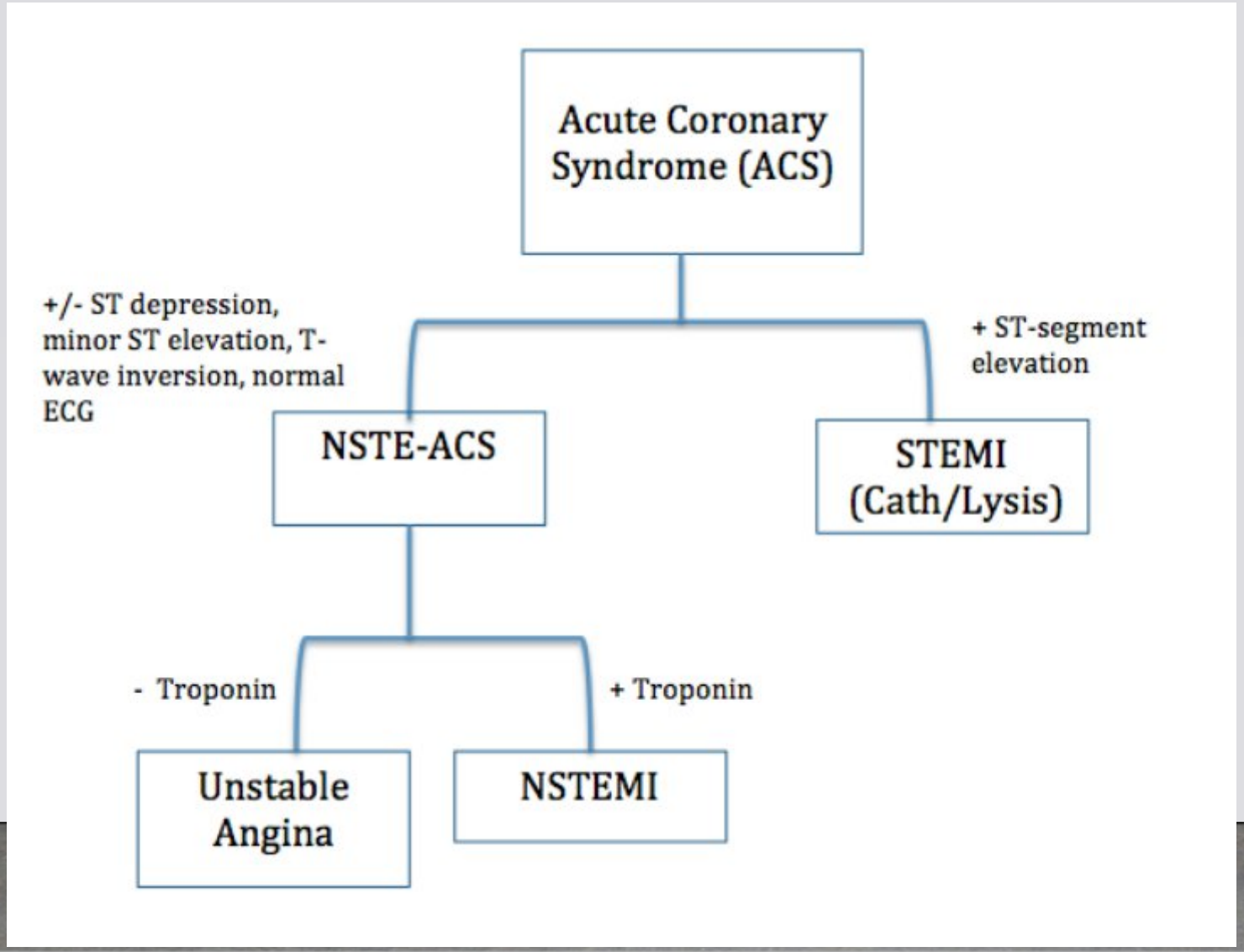
1. ACS protocol – This represents NSTEMI
2. ACS protocol – This represents UA
3. **STEMI – Initiate cath lab**
4. No ACS protocol
5. Turn pager off and hide

Troponin: 161 ng/ml




X5-1
50Hz
19cm
2D
64%
C 52
P Low
HPen
M3
109 bpm

ACS Management



ACS Guidelines

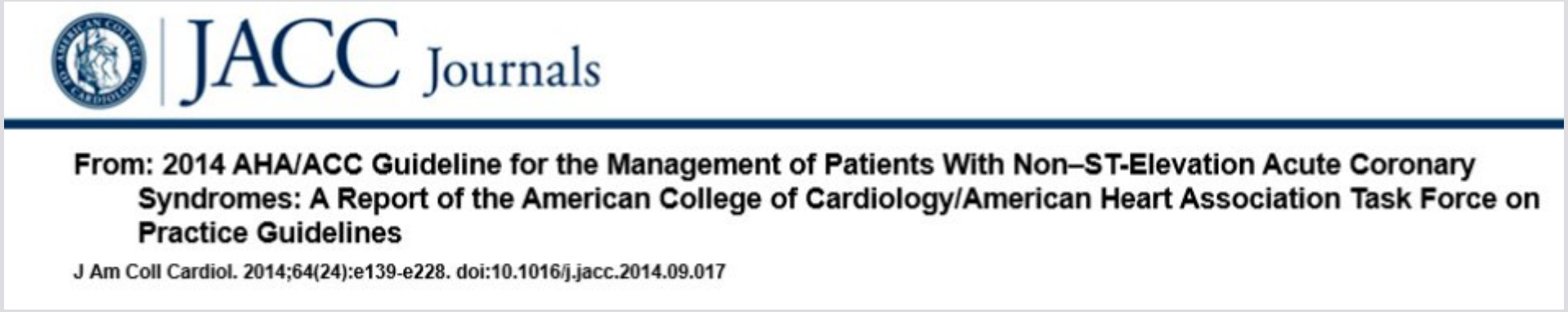


TABLE 1 Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — Benefit ≥ Risk

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — Benefit = Risk

(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

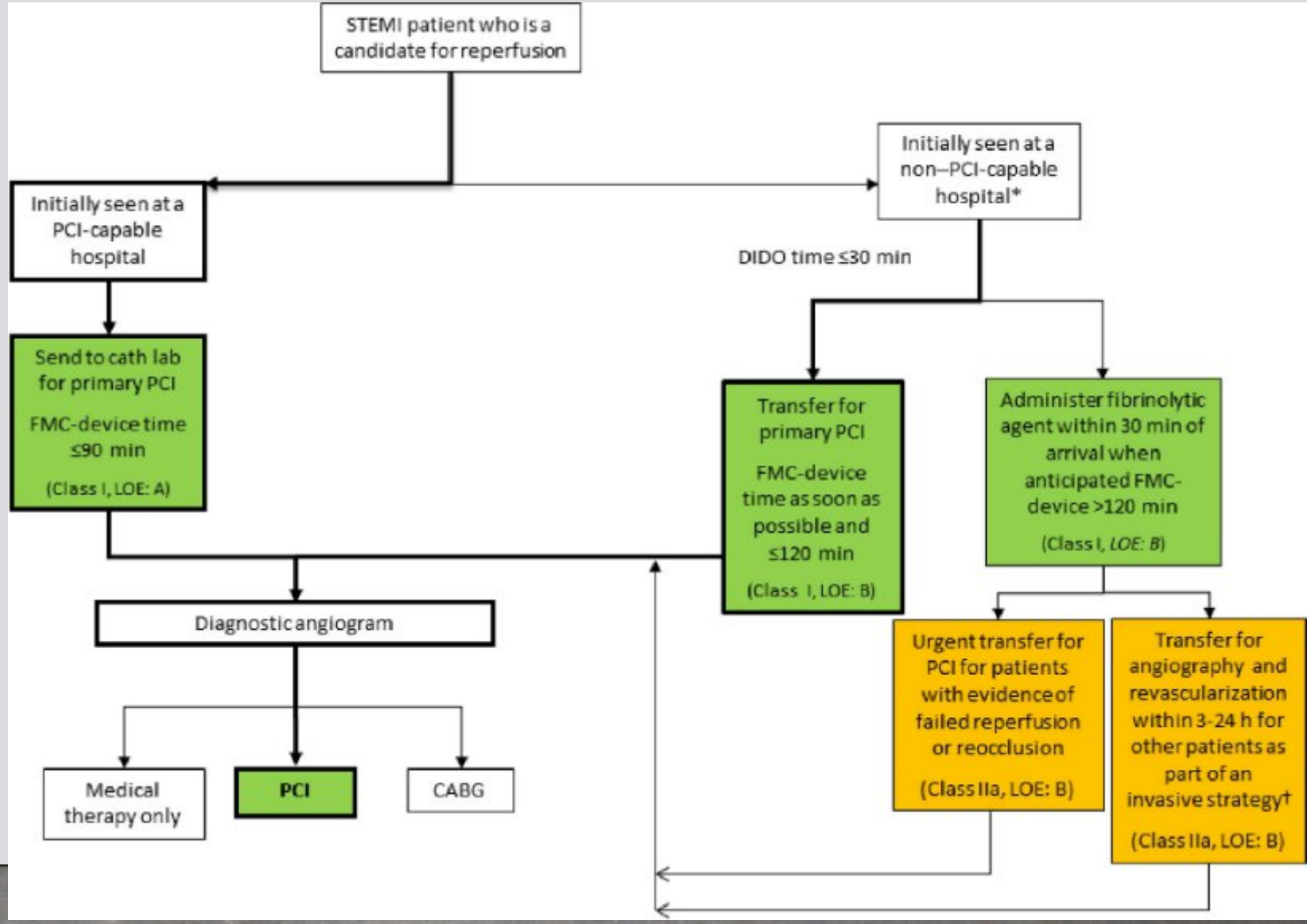
† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

STEMI Therapy

TO THE CATH LAB!



Primary PCI in STEMI

Table 2. Primary PCI in STEMI

	COR	LOE	References
Ischemic symptoms <12 h	I	A	(82,208,209)
Ischemic symptoms <12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC	I	B	(210,211)
Cardiogenic shock or acute severe HF irrespective of time delay from MI onset	I	B	(212–215)
Evidence of ongoing ischemia 12 to 24 h after symptom onset	IIa	B	(94,95)
PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise	III: Harm	B	(216–218)

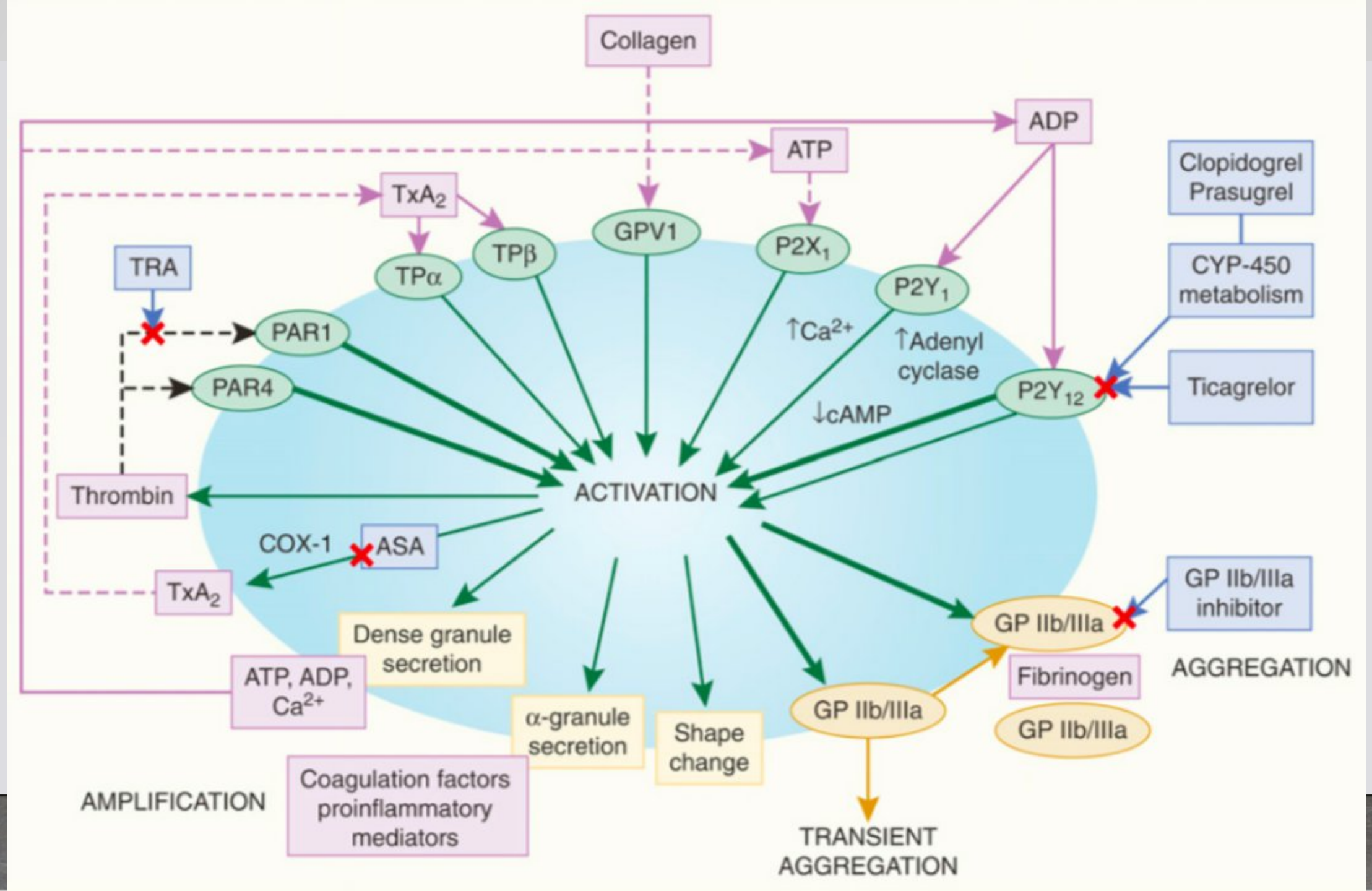
COR indicates Class of Recommendation; FMC, first medical contact; HF, heart failure; LOE, Level of Evidence; MI, myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.

NSTEMI Therapy

- Initial treatment – MONA**
- ABCs:
  - Aspirin, Anti-platelet, Anti-thrombotic, Anti-anginal, ACEi/ARB
  - Beta-blocker
  - Cholesterol (statin)

Anti-thrombotic therapy

Agent	Mechanism	Pro	Con
UFH	Inhibits Xa and thrombin (via ATIII)	Easy to assess effect, quick on/quick off	Variable response, HIT, lab draws
LMWH	Inhibits XA and thrombin (via ATIII)	Ease of use, less platelet activation	Measuring effect, HIT
Bivalirudin	Direct thrombin inhibitor	Easy to assess affect, short half life, no HIT	ONLY FOR INVASIVE APPROACH
Fondaparinaux	Indirect Xa inhibition	Once daiy	Once daily, only for conservative tx


Collagen
ADP
ATP
TxA_2
GPV1
$P2X_1$
TPβ
TPα
$P2Y_1$
TRA
PAR1
PAR4
$\uparrow Ca^{2+}$
↑Adenyl cyclase
$P2Y_{12}$
↓cAMP
Clopidogrel
Prasugrel
CYP-450 metabolism
Ticagrelor
Thrombin
ACTIVATION
COX-1
ASA
TxA_2
Dense granule secretion
ATP, ADP, Ca^{2+}
α-granule secretion
Shape change
GP IIb/IIIa
GP IIb/IIIa inhibitor
Fibrinogen
GP IIb/IIIa
AGGREGATION
AMPLIFICATION
Coagulation factors proinflammatory mediators
TRANSIENT AGGREGATION

Anti-platelet

- Aspirin: 325 mg load, 81 mg daily
- $P2Y_{12}$:
  - Thienopyridines (indirect inhibitors):
    - *Clopidogrel (Plavix)*: 300 or 600 mg load, 75 mg daily
    - Prasugrel (Effient): 60 mg load, 10 mg daily
  - Direct inhibitors:
    - Ticagrelor (Brilinta): 180 mg load, 90 mg BID
    - Cangrelor (Kengreal)

TABLE 7 Summary of Recommendations for Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS and PCI

Recommendations	Dosing and Special Considerations	COR	LOE	References
Aspirin				
• Non-enteric-coated aspirin to *all* patients promptly after presentation	162 mg–325 mg	I	A	(288-290)
• Aspirin maintenance dose indefinitely	81 mg/d–325 mg/d*	I	A	(288-290, 293,391)
$P2Y_{12}$ inhibitors				
• Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin	75 mg	I	B	(291)
• $P2Y_{12}$ inhibitor, in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy: – Clopidogrel – Ticagrelor*	300-mg or 600-mg loading dose, then 75 mg/d 180-mg loading dose, then 90 mg BID	I	B	(289,292) (293,294)
• $P2Y_{12}$ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) continued for at least 12 mo in post-PCI patients treated with coronary stents	N/A	I	B	(293,296,302, 330,331)
• Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy	N/A	IIa	B	(293,294)
GP IIb/IIIa inhibitors				
• GP IIb/IIIa inhibitor in patients treated with an early invasive strategy and DAPT with intermediate/high-risk features (e.g., positive troponin)	Preferred options are eptifibatide or tirofiban	IIb	B	(43,94,295)

$P2Y_{12}$ Inhibitors

Table 1. $P2Y_{12}$ Inhibitors Currently in Clinical Use After Percutaneous Coronary Intervention

	Ticlopidine	Clopidogrel	Prasugrel	Ticagrelor
Class	Thienopyridine	Thienopyridine	Thienopyridine	Cyclopentyl-triazolo-pyrimidine
Pharmacology	Highly CYP-dependent conversion to prodrug	Highly CYP-dependent conversion to prodrug	Requires conversion to prodrug (less CYP dependent)	Directly acting inhibitor
Potency of platelet inhibition	+	+	++	++
Time to peak platelet inhibition[24]	3-4 d	4-5 h (300 mg) 2-3 h (600 mg)	2-4 h	2-4 h
Dosing, daily	Twice	Once	Once	Twice
Time required for antiplatelet effect to dissipate, days	5	5	7	5
Cost for 1 mo, $	≈45.00[a]	14.50 (generic)[a] 218.87 (Plavix)[b]	218.52[b]	260.78[b]

ACC/AHA FOCUSED UPDATE

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

FIGURE 2 Treatment Algorithm for Duration of $P2Y_{12}$ Inhibitor Therapy in Patients Treated With PCI

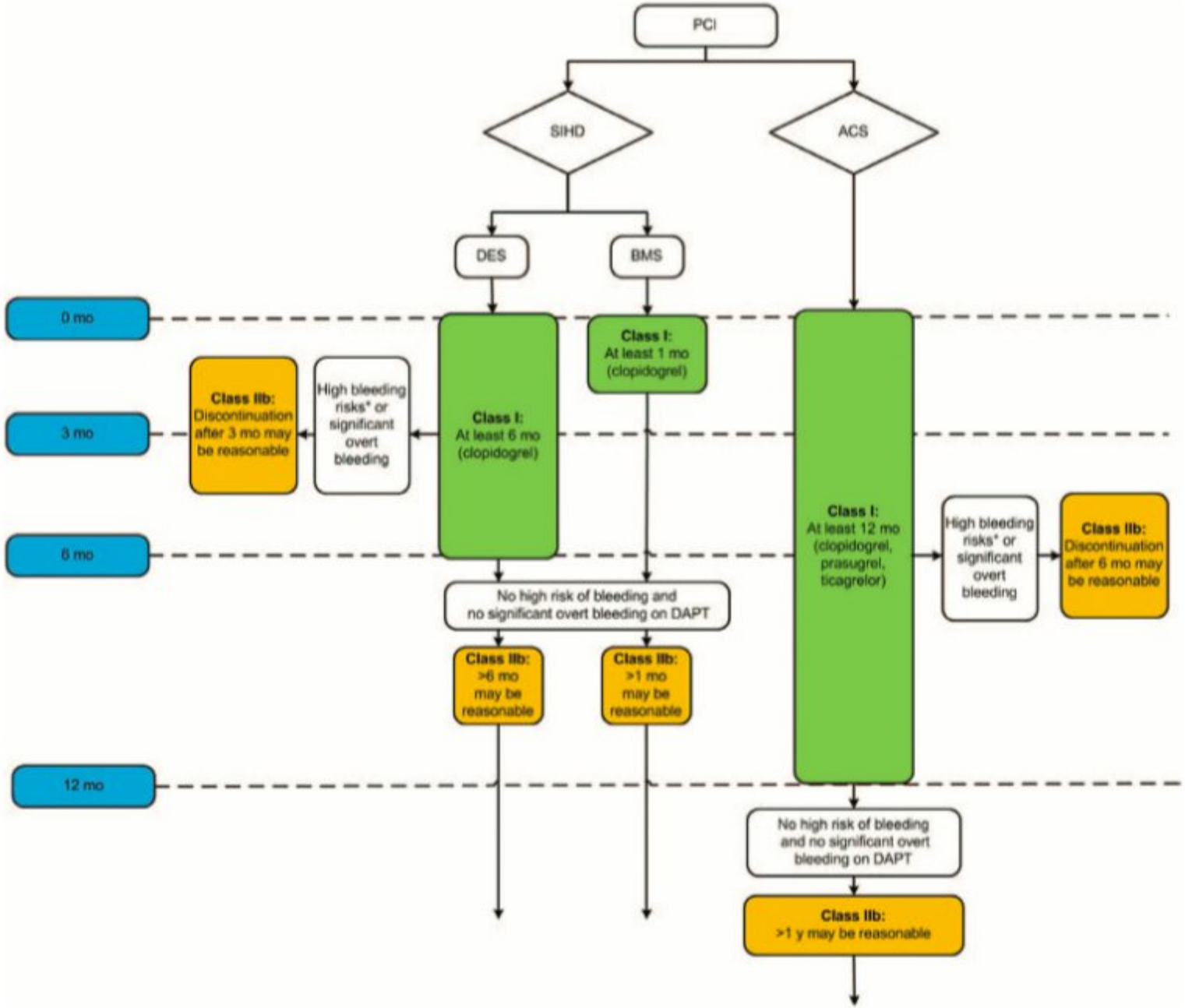


TABLE 6 Summary and Synthesis of Guideline, Expert Consensus Documents, and Comprehensive Review Article Recommendations on the Management of Patients Treated With Triple Therapy (14,88,91-93)

Assess ischemic and bleeding risks using validated risk predictors (e.g., CHA_2DS_2-VASc, HAS-BLED)
Keep triple therapy duration as short as possible; dual therapy only (oral anticoagulant and clopidogrel) may be considered in select patients
Consider a target INR of 2.0-2.5 when warfarin is used
Clopidogrel is the $P2Y_{12}$ inhibitor of choice
Use low-dose (≤100 mg daily) aspirin
PPIs should be used in patients with a history of gastrointestinal bleeding and are reasonable to use in patients with increased risk of gastrointestinal bleeding

Anti-anginal

- Nitroglycerin
  - No mortality benefit
  - Mechanism: selective coronary vasodilation
  - CAUTION: Decrease pre-load
    - Do not use in pre-load dependent RV infarct
    - Careful if severe AS

Medical Therapy

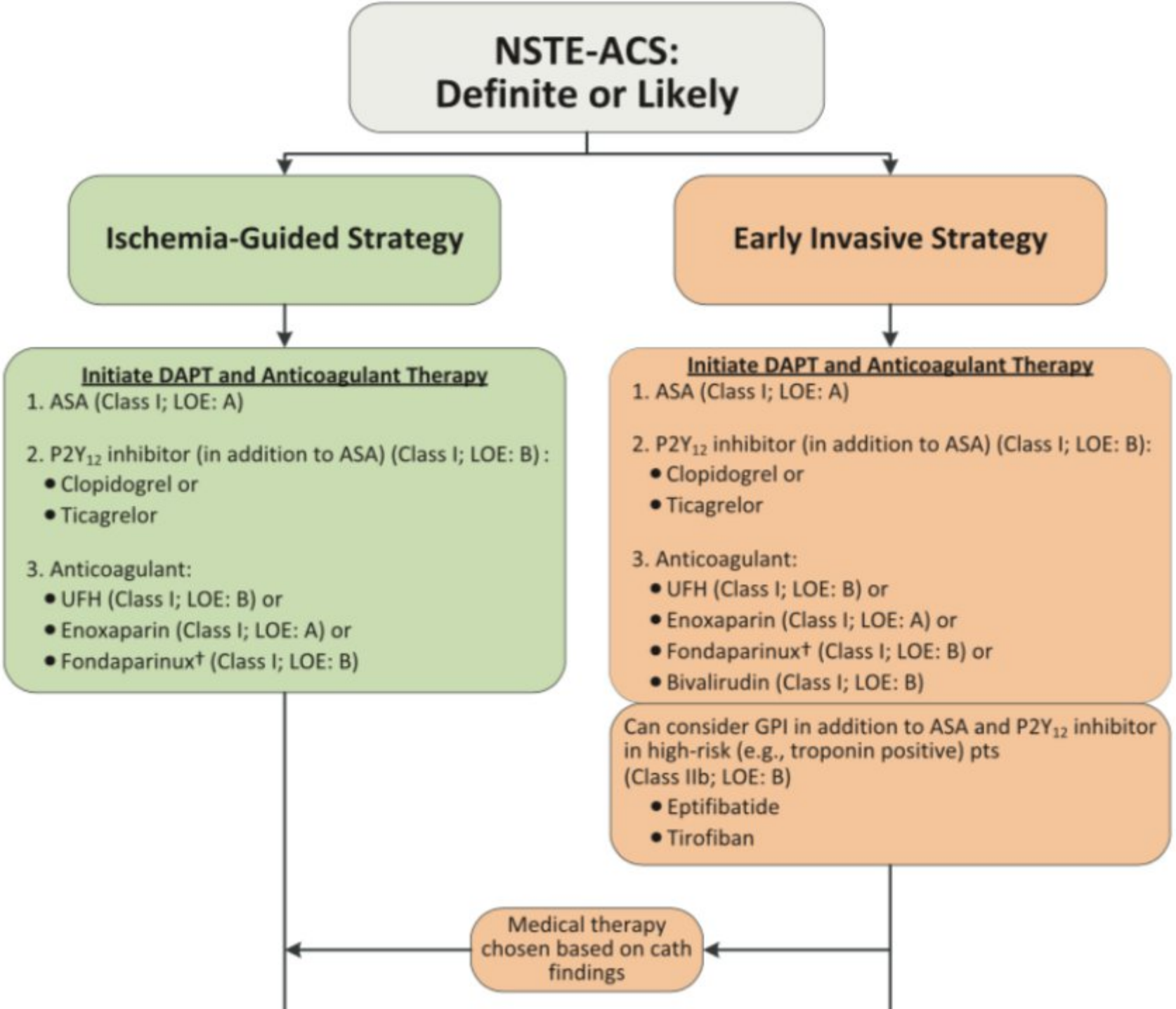
Therapy	Indications	Dose/Administration	Avoid/Caution
Beta-Receptor Antagonists	• Oral: All patients without contraindication • IV: Patients with refractory hypertension or ongoing ischemia without contraindication	Individualize: • Metoprolol tartrate 25 to 50 mg every 6 to 12 h orally, then transition over next 2 to 3 d to twice-daily dosing of metoprolol tartrate or to daily metoprolol succinate; titrate to daily dose of 200 mg as tolerated • Carvedilol 6.25 mg twice daily, titrate to 25 mg twice daily as tolerated • Metoprolol tartrate IV 5 mg every 5 min as tolerated up to 3 doses; titrate to heart rate and BP	• Signs of HF • Low output state • Increased risk of cardiogenic shock • Prolonged first-degree or high-grade AV block • Reactive airways disease

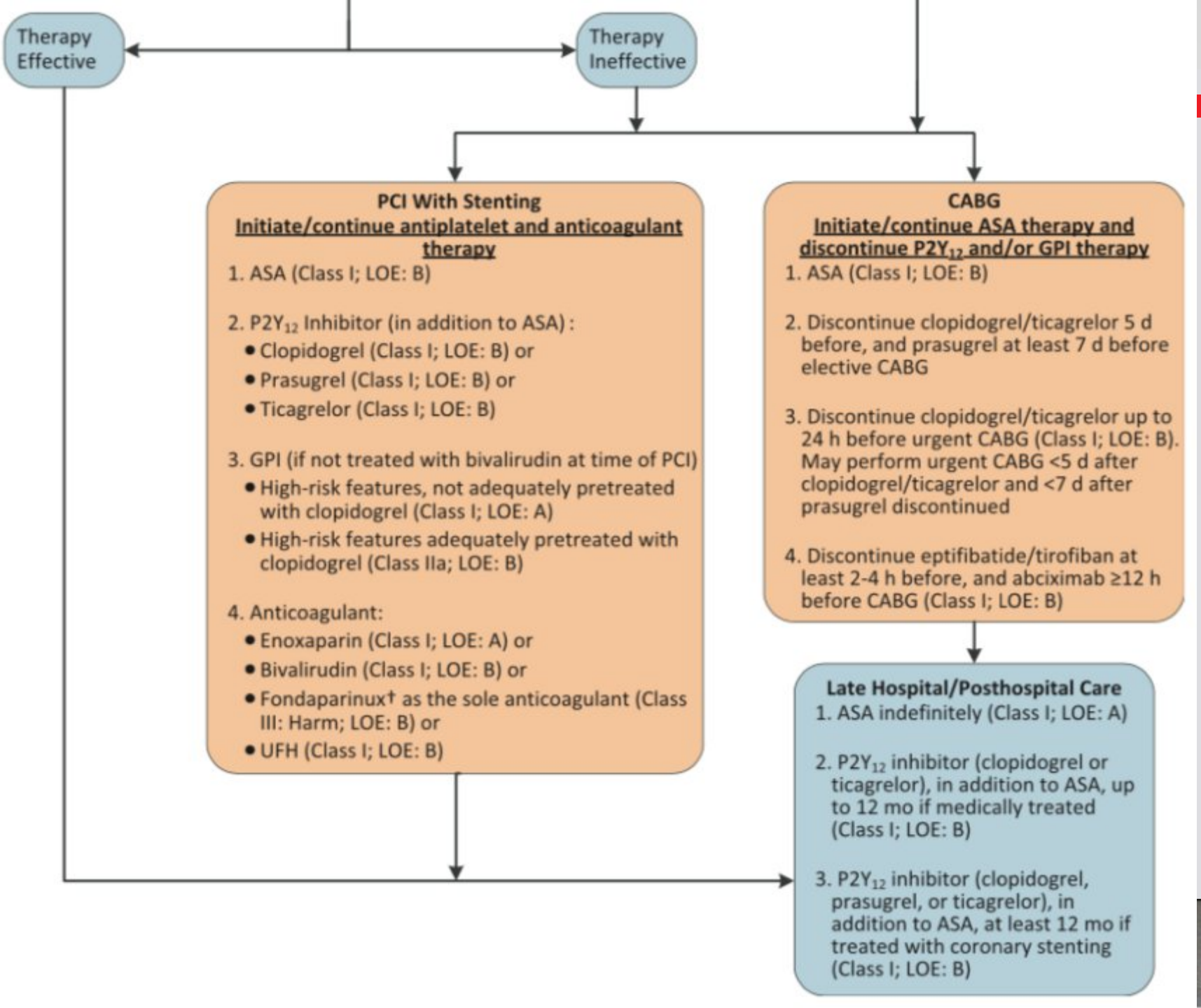
ACE Inhibitors	• For patients with anterior infarction, post-MI LV systolic dysfunction (EF ≤0.40) or HF • May be given routinely to all patients without contraindication	Individualize: • Lisinopril 2.5 to 5 mg/d to start; titrate to 10 mg/d or higher as tolerated • Captopril 6.25 to 12.5 mg 3 times/d to start; titrate to 25 to 50 mg 3 times/d as tolerated • Ramipril 2.5 mg twice daily to start; titrate to 5 mg twice daily as tolerated • Trandolapril test dose 0.5 mg; titrate up to 4 mg daily as tolerated	• Hypotension • Renal failure • Hyperkalemia
ARB	• For patients intolerant of ACE inhibitors	• Valsartan 20 mg twice daily to start; titrate to 160 mg twice daily as tolerated	• Hypotension • Renal failure • Hyperkalemia
Statins	• All patients without contraindications	• High-dose atorvastatin 80 mg daily	• Caution with drugs metabolized via *CYP3A4*, fibrates • Monitor for myopathy, hepatic toxicity • Combine with diet and lifestyle therapies • Adjust dose as dictated by targets for LDL cholesterol and non–HDL cholesterol reduction

NSTEMI Summary

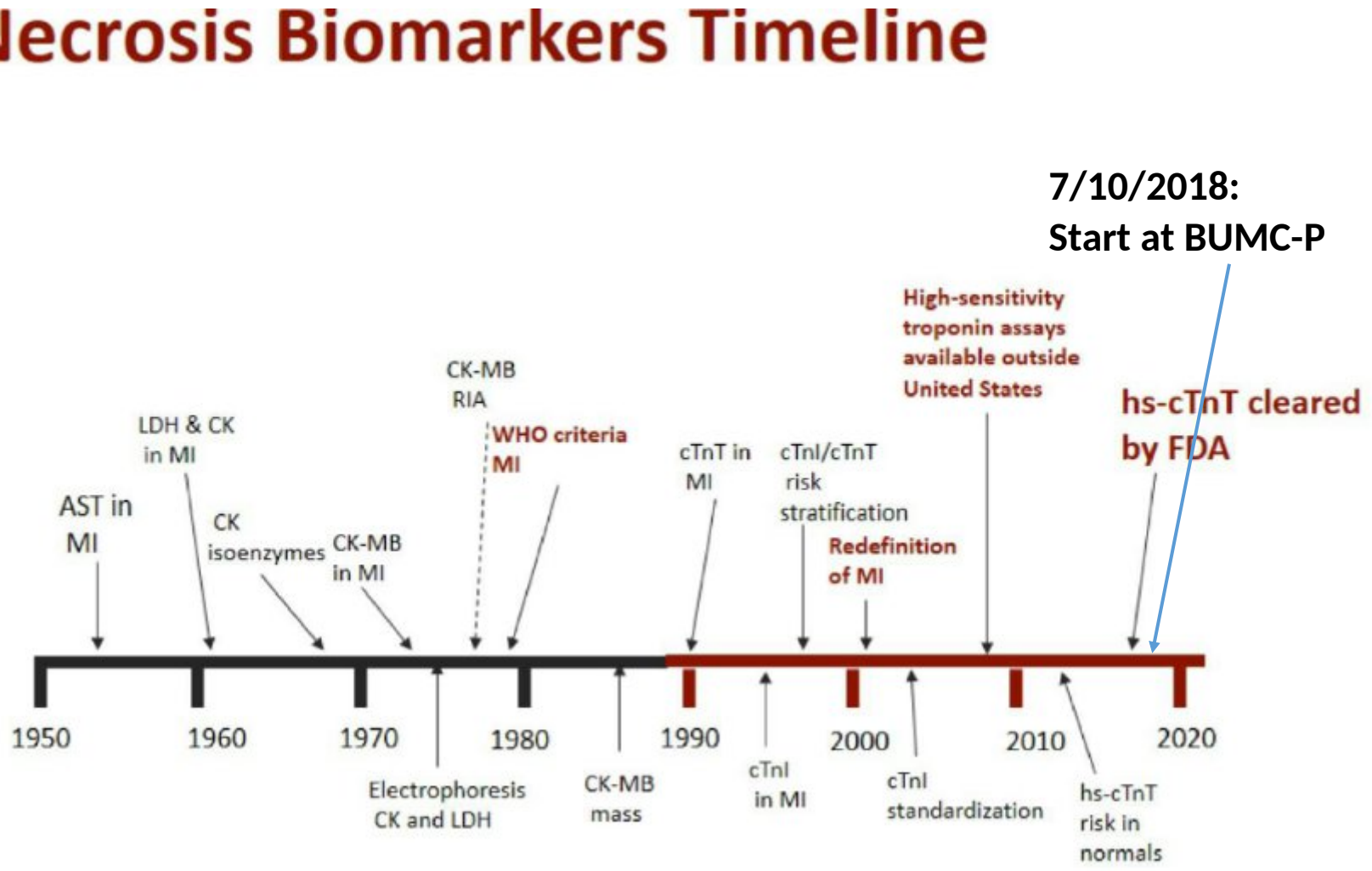
- Serial ECG and cardiac biomarkers
- ABCs
  - ASA 325mg then 81mg QD
  - Anti-platelet (Clopidogrel 600mg or 300mg then 75mg QD)
  - Anti-thrombotic (UFH)
  - Anti-anginal (SL NTG or NTG drip)
  - Beta-blocker (PO Metoprolol)
  - Cholesterol (High intensity Rosuvastatin or Atorvastatin)

NSTEMI Treatment pathway


NSTE-ACS:
Definite or Likely
Ischemia-Guided Strategy
Early Invasive Strategy
Initiate DAPT and Anticoagulant Therapy
1. ASA (Class I; LOE: A)
2. P2Y12 inhibitor (in addition to ASA) (Class I; LOE: B):
• Clopidogrel or
• Ticagrelor
3. Anticoagulant:
• UFH (Class I; LOE: B) or
• Enoxaparin (Class I; LOE: A) or
• Fondaparinux† (Class I; LOE: B)
Initiate DAPT and Anticoagulant Therapy
1. ASA (Class I; LOE: A)
2. P2Y12 inhibitor (in addition to ASA) (Class I; LOE: B):
• Clopidogrel or
• Ticagrelor
3. Anticoagulant:
• UFH (Class I; LOE: B) or
• Enoxaparin (Class I; LOE: A) or
• Fondaparinux† (Class I; LOE: B) or
• Bivalirudin (Class I; LOE: B)
Can consider GPI in addition to ASA and P2Y12 inhibitor in high-risk (e.g., troponin positive) pts
(Class IIb; LOE: B)
• Eptifibatide
• Tirofiban
Medical therapy chosen based on cath findings

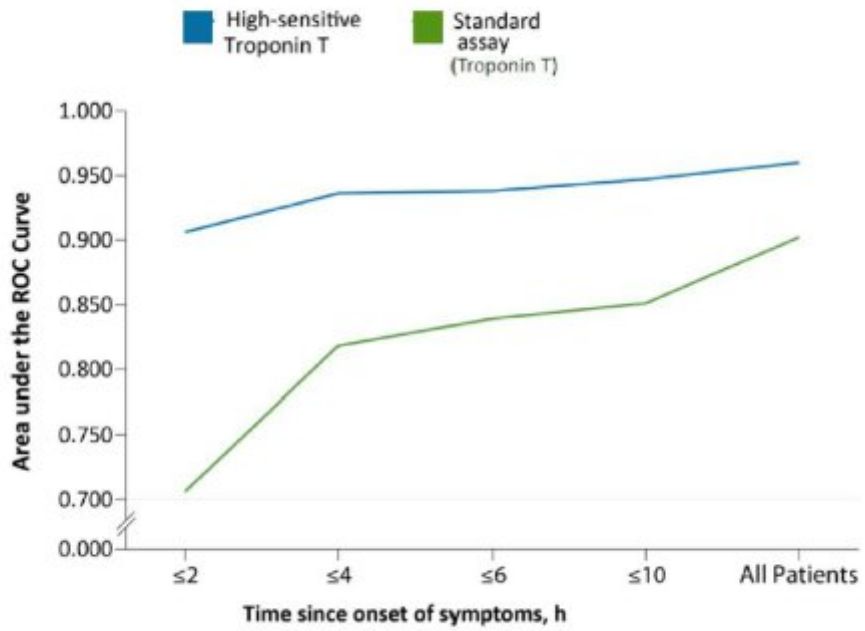

Therapy Effective
Therapy Ineffective
PCI With Stenting
Initiate/continue antiplatelet and anticoagulant therapy
1. ASA (Class I; LOE: B)
2. P2Y12 Inhibitor (in addition to ASA) :
• Clopidogrel (Class I; LOE: B) or
• Prasugrel (Class I; LOE: B) or
• Ticagrelor (Class I; LOE: B)
3. GPI (if not treated with bivalirudin at time of PCI)
• High-risk features, not adequately pretreated with clopidogrel (Class I; LOE: A)
• High-risk features adequately pretreated with clopidogrel (Class IIa; LOE: B)
4. Anticoagulant:
• Enoxaparin (Class I; LOE: A) or
• Bivalirudin (Class I; LOE: B) or
• Fondaparinux† as the sole anticoagulant (Class III: Harm; LOE: B) or
• UFH (Class I; LOE: B)
CABG
Initiate/continue ASA therapy and discontinue P2Y12 and/or GPI therapy
1. ASA (Class I; LOE: B)
2. Discontinue clopidogrel/ticagrelor 5 d before, and prasugrel at least 7 d before elective CABG
3. Discontinue clopidogrel/ticagrelor up to 24 h before urgent CABG (Class I; LOE: B). May perform urgent CABG <5 d after clopidogrel/ticagrelor and <7 d after prasugrel discontinued
4. Discontinue eptifibatide/tirofiban at least 2-4 h before, and abciximab ≥12 h before CABG (Class I; LOE: B)
Late Hospital/Posthospital Care
1. ASA indefinitely (Class I; LOE: A)
2. P2Y12 inhibitor (clopidogrel or ticagrelor), in addition to ASA, up to 12 mo if medically treated (Class I; LOE: B)
3. P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor), in addition to ASA, at least 12 mo if treated with coronary stenting (Class I; LOE: B)

HIGH SENSITIVITY-CARDIAC TROPONIN T
hs-cTnT



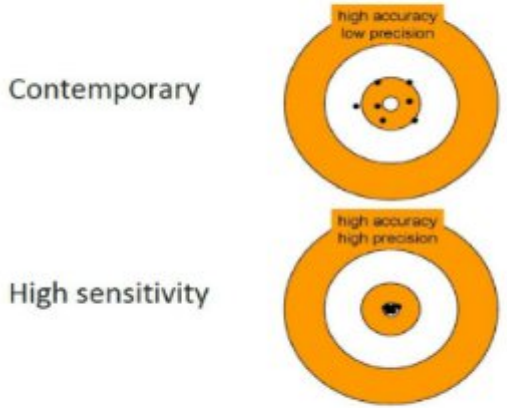
Hs-cTnT Why change?

Area Under ROC Curve and Time of Symptoms Onset



Reichlin T, et al. *N Engl J Med*. 2009;361:858-867.

Cardiac Troponin Assays
High Accuracy, Different Precision



hs-cTn assays are more precise

Courtesy of Robert Christensen, MD.

APACE
Effect of hs-cTn Introduction

- 20% (79 min) reduction in ED LoS
- 35% reduction in stress tests
- No increase in catheterizations
- 20% reduction in total costs

Twerenbold R, et al. *Eur Heart J*. 2016;37:3324-3332.

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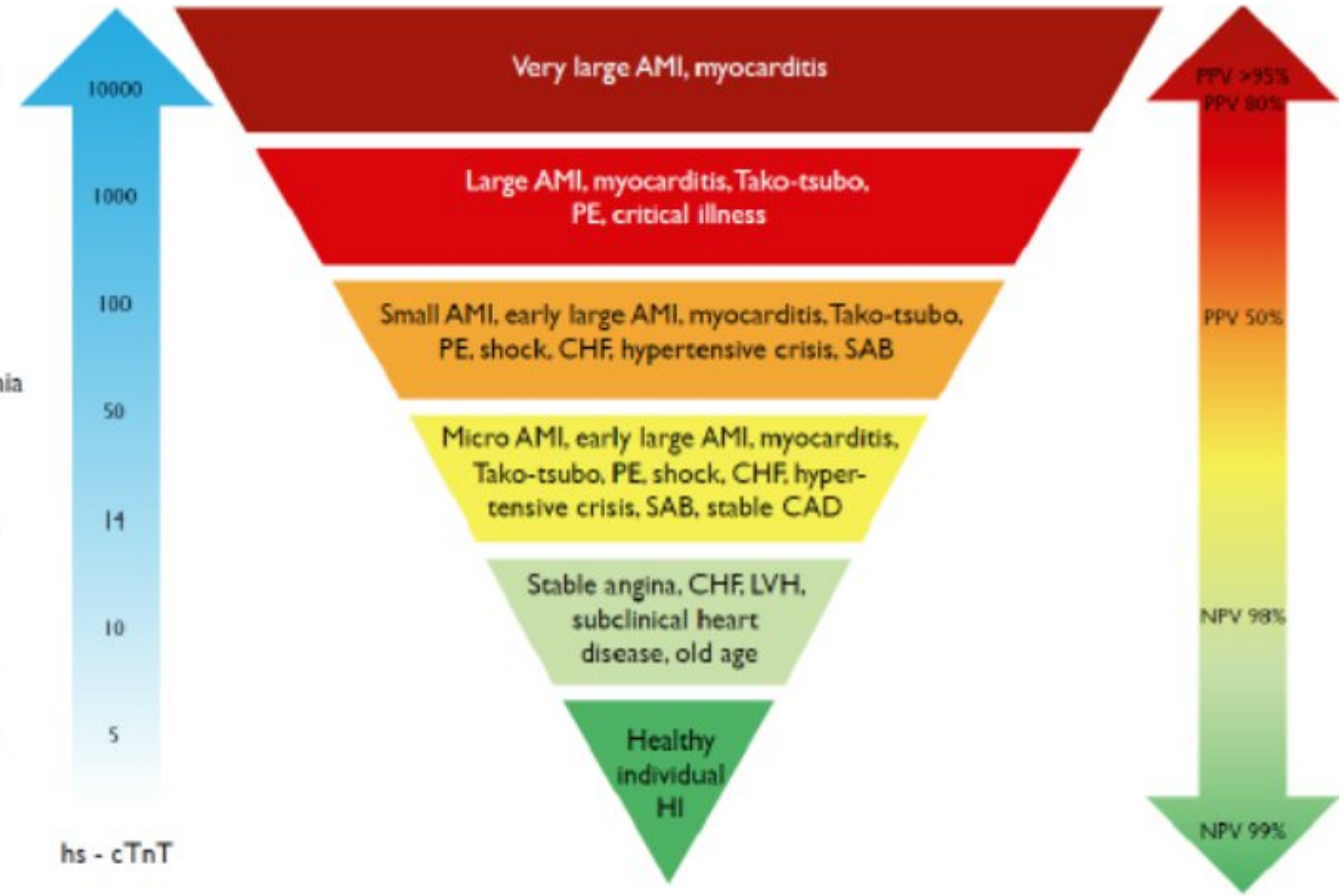
High-sensitivity cardiac troponin as a quantitative marker.

AMI acute myocardial infarction
CAD coronary artery disease
CHF congestive heart failure
HI healthy individual
LVH left ventricular hypertrophy
PE pulmonary embolus
SAB Staphylococcus aureus bacteremia

The lower the level of hs-cTn, the higher the negative predictive value (NPV) for the presence of AMI.

The higher the level of hs-cTN, the higher the positive predictive value (PPV) for the presence of AMI.

Levels just above the 99th percentile have a low PPV for AMI



(derivative of Garg et al, Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin, Intern Emerg Med. (2017) 12:147-155). This work is licensed under Creative Commons Attribution 2.0 Generic License)

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Reporting- How do we avoid confusion in reporting of results?
Current reporting has a line for Troponin I. After the transition,
4 lines of reporting will be available if data is in them.

Triglycerides	107 mg/dL *		
CK, Total			175 IU/L
Troponin-I			0.38 ng/mL H

Troponin T, high sensitivity	**ng/L**
Troponin I, (Backup)	ng/mL
Troponin T Contemporary	ng/mL

Each of these 4 will have their own reporting line with their own reference values and will be reported regardless of where the result is obtained.
(Only Washakie is reporting the cTnT currently).
Note the difference in reporting units.

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Use in evaluation of suspected ACS

For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
Clinical care must not be based on lab values alone.

Initial hs-cTnT Lab Value

Repeat Lab at 2hr

2 hr change in lab value (increase or decrease)

Repeat Lab at 4hr

4 hr change in lab value from baseline

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For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
Clinical care must not be based on lab values alone.

Initial hs-cTnT Lab Value

- NORMAL <12 ng/L
- ELEVATED 12-99 Myocardial Injury
- Critically High >=100 ng/L MI or ACS (or myocardial injury from myocarditis, PE, Takotsubo, etc.)

Repeat Lab at 2hr

2 hr change in lab value (increase or decrease)

Repeat Lab at 4hr

4 hr change in lab value from baseline

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For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
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NORMAL <12 ng/L

ELEVATED 12-99 Myocardial Injury

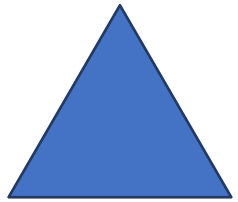
Critically High >=100 ng/L MI or ACS (or myocardial injury from myocarditis, PE, Takotsubo, etc.)

Repeat Lab at 2hr

2 hr change in lab value (increase or decrease)

Repeat Lab at 4hr

4 hr change in lab value from baseline



Delta or Change (Increase or Decrease) in value is compared to the initial value

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For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
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Critically High >=100 ng/L MI or ACS (or myocardial injury from myocarditis, PE, Takotsubo, etc.)

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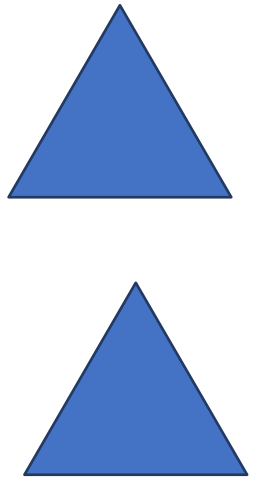
2 hr change in lab value (increase or decrease)

Repeat Lab at 4hr

4 hr change in lab value from baseline



Delta or Change (Increase or Decrease) in value is compared to the initial value

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For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
Clinical care must not be based on lab values alone.

Initial hs-cTnT Lab Value

NORMAL <12 ng/L

ELEVATED 12-99
Myocardial Injury

Critically High >=100 ng/L
MI or ACS
(or myocardial injury from myocarditis, PE, Takotsubo, etc.)

Admit or Place in Obs
Document Severity
Additional Cardiac Evaluation Indicated

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For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
Clinical care must not be based on lab values alone.

Initial hs-cTnT Lab Value

NORMAL <12 ng/L

All Patients
Repeat Lab at 2hr
2 hr change in lab value (increase or decrease)

Δ *<4 ng/L* → No MI- Follow up with Outpatient Provider

Δ *4-9 ng/L* → ED or Observation **Repeat Lab at 4hr**

Δ *>=10 ng/L* → Admit or Place in Obs Document Severity Additional Cardiac Evaluation Indicated

4 hr change in lab value from baseline

Δ *<4 ng/L* → No MI- Follow up with Outpatient Provider

Δ *4-9 ng/L* → Evaluate for non-ACS source of troponin, late presentation MI, etc. Consider non-invasive testing for CAD

Δ *>=10 ng/L* → Admit or Place in Obs Document Severity Additional Cardiac Evaluation Indicated

Banner Health

For STEMI patient– activate CARDIAC ALERT

Evaluation of chest pain must integrate clinical, EKG, and hs-cTnT information.
Clinical care must not be based on lab values alone.

Initial hs-cTnT Lab Value

All Patients
Repeat Lab at 2hr

2 hr change in lab value (increase or decrease)

ELEVATED 12-99 ng/L
Myocardial Injury

△ *<4 ng/L*

△ *4-9 ng/L*

△ *>=10 ng/L*

No MI- Follow up with Outpatient Provider

ED or Observation
Repeat Lab at 4hr

Admit or Place in Obs
Document Severity
Additional Cardiac Evaluation Indicated

4 hr change in lab value from baseline

△ *<4 ng/L* or

△ *4-9 ng/L*

△ *>=10 ng/L*

Evaluate for
non-ACS source of troponin, late presentation MI, etc.
Consider non-invasive testing for CAD

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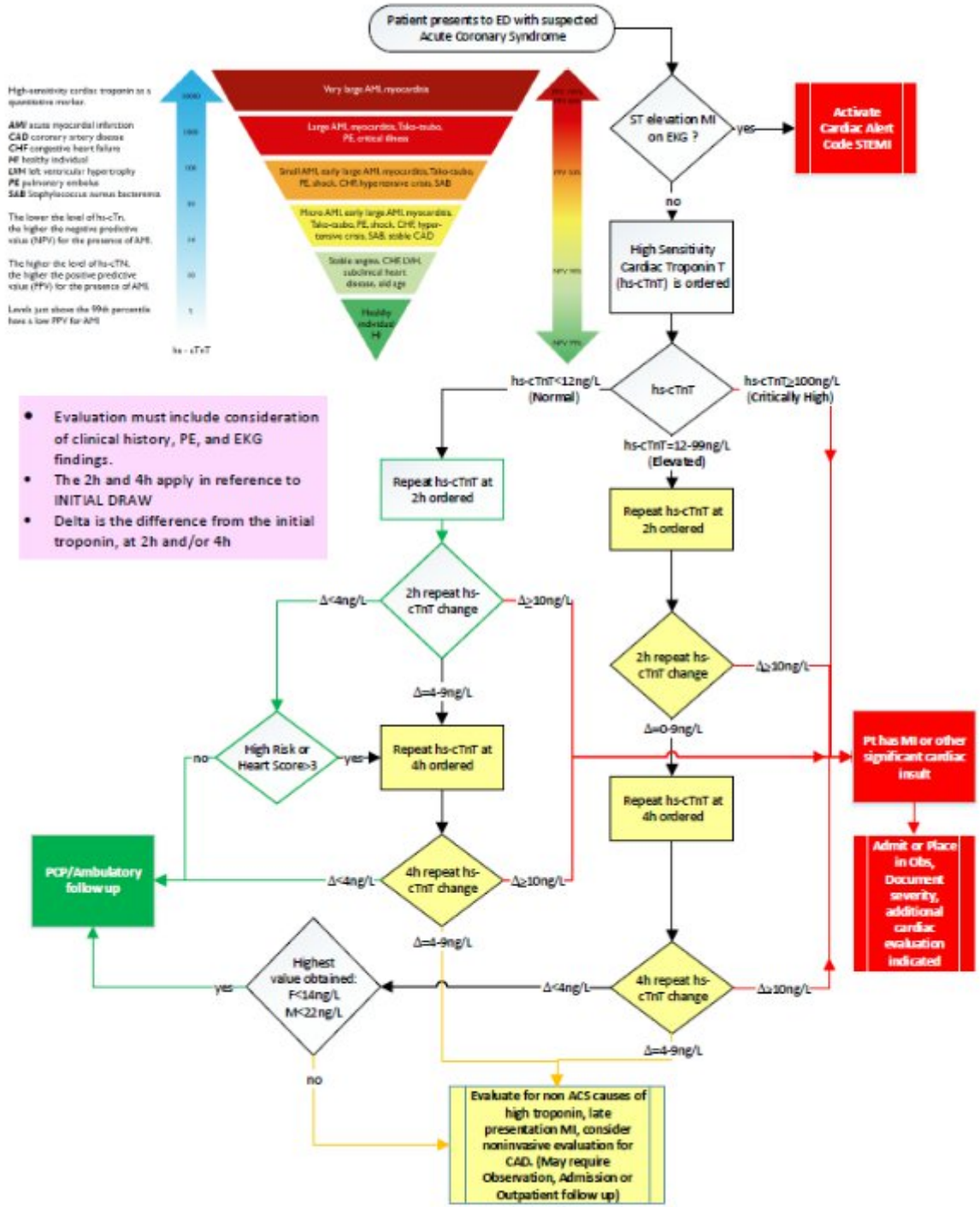
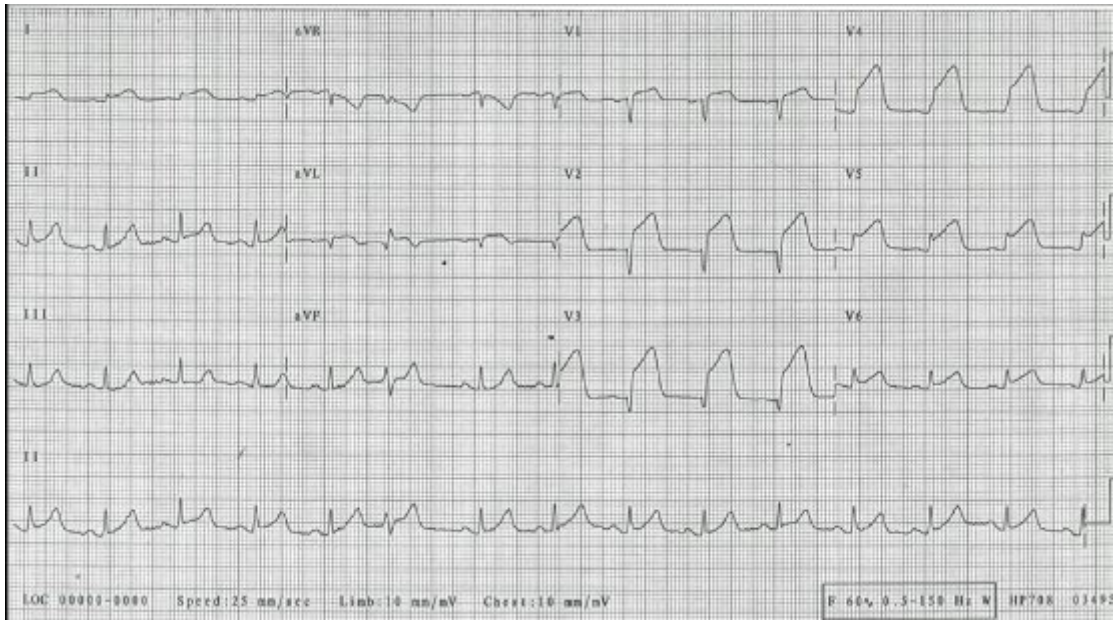
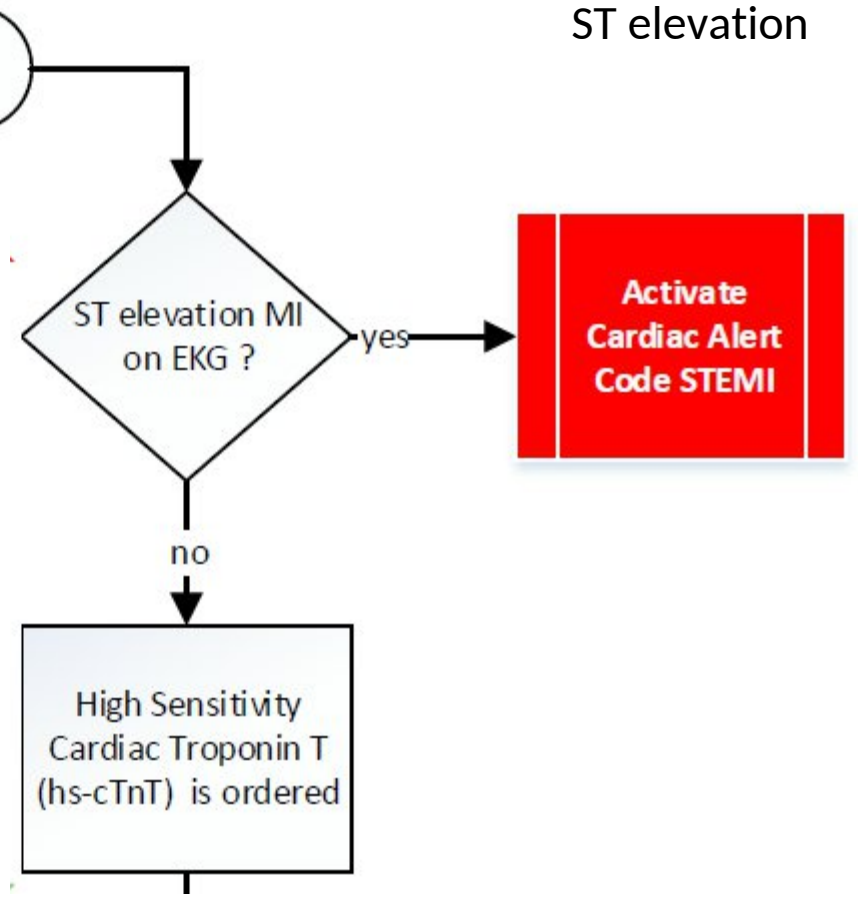


Banner Health

52 y/o Male with chest pain
Abnormal EKG
ST elevation





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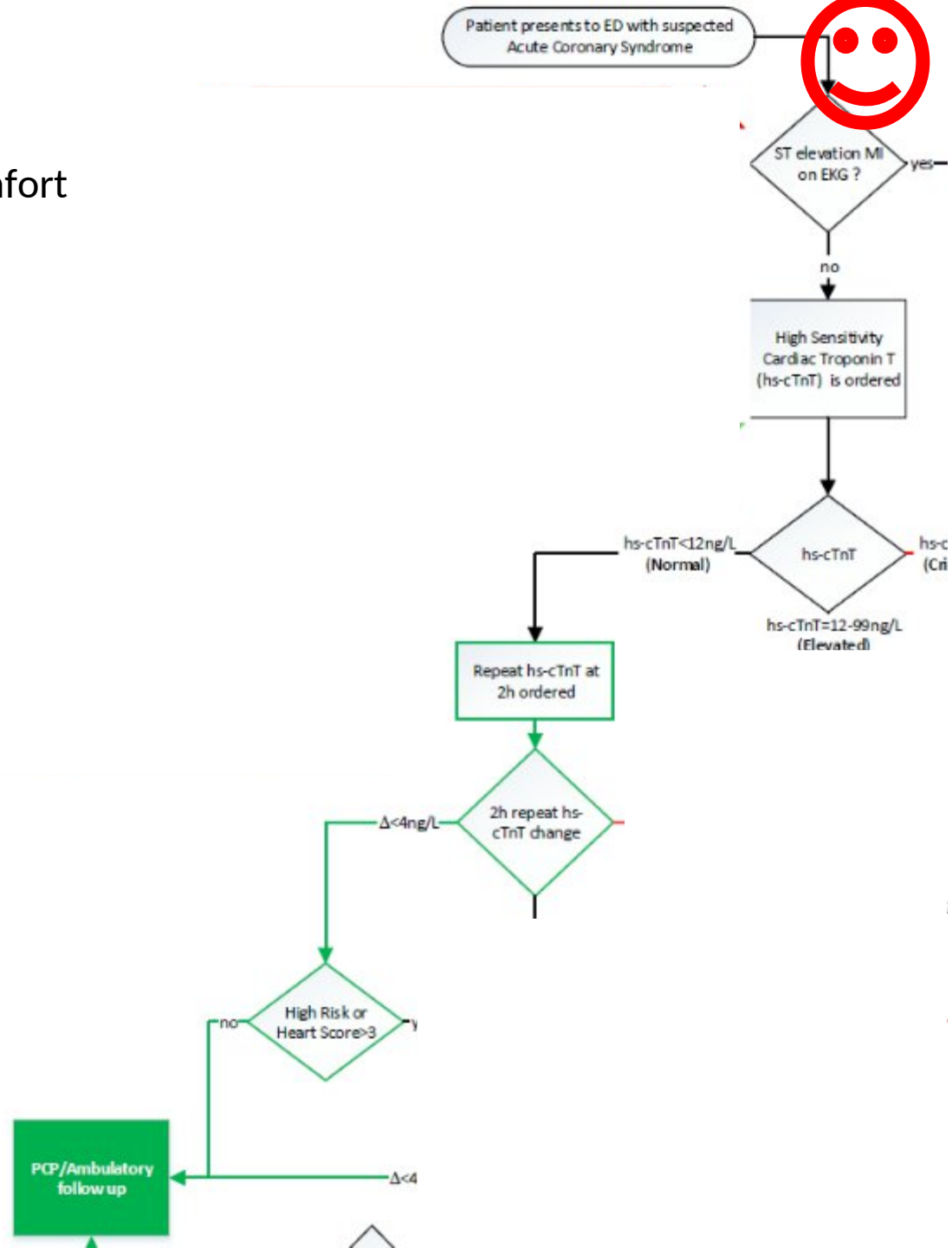
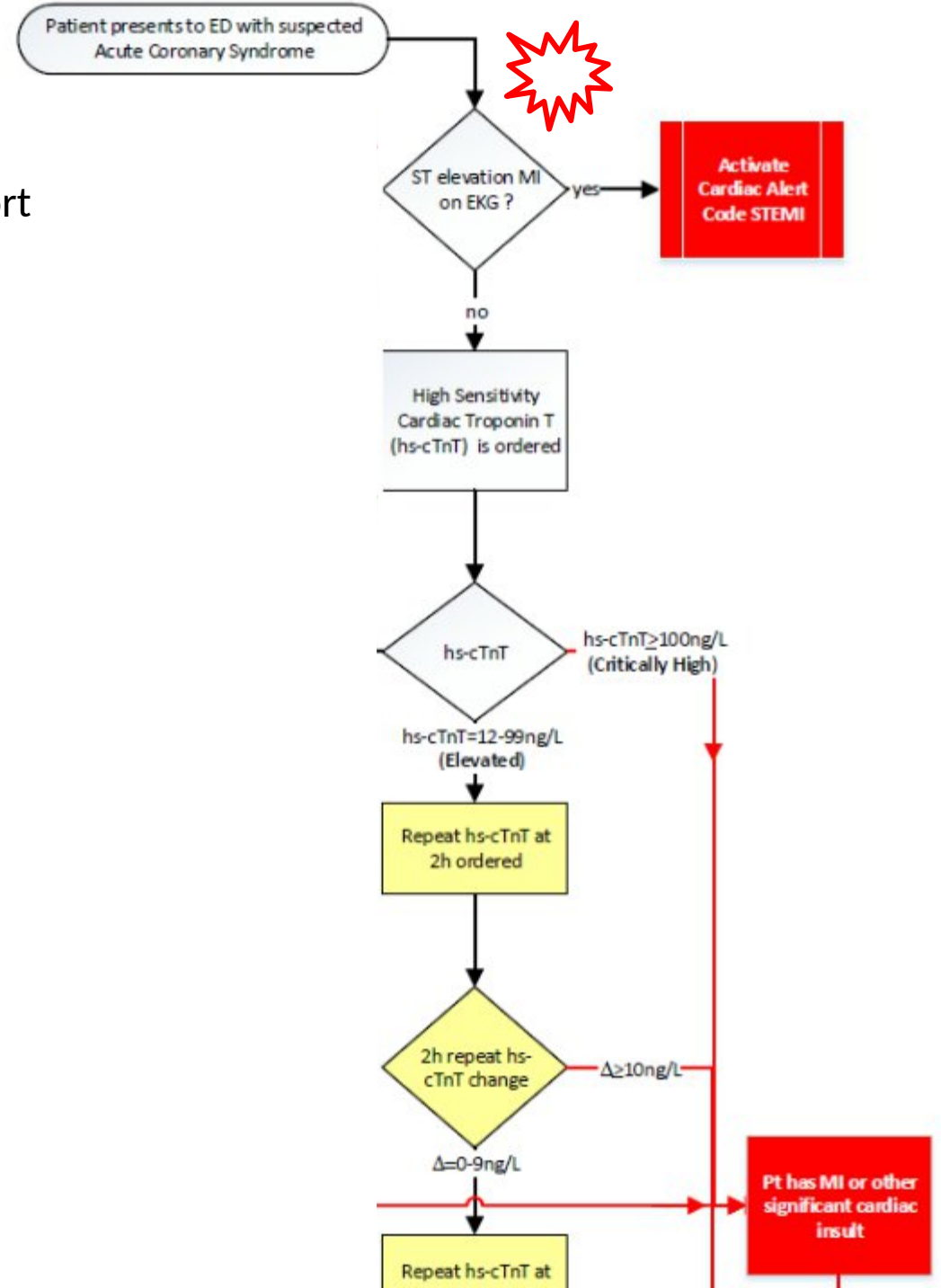
48 y/o female with Chest Discomfort
Nonspecific EKG Changes
t=0hr hs-cTnt 6 ng/L
t=2hr hs-cTnT 8 ng/L



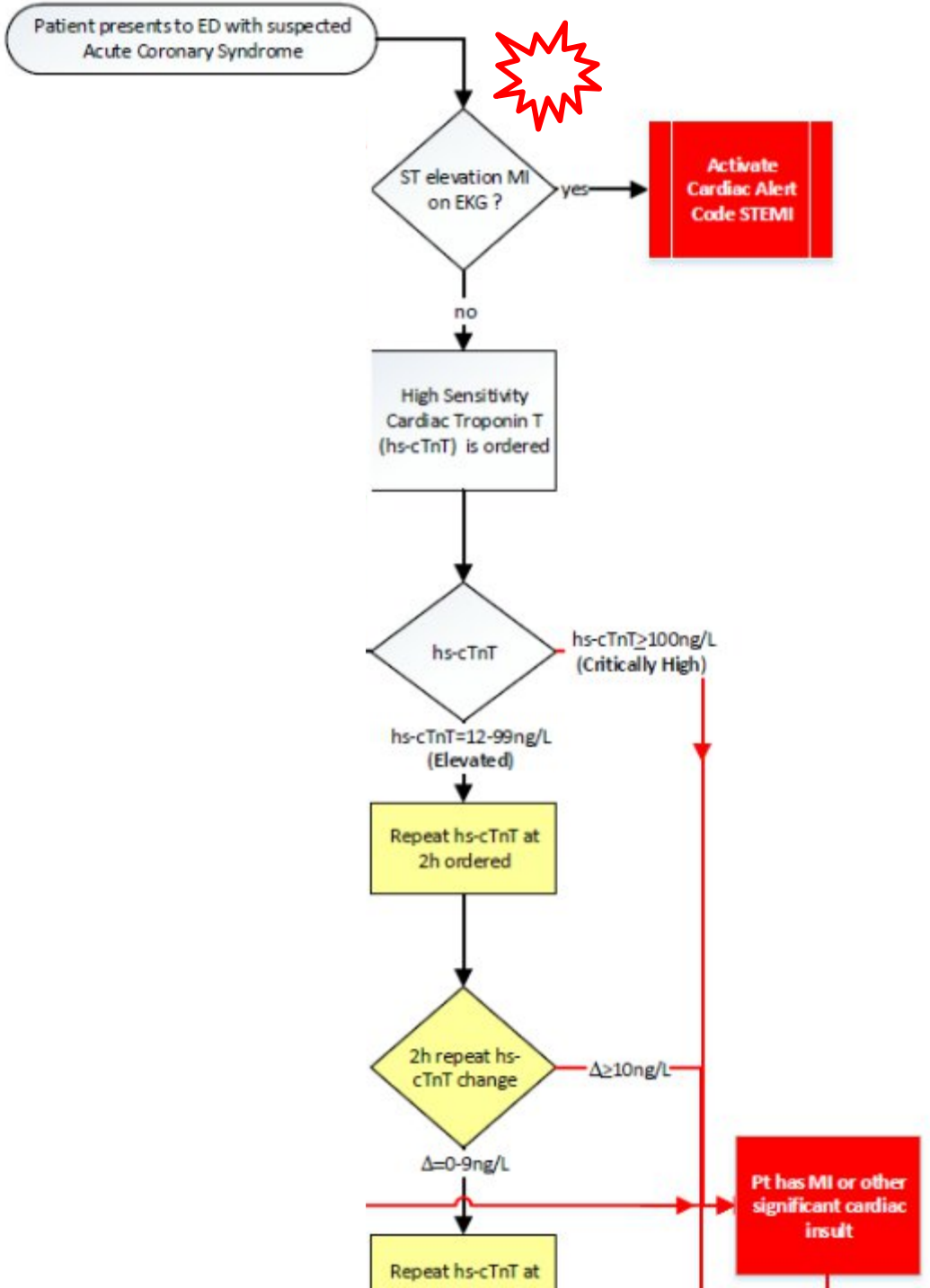
Banner Health

74 y/o female with Chest Discomfort
Nonspecific EKG Changes
t=0hr hs-cTnt 152 ng/L



Banner Health

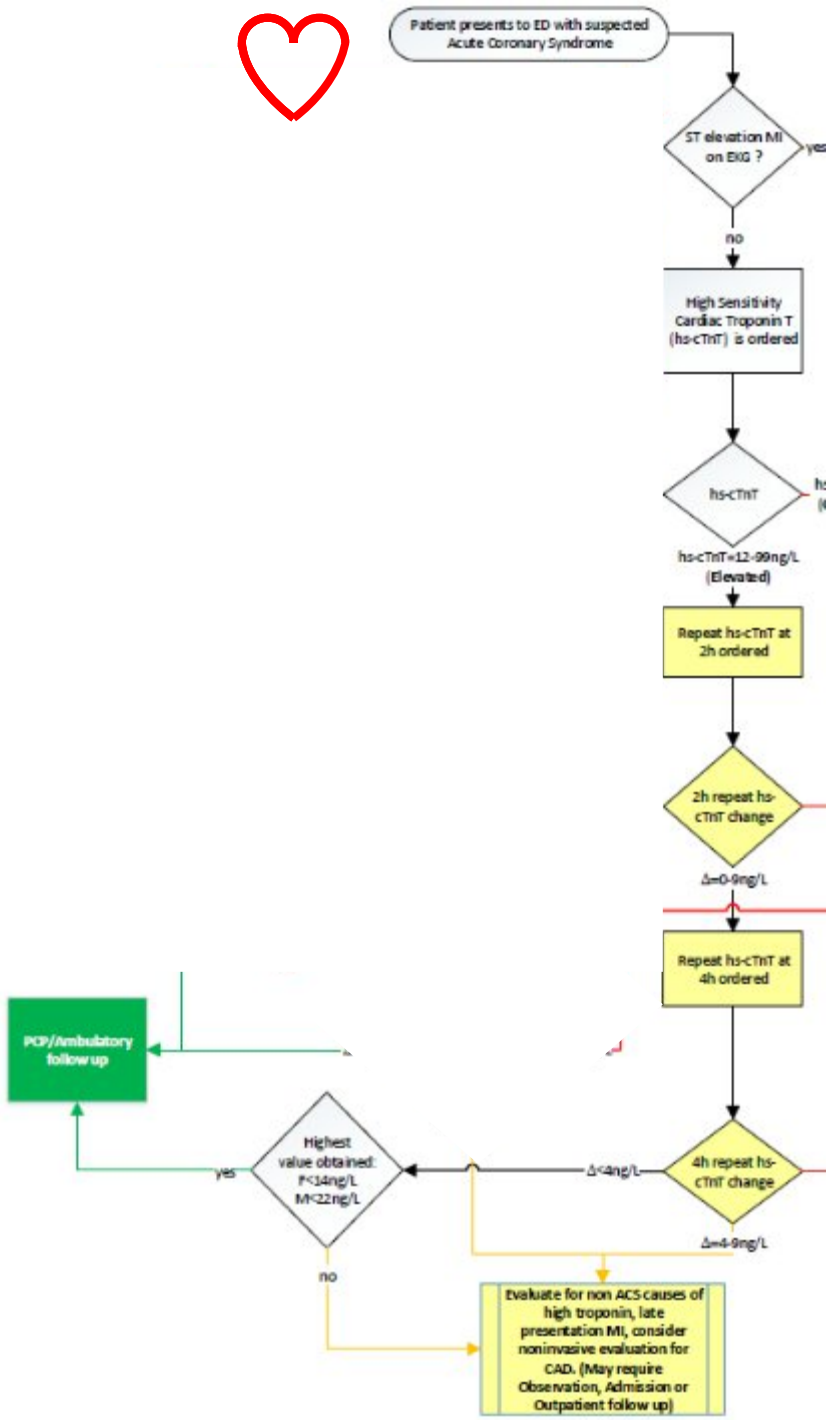
62 y/o Male with Chest Discomfort
Nonspecific EKG Changes
t=0hr hs-cTnt 36 ng/L
t=2hr hs-cTnT 49 ng/L



Banner Health

52 y/o male with Chest Discomfort
Nonspecific EKG Changes

t=0hr hs-cTnt 28 ng/L
t=2hr hs-cTnT 26 ng/L
t=4hr hs-cTnt 25 ng/L



Banner Health

Additional considerations

- hs-cTNT will be decreased with hemolysis- as much as a 20% decrease
  - The lab will not report hemolyzed specimens.
  - The lab will call for a redraw on hemolyzed specimens.
- Hs-cTnT will rise when sympathomimetics are given

Impact in cardiac surgery.

- hs-cTnT will rise after cardiac surgery.
- Rise is more prominent when sympathomimetics are given perioperatively
- Consider obtaining a baseline hs-cTnT level prior to surgery so an elevated post op level can be put in appropriate perspective.