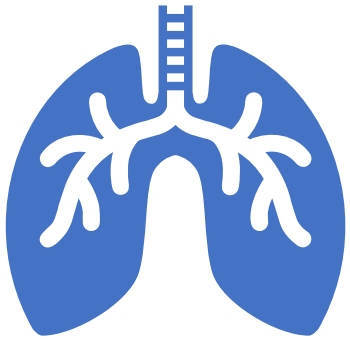
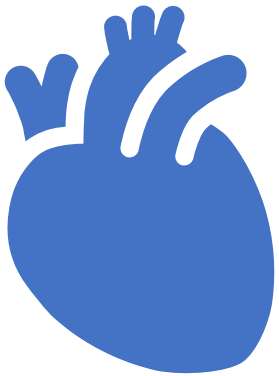




Chest Pain: 3 Deadly Diagnoses

Stephanie Jalaba, MMS, PA-C
Michigan State University
Department of PA Medicine

Adrijana Anderson, MMS, PA-C
Mayo Clinic Arizona
Division of Hospital Medicine

Disclosures

- No disclosures to share.
- No off-label uses will be discussed.

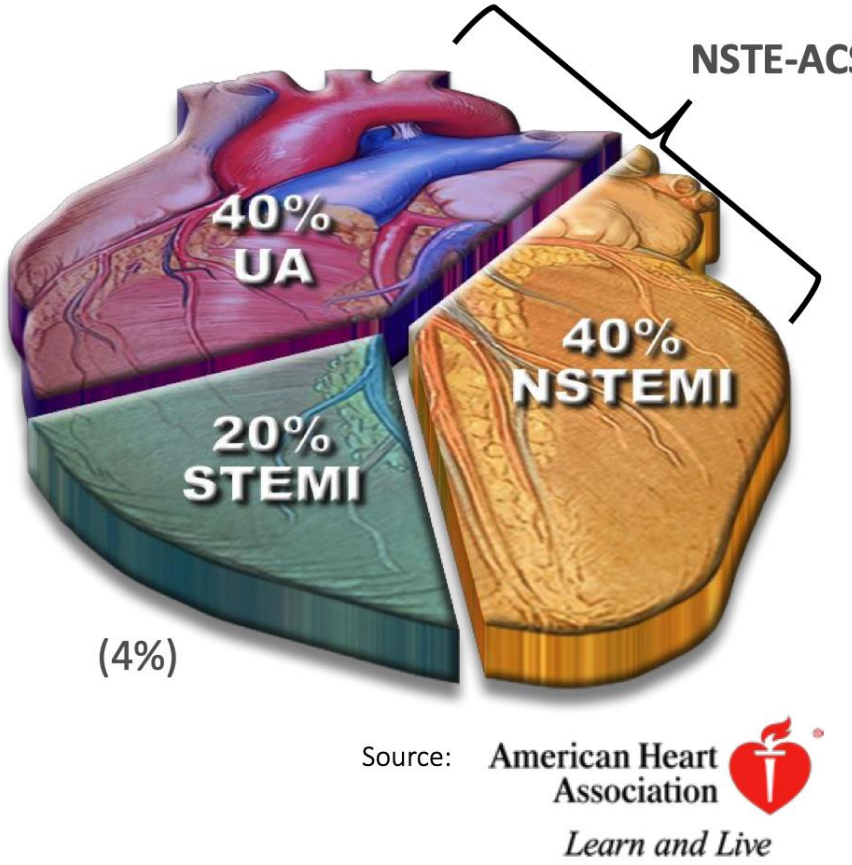
Learning Objectives

Upon conclusion of this lecture, the participant will be able to:

1. Describe approaches to risk stratification for undifferentiated chest pain with suspected ACS.
2. Discuss noninvasive testing in suspected cardiac chest pain, including the recent emergence of Coronary CT Angiography.
3. Recognize advances in PE treatment, including special populations.
4. Explain why high level of suspicion for acute aortic dissection is crucial.

Chest Pain DDX

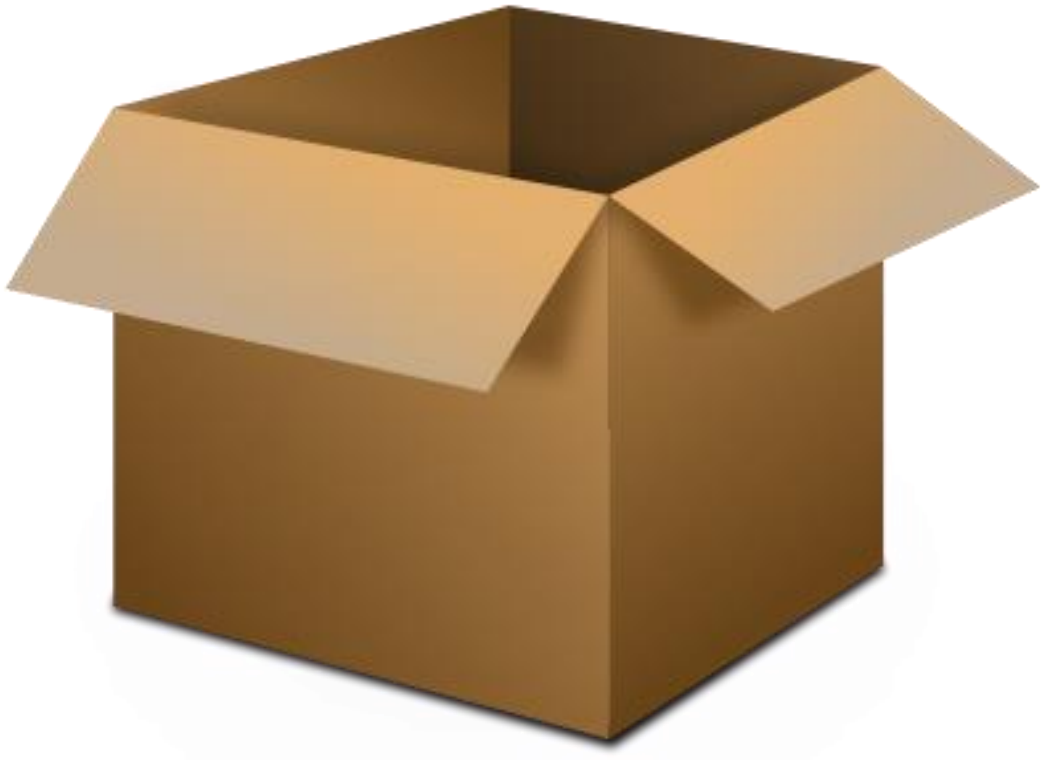
- Myocardial ischemia
  - **ACS**
  - Stable angina
- Aortic dissection
- Pericarditis
- Myocarditis
- Cardiac tamponade
- Arrhythmia
- +/-Heart failure



Chest Pain DDX:

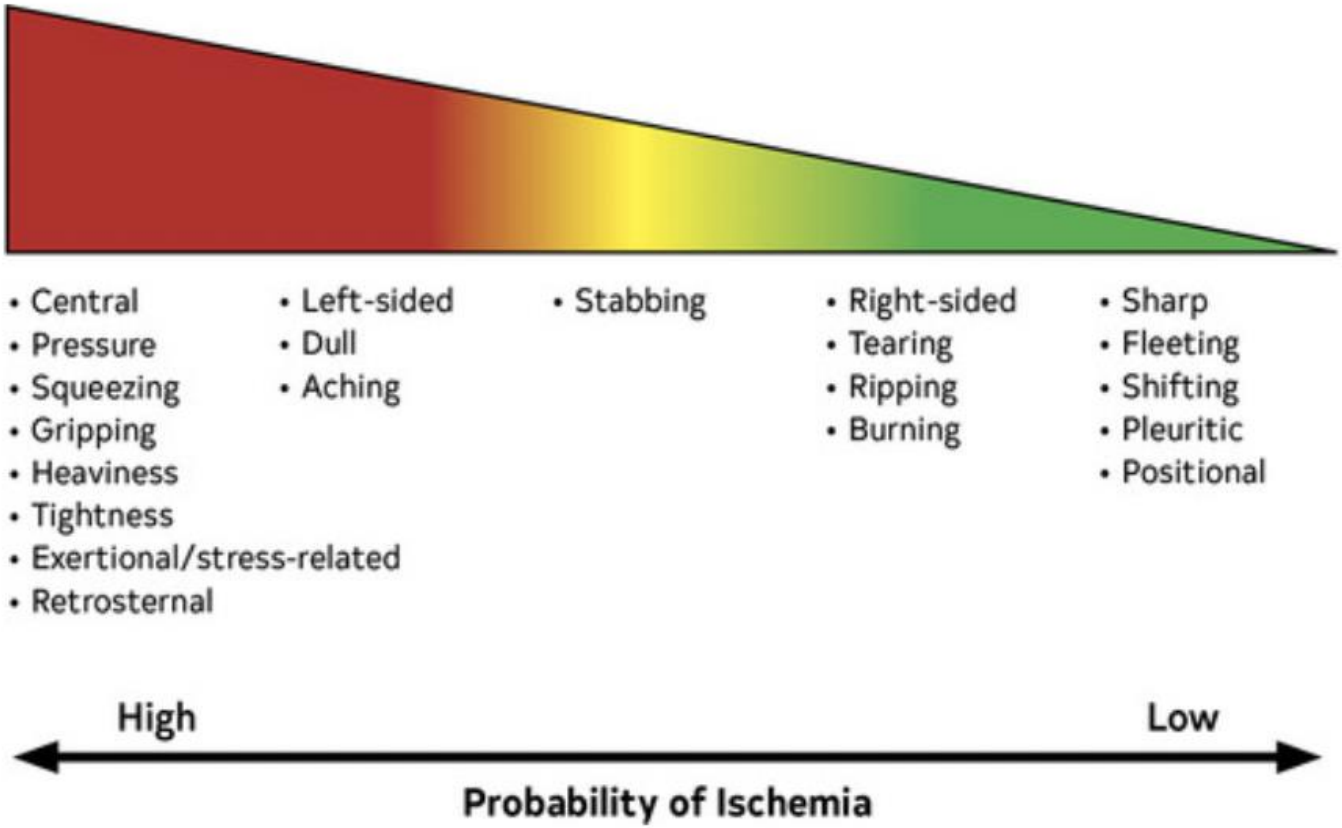
Pulmonary	Gastrointestinal	Musculoskeletal	Psychiatric
Pulmonary embolism	Esophageal spasm	Traumatic injury	Somatization
Pneumothorax	GERD Gastritis	Rib fracture/pain	Depression
Pleural effusion/Pleuritis	Esophagitis	Costochondritis	Panic attack/disorder
Pneumonia	Esophageal rupture/perforation	Rheumatic disease	Generalized Anxiety
Malignancy	PUD	Cervical radiculopathy	
Asthma/COPD exacerbation	Biliary disease	Myositis	
Mediastinitis	Pancreatitis		
	Sliding hiatal hernia		

Thinking Outside the Box…



- Trauma
- Referred pain
- Herpes zoster
- Substance abuse
- Acute chest syndrome
- Collagen vascular disease

Clinical Features With Increased Probability of MI



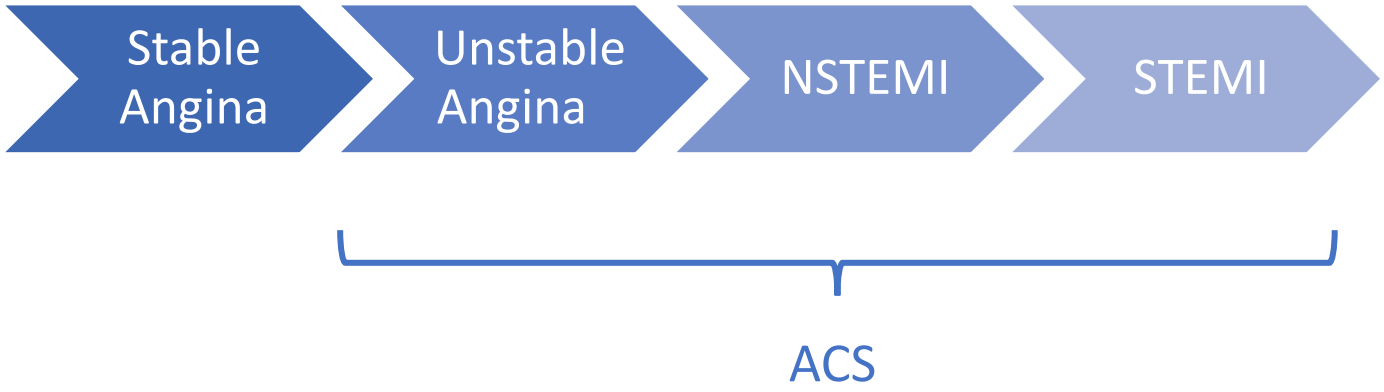
Circulation. 2021;144:e368–e454

Mr. S

- 66 yo male presents with recurring substernal chest pressure over the past day.
- Each episode has lasted about 2 minutes, described as “a sandbag sitting on my chest”, and is relieved with rest. There are no associated symptoms and no radiation of pain.

- **PMH:** HTN, HLD, Type 2 DM
- **SH**: Current smoker, 20 pack-year history. Social EtOH use. No drug use. He has a high stress job as a director of a parks and recreation department. Diet mostly consists of meat.
- **FH:** Unknown, he didn’t want to share much about his family history.

Coronary Artery Disease (CAD)



Coronary Artery Disease (CAD)

Stable angina

- Symptoms are stable, and resolve with rest.

Acute Coronary Syndrome

- **Unstable angina**
  - Increasing severity/frequency/duration **OR** occurs at rest
- **Myocardial Infarction**
  - **NSTEMI**
    - Non-occlusive thrombus
    - Ischemia with elevated cardiac enzymes
  - **STEMI**
    - Occlusive thrombus, transmural infarction

Stable Angina

- **<u>Classic history</u>:** pressure, heaviness, tightness, fullness, or squeezing in the center or left of the chest
  - Precipitated by exertion and relieved by rest
  - Can radiate to shoulder, arms, neck or jaw

Anginal Equivalents

- Study of 14,722 ACS patients from 2000 to 2016[51]
  - 78% presented with typical chest pain
  - **21% presented with atypical complaint****

Shortness of Breath	Nausea and/or Vomiting	Diaphoresis	Fatigue
Dizzy/lightheaded	**Weak**	**Palpitations**	Syncope

- More likely to be elderly, female, and with more comorbidities (esp. diabetes)

Hammer et al., 2019

Anginal Equivalents

- **Female Patients:**
  - Women with moderate-to-severe ischemia are **more symptomatic** than men
  - Women are less likely to have timely and appropriate care
  - Women were more likely to report ≥3 associated symptoms than men

- **Elderly Patients:**
  - Patients >75 years of age more likely to present with shortness of breath, syncope, altered mental status, abdominal pain, or to have experienced an unexplained fall

Risk Stratification

- Goal = identify the **largest** number of **low-risk patients** *without* compromising safety

- Why use?
  - Cost
  - Efficiency
  - Length of stay
  - Incidentalomas

- Should **always** couple clinical judgement with risk scoring!

Risk Stratification Tools

- Derived among patients with ACS:
  - GRACE
  - **TIMI**

- Derived among patients with undifferentiated chest pain in the ED:
  - **HEART score and pathway**
  - T-MACS
  - EDACS
  - ADAPT

HEART Score

Predicts **6-week** risk of major adverse cardiac event (MACE)

	0 points	1 point	2 points
History	Incompatible with ACS	Potentially compatible with ACS	Strongly suggestive of ACS
ECG	Normal	Nonspecific repolarization abnormalities	ST depression or transient ST elevation
Age	<45	45-65	>65
Risk Factors	None	1-2 Risk Factors	3 Risk Factors or known CAD
Troponin Levels	Normal	1-3x upper limit of normal	>3x upper limit of normal

Score	Risk	Recommendation
0-3	Low Risk	Outpatient follow up
4-6	Moderate Risk	Admission to hospital
7	High Risk	Admission to hospital

Risk Stratification

- Is the HEART score perfect?
  - NO!
  - MACE 2.5% even in the low risk group
    - Improved when high-sensitivity troponin used
  - *HEART Pathway* created to address high MACE

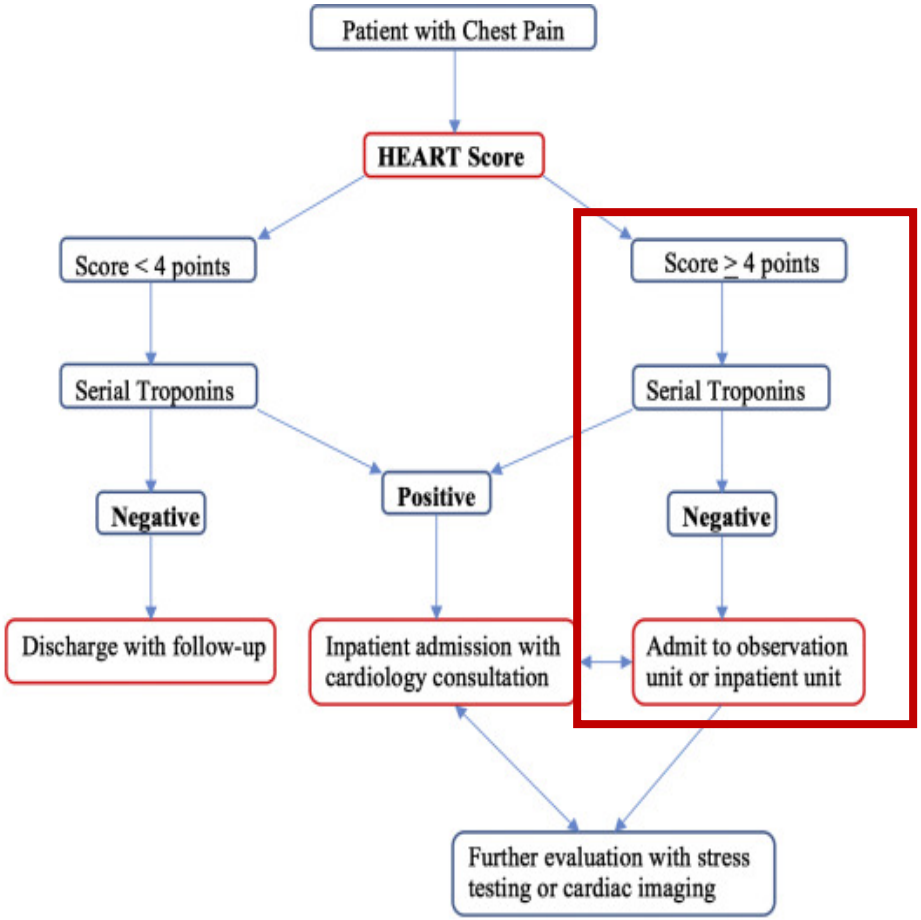
HEART Pathway

Combines the HEART score and serial cardiac troponins

- **Low risk score < 4**
- **High Risk score ≥ 4**

✓Sensitive

✓Good negative predictive value



Mr. S

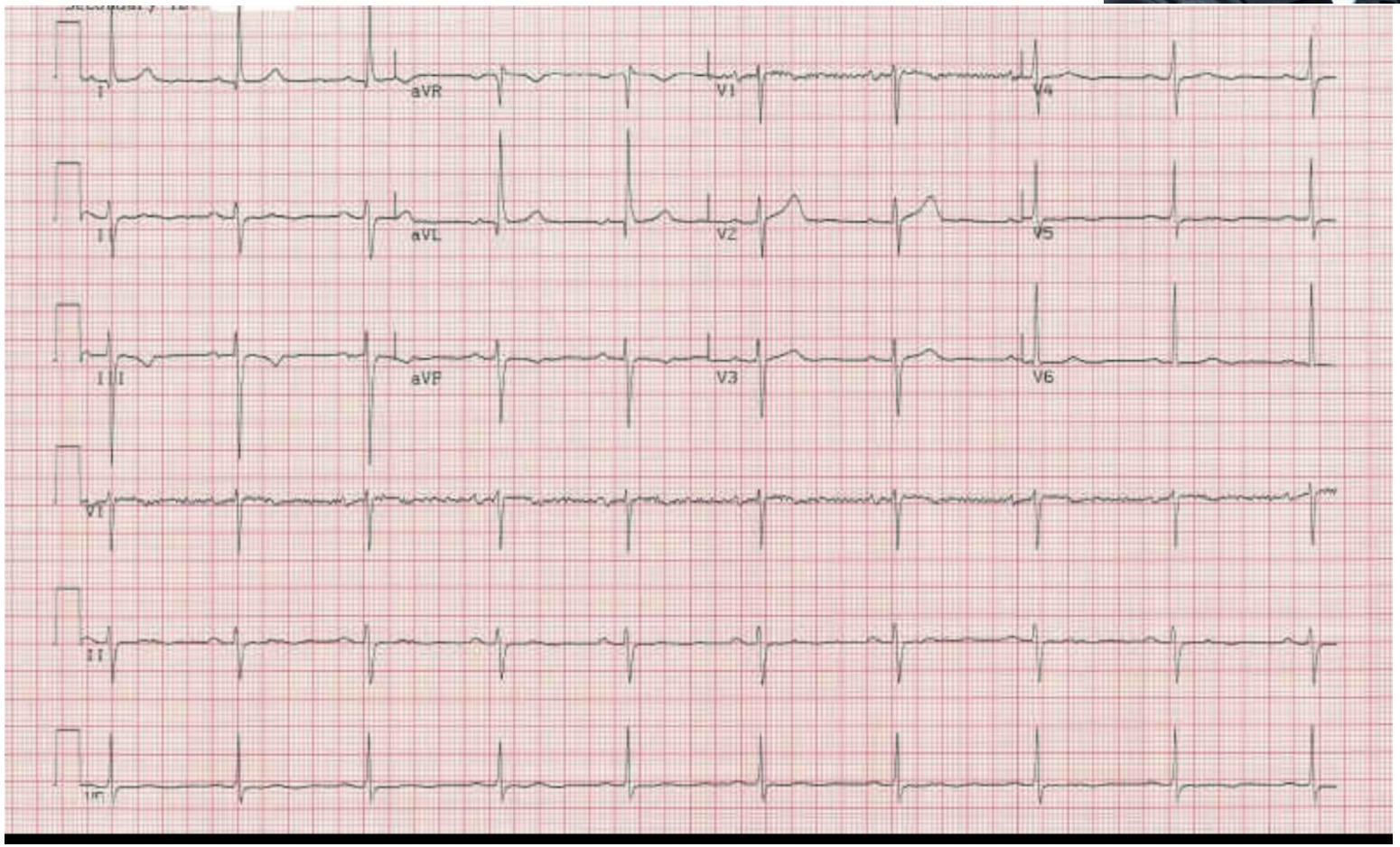
- **Vitals:**
  - T 36.7 C; HR 78 bpm; BP 133/85; RR 18; 97% RA
- **CXR:**
  - No focal consolidation, pleural effusion, or pneumothorax. Heart size appears normal.
- **Labs:**

7.3	15.9	176
	44.8	

140	102	12.2	99
4.6	27	0.9	

  - Troponin T: <0.01
  - hs-cTnT hour 0: 7 ng/L (male ≤ 15 ng/L)
  - hs-cTnT hour 2: 8 ng/L

Mr. S's ECG



High-Sensitivity Troponin (hs-cTn)

- Shorter time intervals between repeat values and earlier rise = more rapid “rule out” and “rule in”
- Gender specific reference ranges
- Emphasized the **delta** between the 2 troponin values
- High negative predictive value when used appropriately

Mr. S

- You admit Mr. S for observation. He is monitored on cardiac telemetry overnight.

- A stress test is planned for the following morning…

Stress Test Modalities

Exercise Stress Test/ECG

- Simple, widely available, low cost
- Many limitation, but may be appropriate initial test in some

Stress Echocardiogram

- Exercise vs. pharmacologic (typically with dobutamine)
- Localizes ischemia, provides structural information, fast results
  - Limited utility with resting RWMA's

Radionucleotide Myocardial Perfusion Imaging (nuclear stress test)

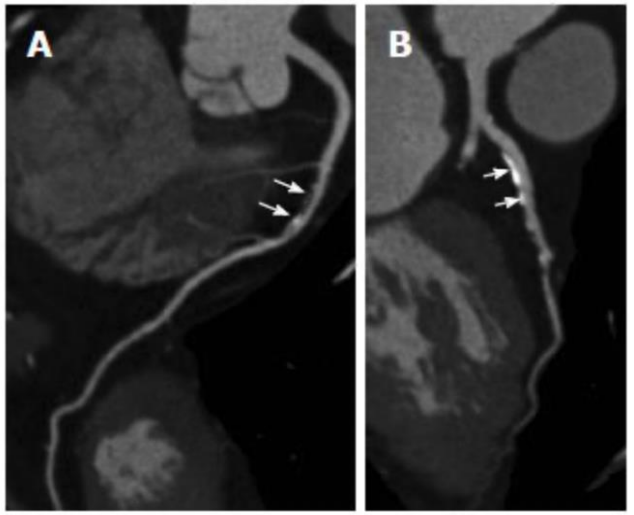
- Perfusion defect can be visualized in areas of hypoperfusion
- Can quantify involved myocardium and assess viability, good for known CAD
- More expensive, radiation exposure, longer interpretation times; limited utility with balanced ischemia (3-vessel disease)

Stress Echo vs. Nuclear Stress

Stress Echo	Nuclear Stress
• Faster • Less costly • No radiation • Provides additional information about heart anatomy, valves, etc.	• More reliable at detecting ischemia • Easier to interpret in pt with baseline cardiac dysfunction • Better for obese patients or others whose body habitus or anatomy may prevent good echo images

Coronary CT Angiography

- Can visualize and help to diagnose the extent and severity of nonobstructive and obstructive CAD
  - Provides an estimation of lesion-specific ischemia
  - Recommended with a previously inconclusive or mildly abnormal stress test in the past year.
  - Among those without a previous diagnostic evaluation and no known CAD, CTA (or stress testing) may be the initial method of testing.



Coronary CT Angiography

- Scottish Computed Tomography of the Heart (SCOT-HEART) investigators
  - CTA had significant effect in diagnosis and treatment of patients referred for stable chest pain
  - CTA group had significantly lower death rate from coronary heart disease or nonfatal myocardial infarction than standard care alone (5 year outcome)

N Engl J Med 2018; 379:924-933

Back to Mr. S

- He underwent stress myocardial perfusion imaging.
- Per his RN, he tolerated the procedure well. He is anxious to discharge.

MYOCARDIAL PERFUSION TOMOGRAM INTERPRETATION: No evidence of ischemia or infarction. There is mild dilation of left ventricle with ESV 88 mL. The post-stress left ventricular ejection fraction is 46%. There is global mild degree hypokinesis.

*** ADDITIONAL REPORT - 23-Apr-2018 14:32 ***

NM MPI Rest+Pharm Multi 1 Day

IMPRESSION/SUMMARY INTERPRETATION: Abnormal study.

No myocardial ischemia or infarction.

Mild dilation of left ventricle with mild degree global hypokinesis.
Post-stress LVEF at 46%.

HISTORY: Chest pain. Coronary artery disease. Status post stent placement.

STRESS STUDY: At baseline, blood pressure was 144/87, with a heart rate of 65 beats per minute. Oxygen saturation was 96%.

Regadenoson 0.4 mg was given IV over 15 seconds, followed by 5 mL normal saline given over 15 seconds. Heart rate at baseline was 65 beats per minute and rose to a maximum of 81 beats per minute. The patient's baseline ECG demonstrated sinus rhythm with nonspecific ST-segment changes inferolaterally. Due to presence of baseline ST-segment changes, the stress portion was nondiagnostic. There were no significant arrhythmias noted. The patient complained of shortness of breath with regadenoson infusion. However, this had resolved by the conclusion of the study. Technetium-99m was injected about 30 seconds after completing the IV regadenoson infusion, and the patient was observed for 4 to 5 minutes longer. The patient tolerated the procedure well.

Myocardial Perfusion Imaging

MYOCARDIAL PERFUSION TOMOGRAM INTERPRETATION: No evidence of ischemia or infarction. There is mild dilation of left ventricle with ESV 88 mL. The post-stress left ventricular ejection fraction is 46%. There is global mild degree hypokinesis.

*** ADDITIONAL REPORT - 23-Apr-2018 14:32 ***

NM MPI Rest+Pharm Multi 1 Day

IMPRESSION/SUMMARY INTERPRETATION: Abnormal study.

No myocardial ischemia or infarction.

Mild dilation of left ventricle with mild degree global hypokinesis.
Post-stress LVEF at 46%.

[redacted]

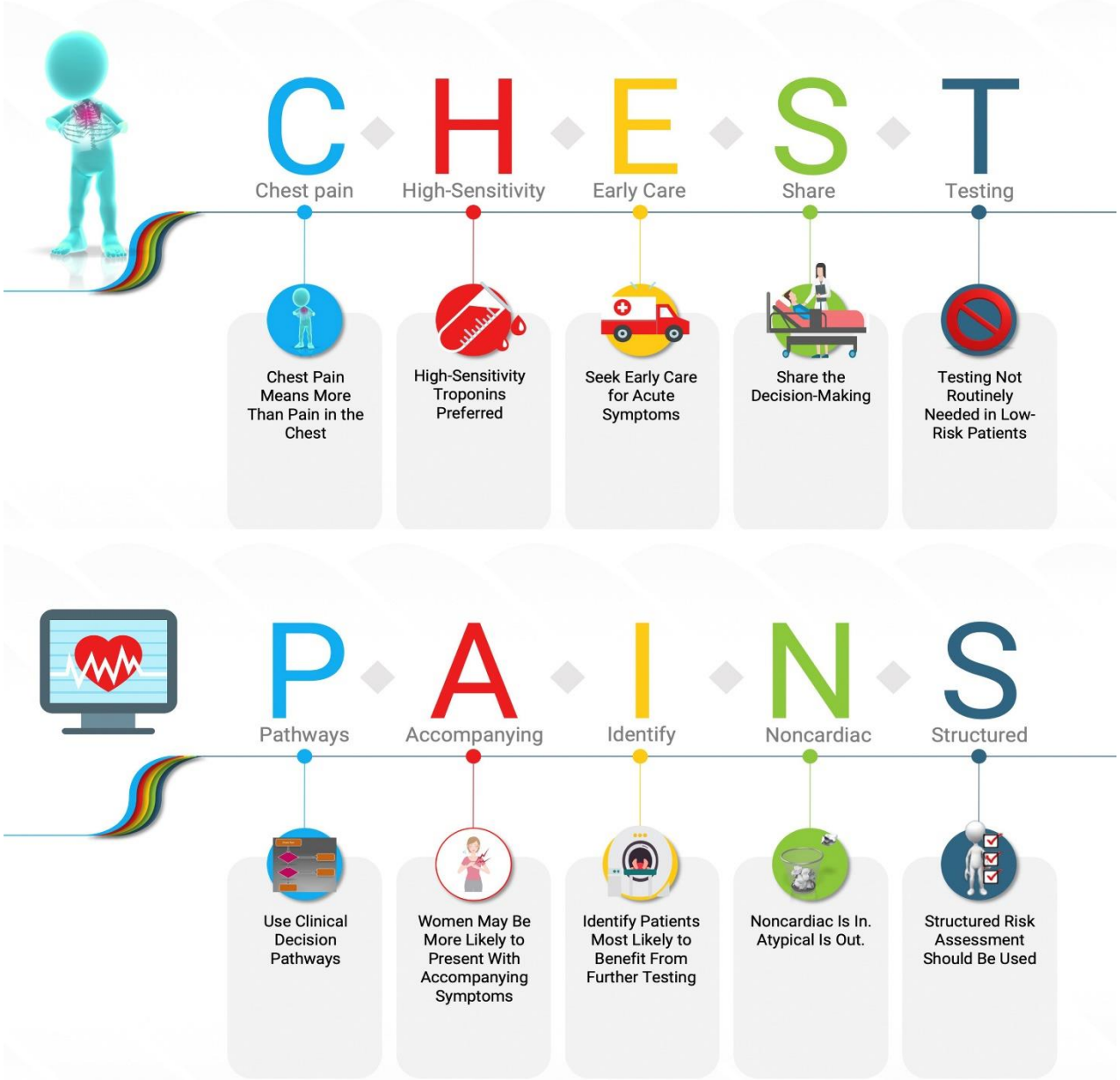
STRESS STUDY: At baseline, blood pressure was 144/87, with a heart rate of 65 beats per minute. Oxygen saturation was 96%.

Regadenoson 0.4 mg was given IV over 15 seconds, followed by 5 mL normal saline given over 15 seconds. Heart rate at baseline was 65 beats per minute and rose to a maximum of 81 beats per minute. The patient's baseline ECG demonstrated sinus rhythm with nonspecific ST-segment changes inferolaterally. Due to presence of baseline ST-segment changes, the stress portion was nondiagnostic. There were no significant arrhythmias noted. The patient complained of shortness of breath with regadenoson infusion. However, this had resolved by the conclusion of the study. Technetium-99m was injected about 30 seconds after completing the IV regadenoson infusion, and the patient was observed for 4 to 5 minutes longer. The patient tolerated the procedure well.

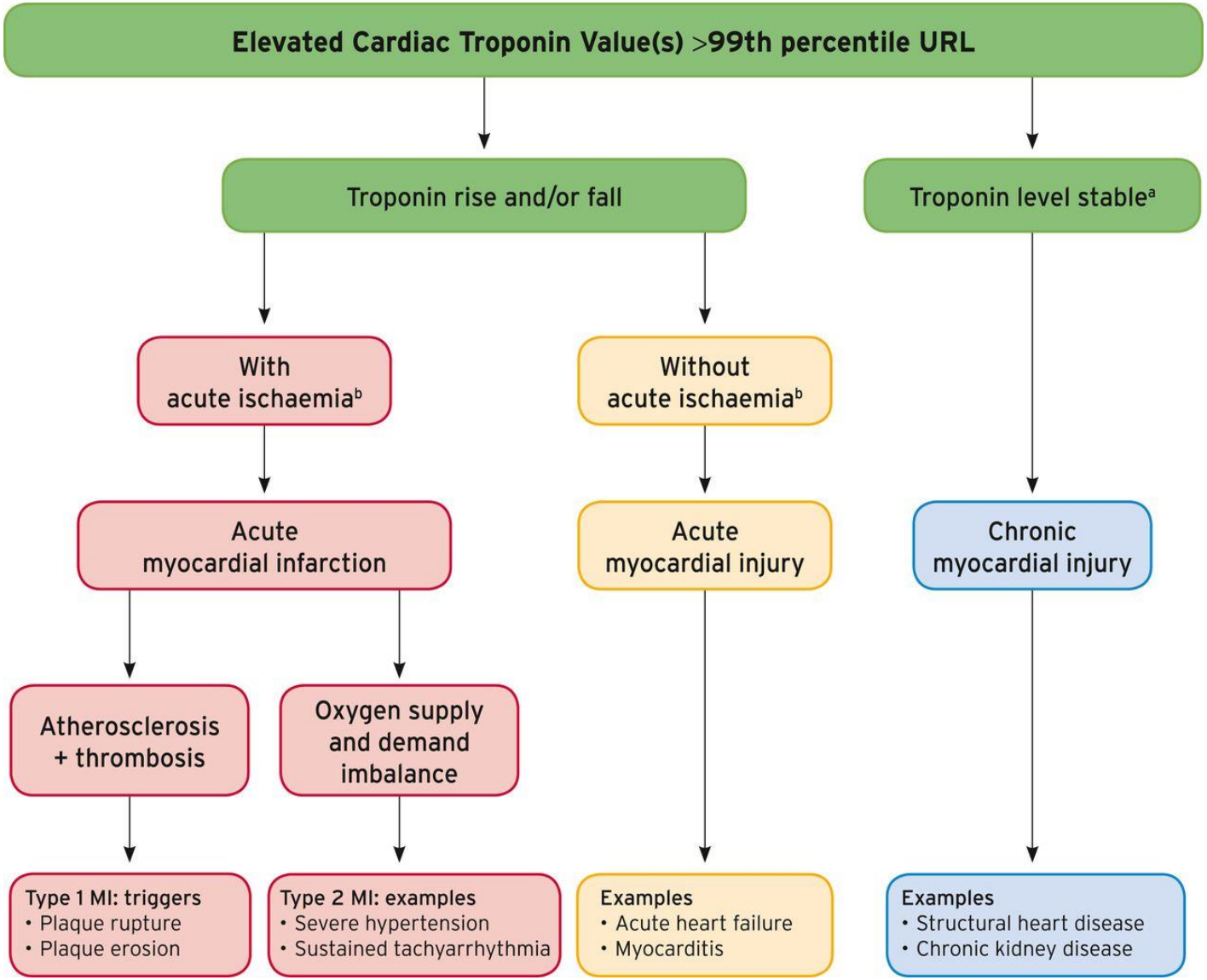
Balanced ischemia

Mr. S

- He was eventually taken to the OR and underwent 3-vessel CABG
- Unfortunately, he is having a hard time with the recommended “lifestyle changes”



Circulation. 2021;144:e368–e454

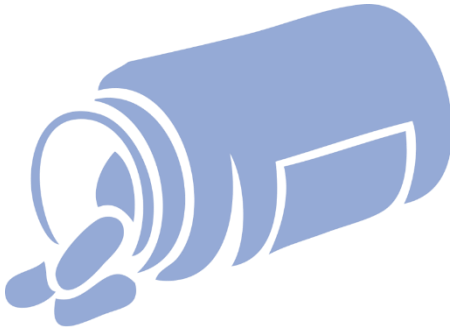


Thygesen K, et al. Journal of American College of Cardiology. DOI: 10.1016/j.jacc.2018.08.1038.

ACS Treatment

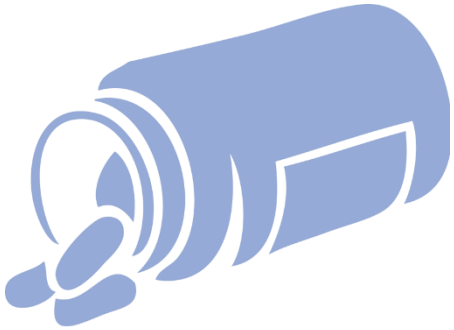
- MONA is no more…

ACS Treatment: What's New-ish?



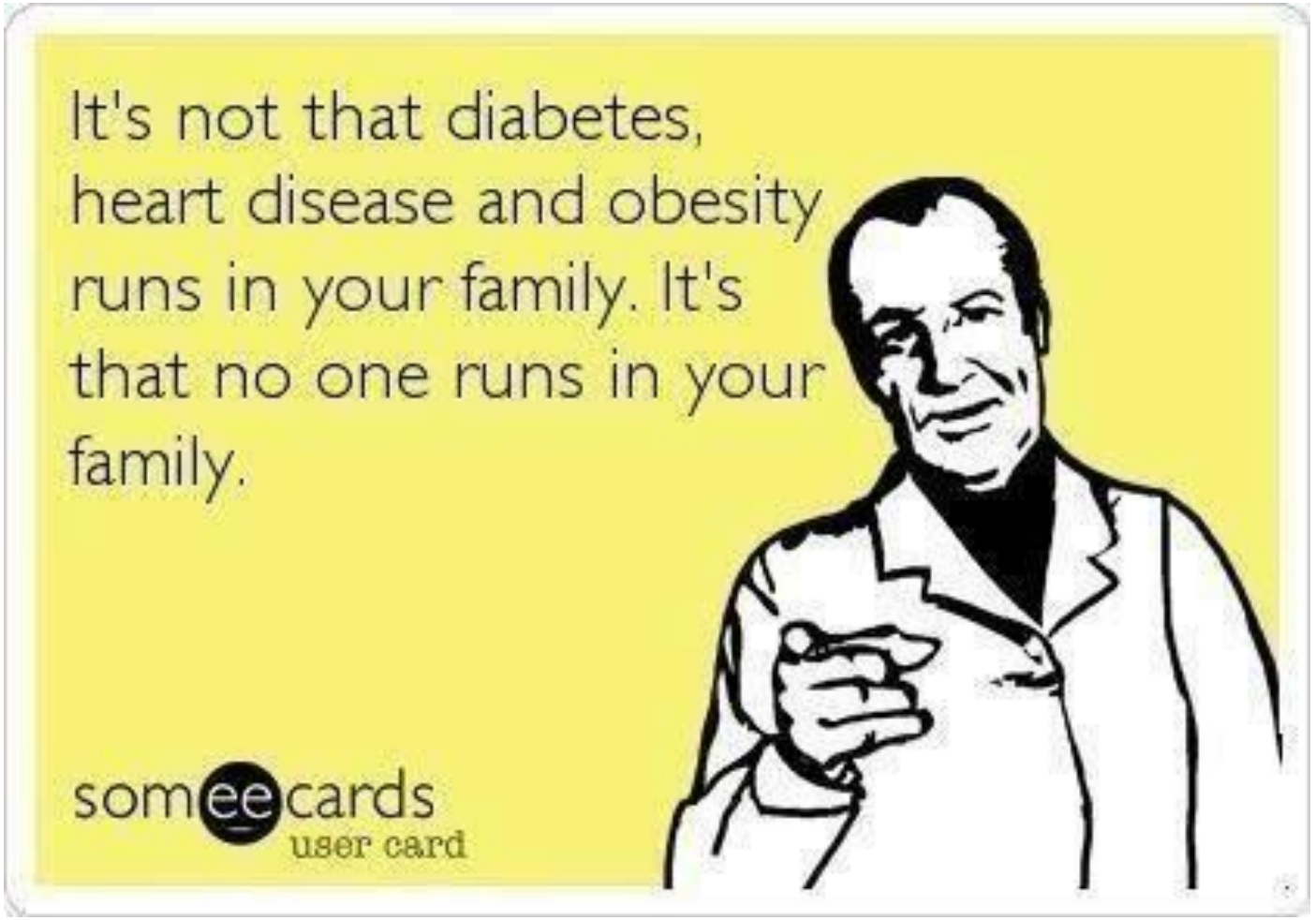
- **P2Y12 Inhibitors**
  - Ticagrelor and prasugrel provide the greatest reductions in risk of recurrent MI and stent thrombosis
    - Of the two, **ticagrelor** is best!
      - Better CV and all-cause mortality
      - Lower bleeding risk
  - **POPular AGE** trial suggests **clopidogrel** as reasonable alternative for older patients[31]
    - Lowest bleeding risk associated with clopidogrel
- **Analgesics**
  - **Morphine** = is it still the best analgesic in ACS?
    - Recent studies show decreased antiplatelet effect, possible increased risk of in-hospital mortality, in-hospital MI, and recurrent ischemia[34, 36]

ACS Treatment: What's New-ish?



- **Oxygen**
  - Only in hypoxic patients!
  - Above-normal oxygen levels can cause vasoconstriction[13]
  - Supplemental O2 with normal O2 sats associated with:
    - ↑ early myocardial injury
    - larger myocardial infarct size assessed at 6 months

- **PCSK9 Inhibitors**
  - **Alirocumab** – now indicated for risk reduction of MI, stroke, and unstable angina requiring hospitalization in those with established coronary artery disease
  - **EVOPACS** trial[37]: Evolocumab + high-intensity statin therapy substantially reduced LDL-C, >95% of patients in target range LDL-C, safe
    - Enough evidence to warrant in-hospital use?



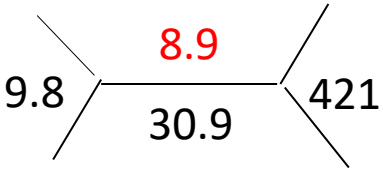
https://www.someecards.com/usercards/viewcard/MjAxMy1jN2Q2ZjExODBmZmIwNGY0/

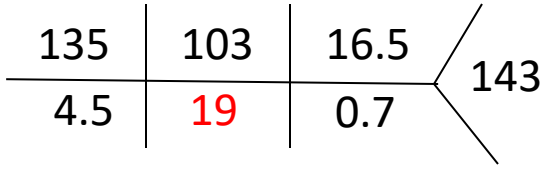
Mrs. F

- 48 YO F with asthma, microcytic anemia 2/2 menorrhagia and uterine fibroids presents to the ED with DOE X 4 weeks and R shoulder and chest pain X 4 days.

Mrs. F

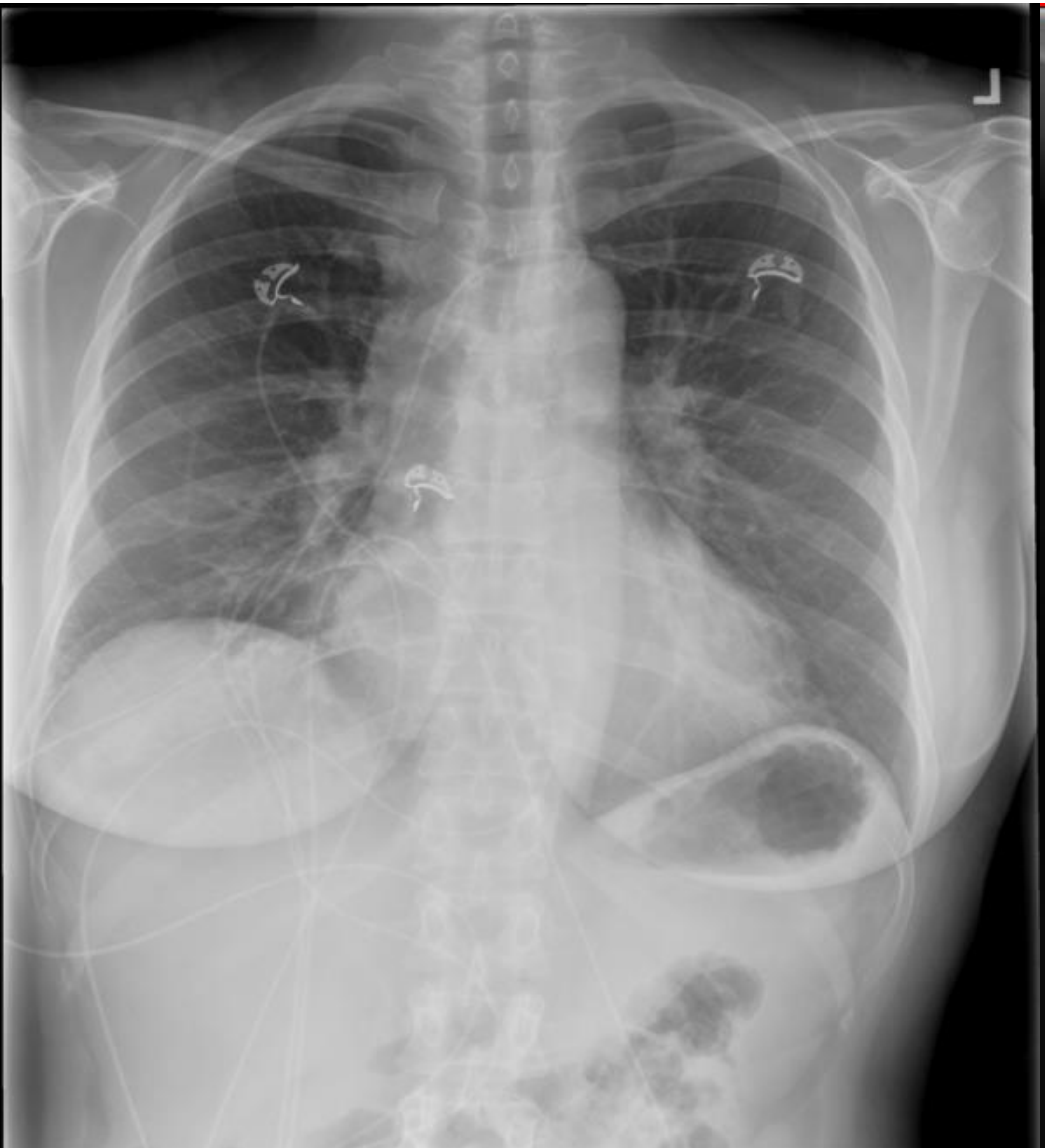
- **Vitals:**
  - T 36.5 C; HR 117 bpm; BP 150/94 mmHg; RR 24 br/min; SpO2 85% RA
- **Labs:**



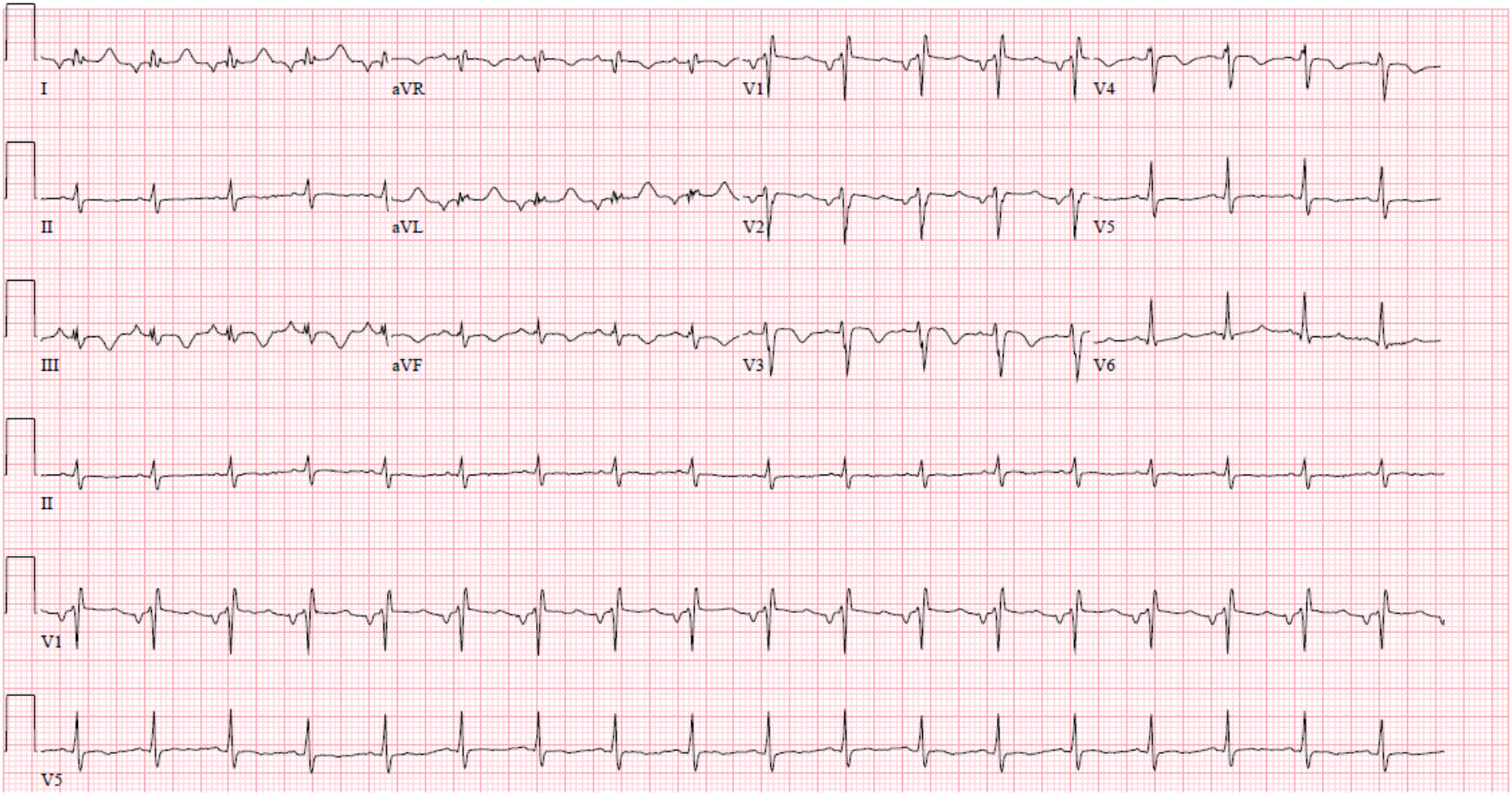


hs-cTnT: 5 ng/L (female ≤ 10 ng/mL)
NT-Pro BNP: **6,204** pg/mL (<248 pg/mL)
D-Dimer: **5,924** ng/mL (< 500 ng/mL*)

Chest X-ray



Admission ECG (no priors)



(Modified) Wells Score for PE

Criteria	Scoring
Clinical symptoms of DVT	3.0
Other diagnosis less likely than PE	3.0
HR > 100	1.5
Immobilization ≥ 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy	1.0

Pretest Probability	Score
High	> 6.0
Moderate	2.0 to 6.0
Low	< 2.0

Modified Wells Criteria	Score
PE likely	> 4.0
PE unlikely	≤ 4.0

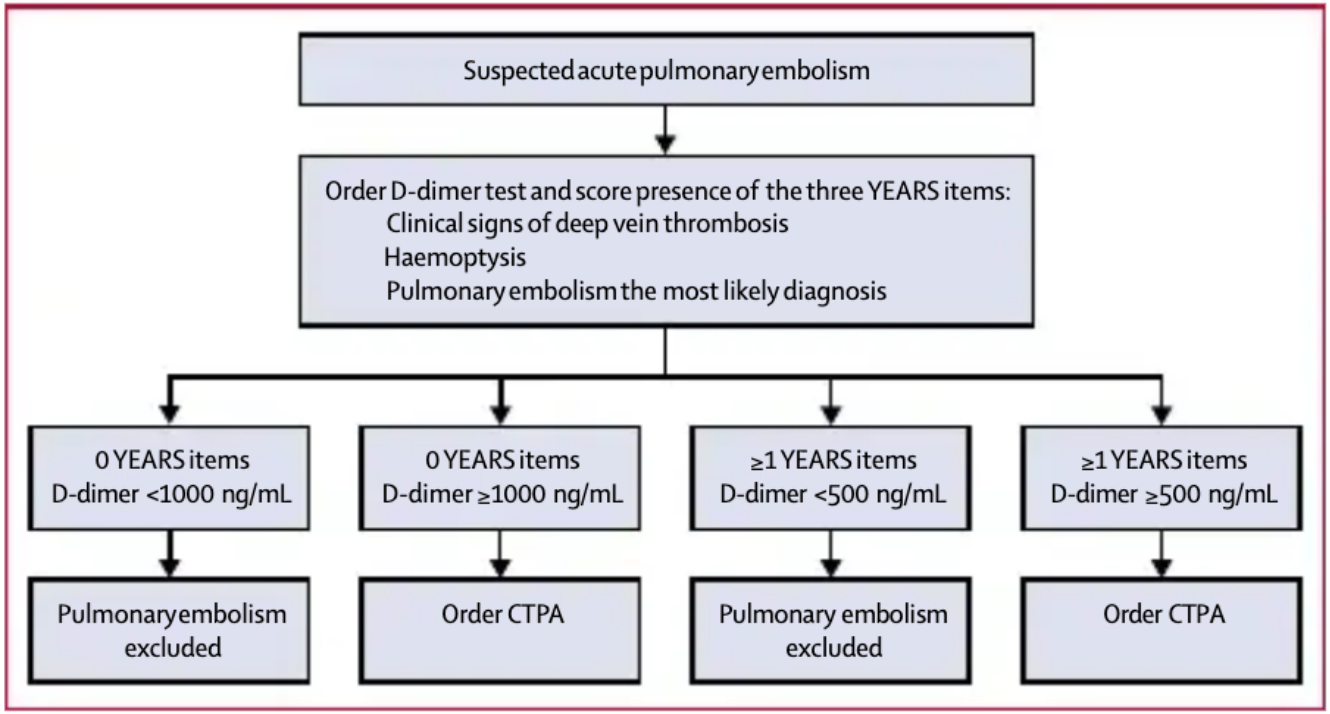
(Modified) Wells Score for PE

Wells Category	Recommendation
Low risk (< 2 points) 1.3% incidence of PE	Consider d-dimer testing or applying PERC rule
Intermediate risk (2-6 points) 16.2% incidence of PE	Consider high sensitivity d-dimer or CTA
High risk (> 6 points) 37.5% incidence of PE	D-dimer NOT recommended, consider CTA

Modified Wells Category	Recommendation
PE unlikely (0-4 points) 12.1% incidence of PE	Consider high-sensitivity d-dimer testing
PE likely (> 4 points) 37.1% incidence of PE	Consider CTA

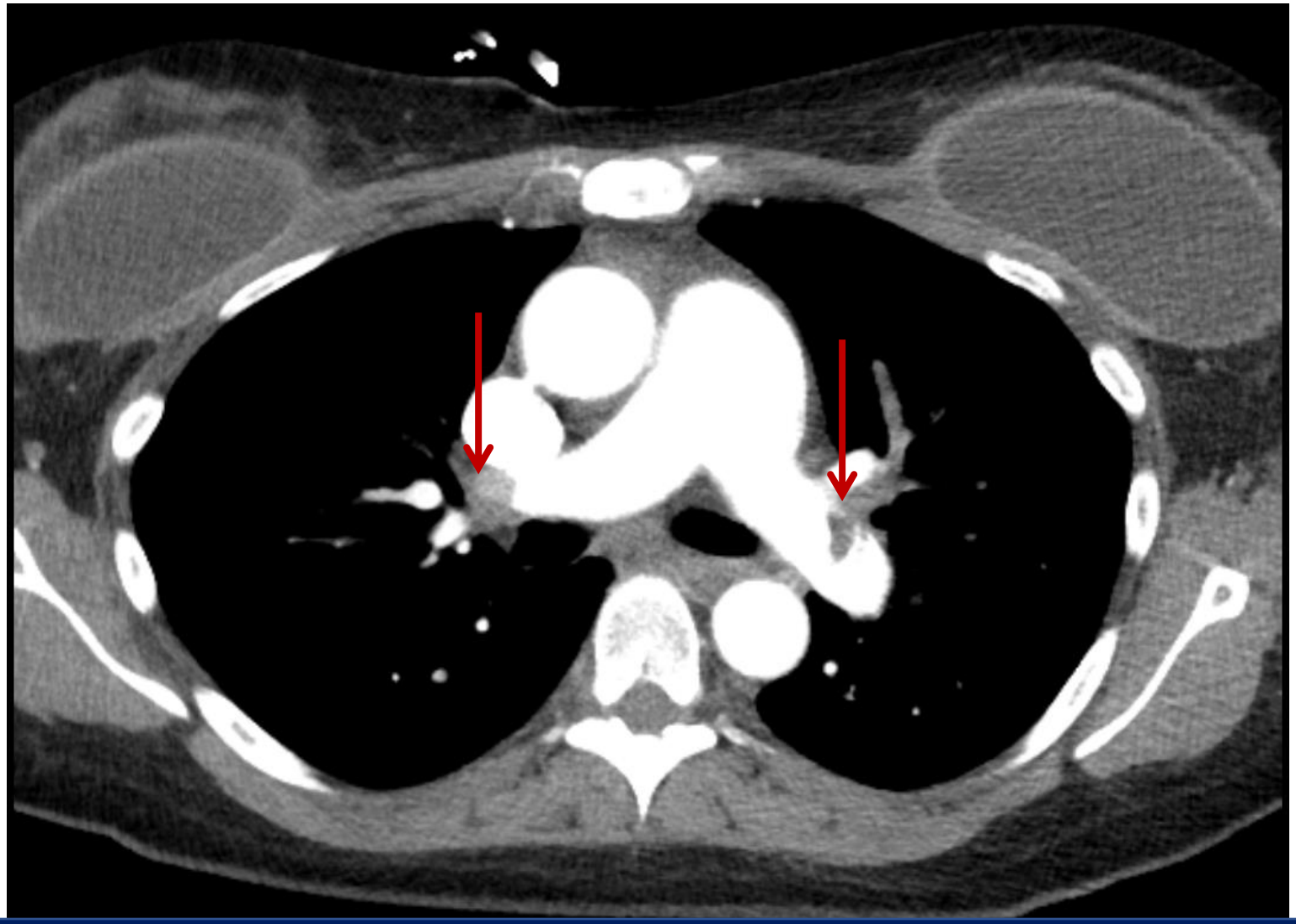
- If d-dimer is + in any scenario, proceed to CTA; d-dimer alone is not enough to make diagnosis.
- Use age adjusted d-dimer if appropriate.
- Before ordering, consider that d-dimer may be elevated for a variety of other reasons.

YEARS Clinical Decision Rule[48]



- 14% decrease in CTPA as compared to Wells'
  - Age adjusted D-dimer would decrease this %
- 3-month incidence of VTE in patients who did not undergo CTPA was 0.43% in YEARS vs 0.34% in a meta-analysis of similarly structured 2 tier algorithm)

CT Pulmonary Angiography



Latest Guidelines

- **ESC Guidelines for Acute PE in collaboration with ERS 2019** [45]
  - Some Highlights:
    - Definition of hemodynamic instability, high-risk PE, algorithm for high-risk tx
    - Assessment of PE severity and early PE-related risk recommended
    - Assessment of RV by imaging/biomarkers should be considered even in lowest PESI
    - Risk factors for recurrence classified to high, intermediate, low risk

Latest Guidelines

- **American Society of Hematology (ASH) Guidelines for Management of VTE 2020: Treatment of DVT and PE [52]**
  - PE highlights:
    - DOAC > Vitamin K
      - No specific recommendation as to which DOAC – consider cost, once vs. twice daily dosing, the need for parenteral anticoagulation, and renal function
      - DOACs may not be best choice in those with CrCl < 30, moderate to severe liver disease, antiphospholipid syndrome
    - PE and hemodynamic compromise >> thrombolytic therapy followed by anticoagulation rather than anticoagulation alone
    - RV dysfunction but no hemodynamic compromise (submassive PE) >> anticoagulation alone
    - PE and thrombolysis appropriate >> use systemic over catheter-directed (conditional, low certainty)
    - No IVC filter unless AC contraindicated
    - Breakthrough PE with therapeutic VKA >> use LMWH over DOAC

Latest Guidelines

- **Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline 2021** [53]
- PE highlights
  - PE >> DOAC over VKA (apixaban, dabigatran, edoxaban, or rivaroxaban)
  - PE with cancer >> Oral Xa inhibitor (apixaban, edoxaban, rivaroxaban) over LMWH
  - PE and associated hypotension (w/o high risk of bleed) >> systemic thrombolytics (weak, low certainty)
  - PE and thrombolytics appropriate >> systemic thrombolysis over catheter-directed (weak, low certainty)
  - PE and hypotension WITH either high bleed risk, failed systemic lytics, or shock that may cause death before systemic lytics take effect >> catheter-directed thrombolysis (weak, low certainty)

Baseline Assessment of Severity/Risk Stratification [45]

PE Severity Index (PESI)

Parameter	Original version[226]	Simplified version[229]
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic BP <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per min	+20 points	–
Temperature <36°C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point

	Original Classification	Simplified Classification
Risk strata[a]		
	Class I: ≤65 points very low 30 day mortality risk (0–1.6%) **Class II: 66–85 points** low mortality risk (1.7–3.5%)	**0 points =** 30 day mortality risk 1.0% (95% CI 0.0–2.1%)
	Class III: 86–105 points moderate mortality risk (3.2–7.1%) **Class IV: 106–125 points** high mortality risk (4.0–11.4%) **Class V: >125 points** very high mortality risk (10.0–24.5%)	**≥1 point(s) =** 30 day mortality risk 10.9% (95% CI 8.5–13.2%)

Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolisms developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart Journ 2020;41(4):543-603. https://doi.org/10.1093/eurheartj/ehz405

Prognostic Risk Assessment [45]

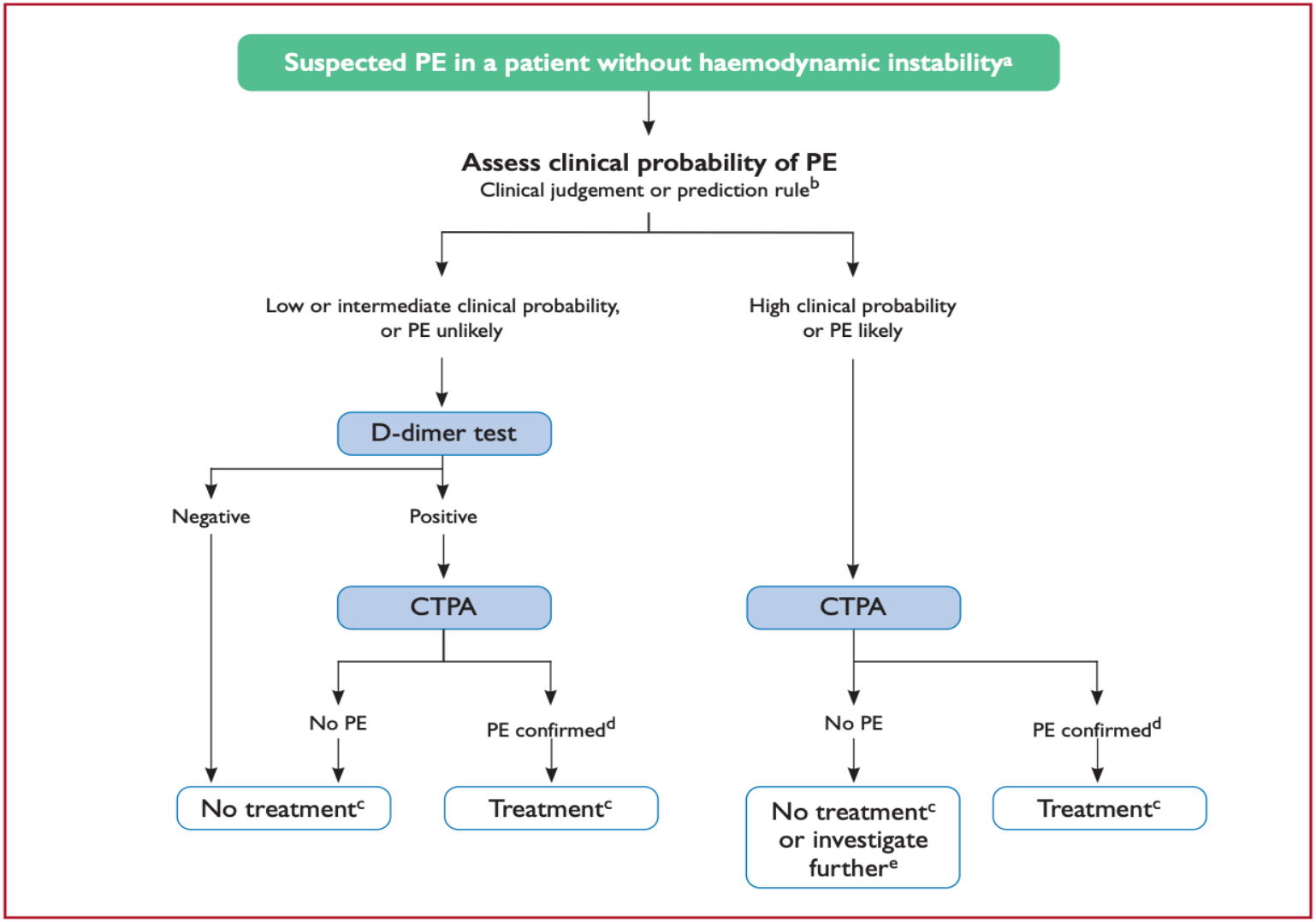
Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

©ESC 2019

- Hemodynamic instability defined by ESC as one of the following:
  - Cardiac arrest
  - Obstructive shock (SBP < 90mmHg / vasopressors required to achieve SBP ≥ 90 + end organ hypoperfusion)
  - Persistent hypotension (SBP < 90 or SBP drop ≥ 40 for >15 min)

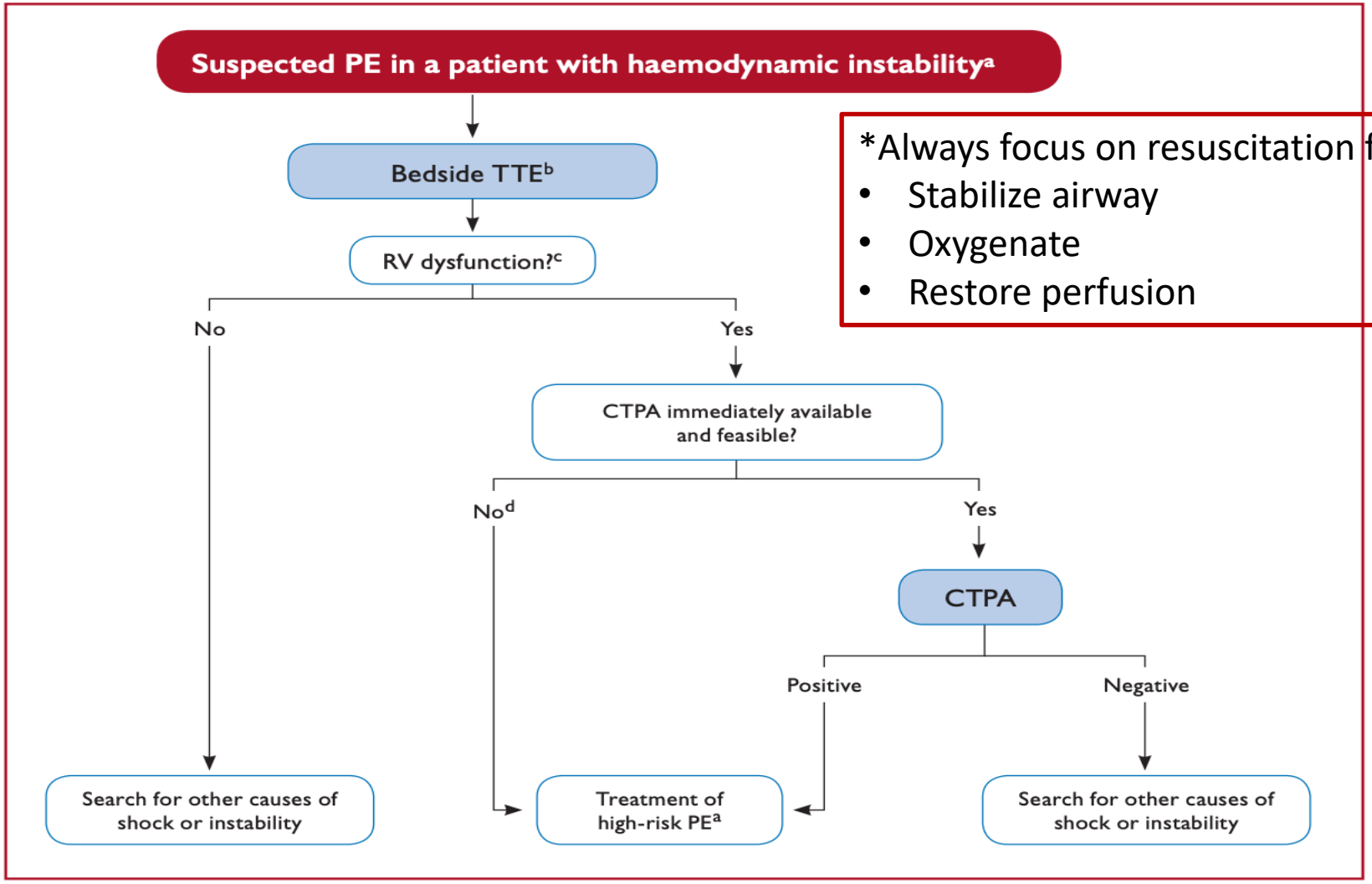
Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolisms developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart Journ 2020;41(4):543-603. https://doi.org/10.1093/eurheartj/ehz405

ESC Acute PE Guideline Update[45]



Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolisms developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart Journ 2020;41(4):543-603. https://doi.org/10.1093/eurheartj/ehz405

ESC Acute PE Guideline Update[45]

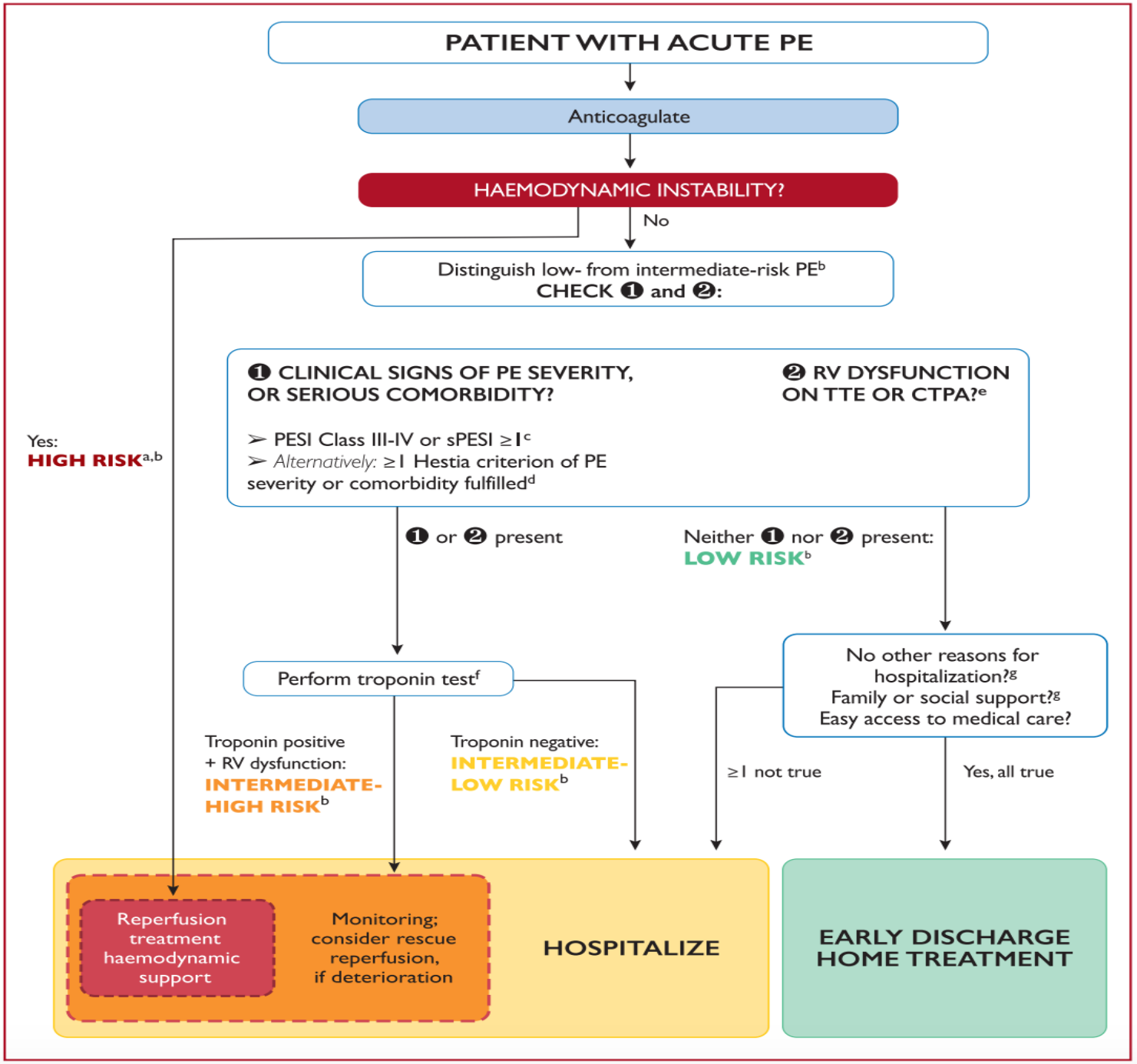


*Always focus on resuscitation first!!

- Stabilize airway
- Oxygenate
- Restore perfusion

Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolisms developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart Journ 2020;41(4):543-603. https://doi.org/10.1093/eurheartj/ehz405

ESC Acute PE Guideline Update[45]



Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolisms developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart Journ 2020;41(4):543-603. https://doi.org/10.1093/eurheartj/ehz405

PE in COVID-19

- **Pulmonary Thrombosis and Thromboembolism in VTE in COVID-19: CHEST Review (Oct. 2021)**
  - at least two distinct, but interrelated, processes: a hypercoagulable state responsible for large-vessel thrombosis and thromboembolism and direct vascular and endothelial injury responsible for in situ microvascular thrombosis
  - Jimenez et al. -- pooled incidence of VTE in patients with COVID-19 was 17% (12% for DVT, 7.1% pulmonary embolism [PE])
  - Klok et al -- 31% incidence of thrombotic events in 184 **critically ill** patients, 81% of the thrombotic events being PE
- **Aggressive prophylactic strategy??**
  - **Therapeutic dose vs. standard prophylactic dose**

Back to Mrs. F

Transthoracic Echocardiogram:

Final Impressions
1. Findings consistent with cor pulmonale - possibly acute.
2. Moderate right ventricular enlargement with moderate-severe systolic dysfunction (FAC 26%).
3. Estimated right ventricular systolic pressure 93 mmHg (systolic blood pressure 170 mmHg).
4. Tricuspid annulus dilatation with moderate-severe functional tricuspid regurgitation.
5. Severely dilated inferior vena cava with no inspiratory collapse and dilated hepatic veins.
6. Normal left ventricular systolic function with concentric remodeling and D-shaped left ventricle, LVEF estimated 65-70%.
7. No significant mitro-aortic valve disease.
8. No pericardial effusion.
9. No previous studies available for comparison.
10. Emergency communication to Palermo, J (1-5431) at Internal Medicine regarding the critical echocardiography results was completed and acknowledged.

Findings
Echocardiographic images interpreted at MCA - Hospital campus.
Color flow and spectral Doppler performed in part to assess valvular heart disease.
Emergency communication to Palermo, J (1-5431) at Internal Medicine regarding the critical echocardiography results was completed and acknowledged.
LEFT VENTRICLE:
Normal left ventricular systolic function.
Estimated ejection fraction range 65 % - 70 %.
No regional wall motion abnormalities.
Flattening of the ventricular septum.
RIGHT VENTRICLE:
Moderate right ventricular enlargement.
Severe decrease in right ventricular systolic function.
Estimated right ventricular systolic pressure 93 mmHg (systolic blood pressure 170 mmHg).
Calculated right ventricular fractional area change; 26%.

Mrs. F

- Underwent emergent **US guided catheter-directed thrombolysis**

IR Angiogram Pulmonary Bilat
IMPRESSION:
1. Pulmonary angiogram demonstrates acute thrombus within the bilateral pulmonary arteries.
2. Bilateral ultrasound directed thrombolysis catheters (EKOS catheters) were placed.
3. Elevated pulmonary artery pressures.

Orders were placed to have each EKOS catheter running at 0.5 mg tPA per hour. Each EKOS catheter also should have a coolant running at 35 mL/h of normal saline. Each of the sheaths should be running at 500 units per hour of heparin. Hence, the patient will receive 1000 units of heparin per hour. The PTT should not be in the therapeutic range. The patient should not receive any more heparin during the thrombolysis phase.

The TPA should be turned off at 8:00 AM on 1/4/18. We will remove the EKOS catheters at this time.

Mrs. F

- At 24 hours → catheter pulled and placed on heparin drip
  - COMPLETE resolution of symptoms!

- Transitioned to rivaroxaban upon discharge
  - IUD placed for her vaginal bleeding

TTE Post-intervention:

Final Impressions
1. D-shaped left ventricle.
2. Calculated left ventricular ejection fraction 55 %.
3. Moderate right ventricular enlargement.
4. Moderate-severe decrease in right ventricular systolic function.
5. Estimated right ventricular systolic pressure 63 mmHg (systolic blood pressure 137 mmHg).
6. Findings consistent with moderate pulmonary hypertension.
7. Averaged right ventricular free wall longitudinal peak systolic strain is -10 %.
8. Moderate tricuspid valve regurgitation.
9. Main pulmonary artery dilatation.
10. Severely dilated inferior vena cava with no inspiratory collapse.
11. Tiny circumferential pericardial effusion.
12. Compared to the report of 01/03/2018 the following changes have occurred: RV size is smaller, RV function has improved slightly, PAP is lower..

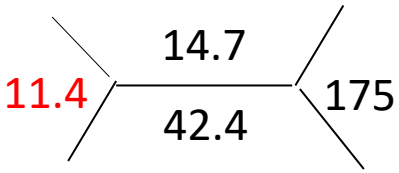
She is still following up with the Vascular Medicine clinic and is planning to undergo a VO2 max test to assess her persistent, significant tachycardia with exertion.

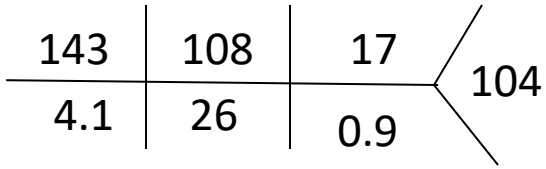
Mr. S

45 YO M with untreated HTN presents to the ED with acute onset of dizziness and severe chest pain with radiation to his back, of acute onset while he was in the shower. He also described bilateral 9/10 flank pain and nausea & emesis.

Mr. S

- **Vitals:**
  - T 37 C; HR 78; BP 189/99; RR 20 br/min; 96% RA
- **Labs:**

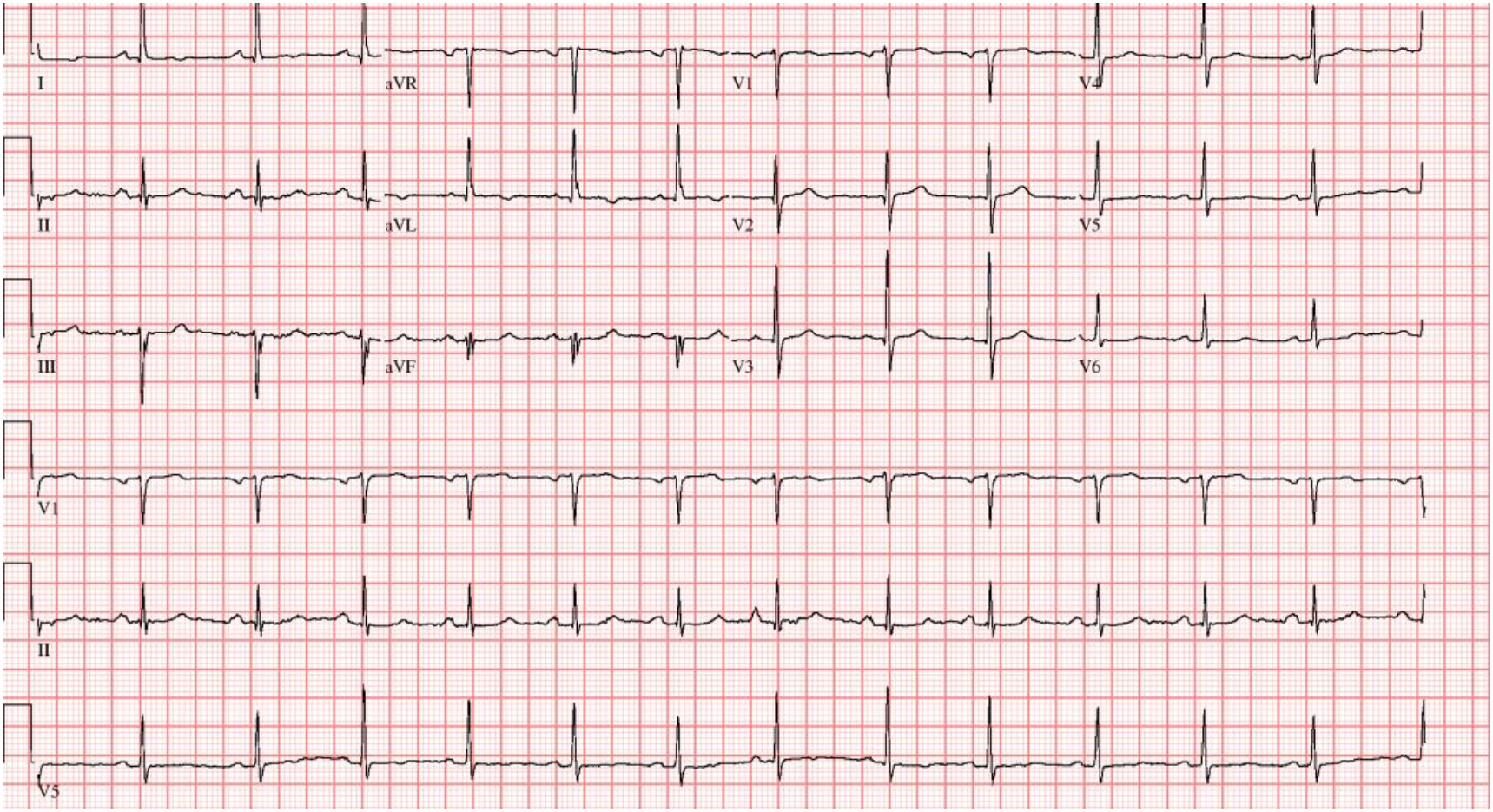




hs-cTnT: 8 ng/L (male ≤ 15 ng/L)

D-dimer: 1,208 ng/mL (< 500 ng/mL*)

Admission ECG



Chest X-ray

Mr. S

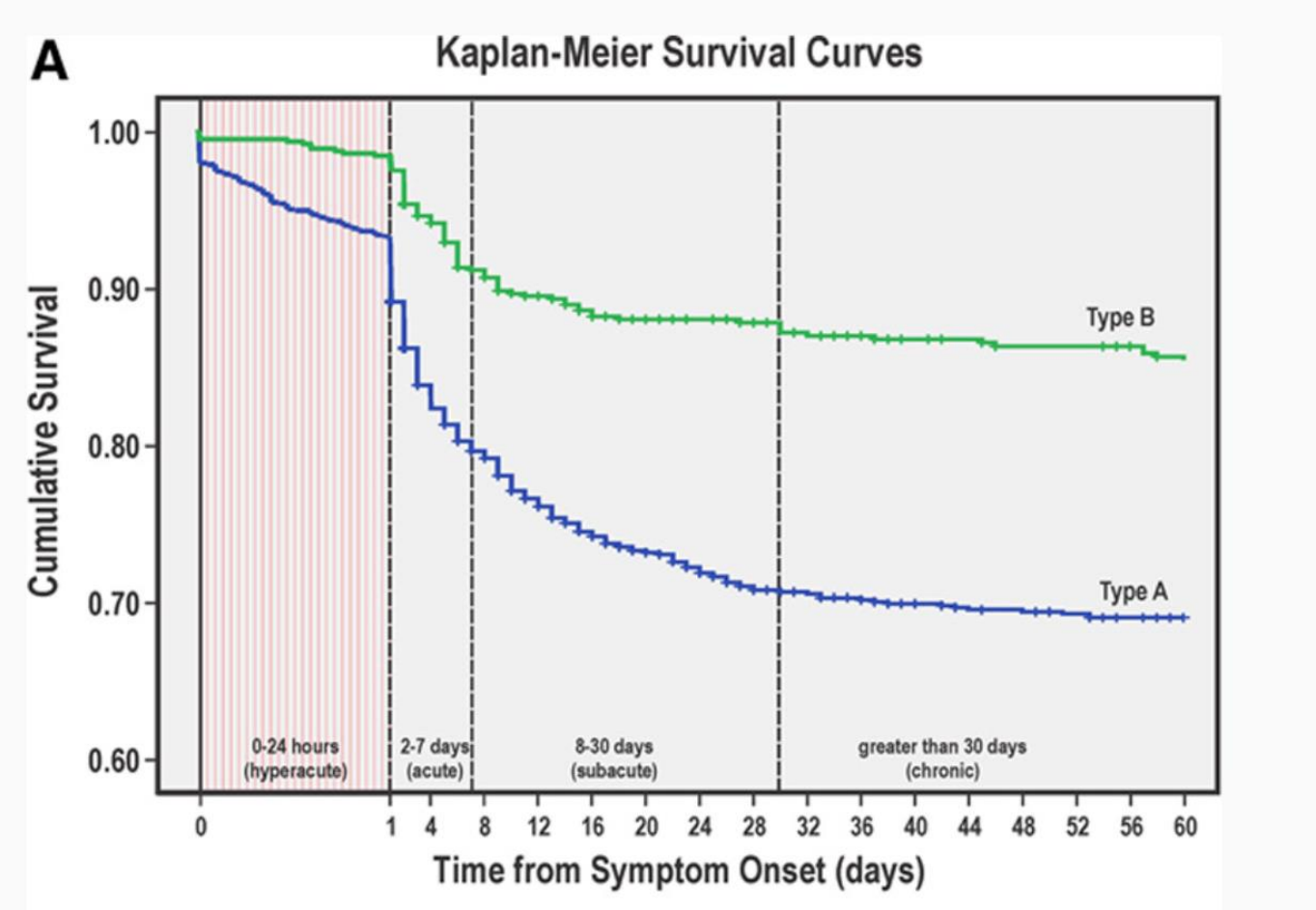
- You are called to see the patient in the ED, so you quickly review his records from when he was admitted to the hospital with atypical chest pain 1 month prior…

TTE (one month prior):

Final Impressions
1. Normal left ventricular chamber size. Hyperdynamic left ventricular systolic function.
2. Calculated 2-D monoplane volumetric left ventricular ejection fraction 73 %.
3. Mid left ventricular maximal instantaneous Doppler gradient rest 6 mm Hg; Valsalva 28 mm Hg.
4. Concentric remodeling (increased wall thickness to cavity ratio).
5. Findings consistent with normal left ventricular filling pressure.
6. Mild right ventricular enlargement with normal systolic function.
7. Normal left atrial size.
8. No hemodynamically significant valvular heart disease.
9. Normal inferior vena cava size with normal inspiratory collapse (>50%).
10. Mild ascending aorta dilatation (diameter 41 mm at proximal level).
11. No pericardial effusion.

ECG and CXR are unchanged.

Acute Aortic Dissection



Evangelista A, Isselbacher EM, Bossone E, et al. Insights From the International Registry of Acute Aortic Dissection: A 20-Year Experience of Collaborative Clinical Research. Circulation 2018;137:1846-1860. https://doi.org/10.1161/CIRCULATIONAHA.117.031264

Acute Aortic Dissection

Risk Factors:
- Hypertension (76.6%)
- Hx of atherosclerosis (27%)
- Known aortic aneurysm or previous aortic dissection
- Previous cardiac surgery
- Bicuspid aortic valve
- Marfan syndrome
- Iatrogenic
- Cocaine use
- Age
- Male sex

Signs:
- Diastolic murmur (40% of type A)
- Hypotension (>25%)
- Syncope (13%)
- Pulse deficits
- Aortic regurgitation
- CHF
- MI
- Cardiogenic shock
- Neurologic symptoms

Symptoms:
- Sudden onset of severe chest pain (type A) or back pain (type B)
  - Abrupt onset
- Painless (6.3%)
- Atypical presentation – abdominal pain

Aortic Dissection Detection Risk Score (ADD-RS)

- **ADD-RS:**
  1. **High risk conditions**: Marfan syndrome or other CT disease, aortic valvular disease, family history, gene mutation, known thoracic aortic aneurysm, previous cardiac surgery or aortic manipulation

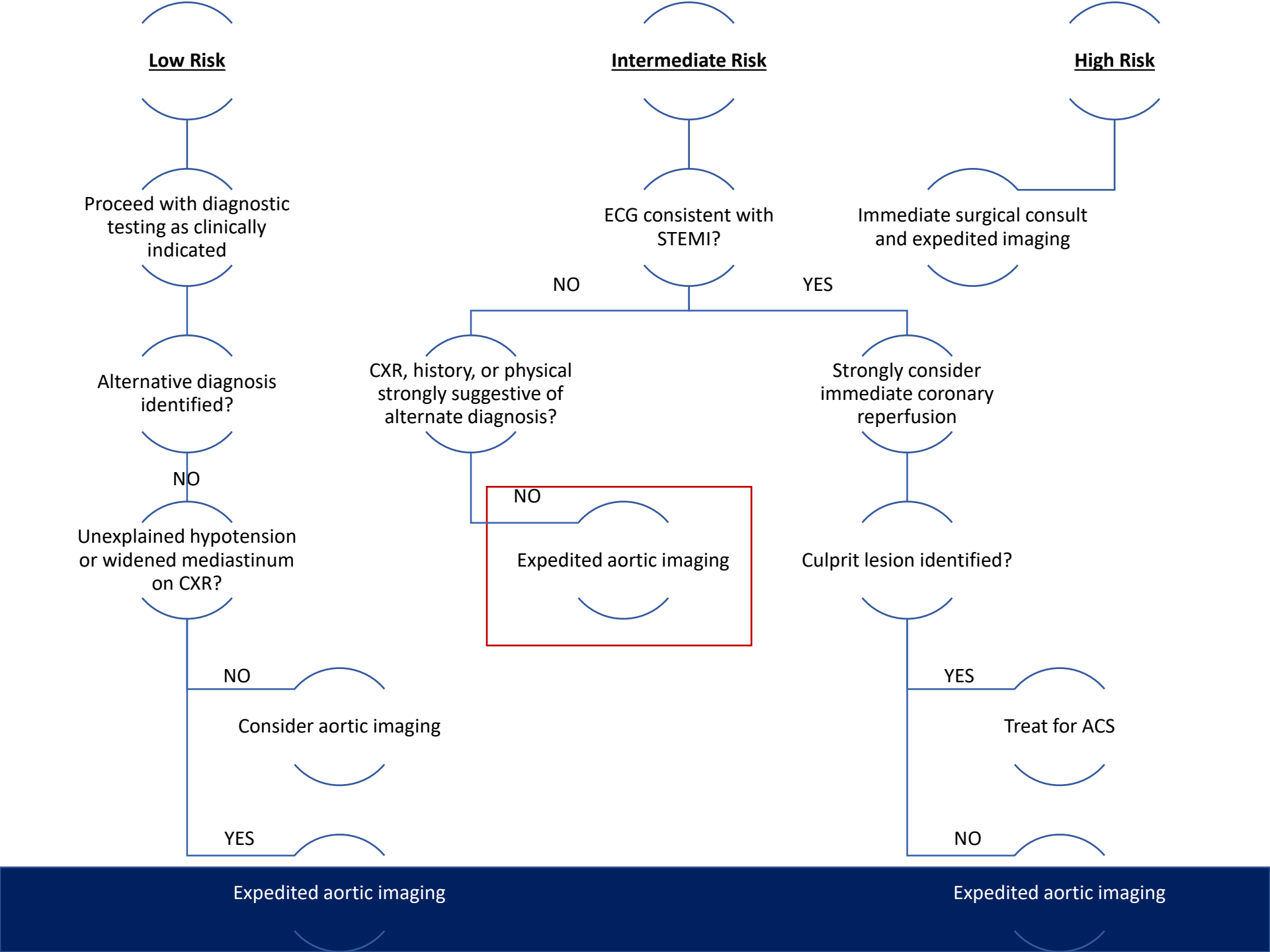
  1. **High risk features:** pain in the chest back or abdomen that is abrupt, severe, or a ripping/tearing sensation

  1. **High risk exam findings:** pulse deficit, SBP difference, focal neurologic deficit, aortic diastolic murmur, shock

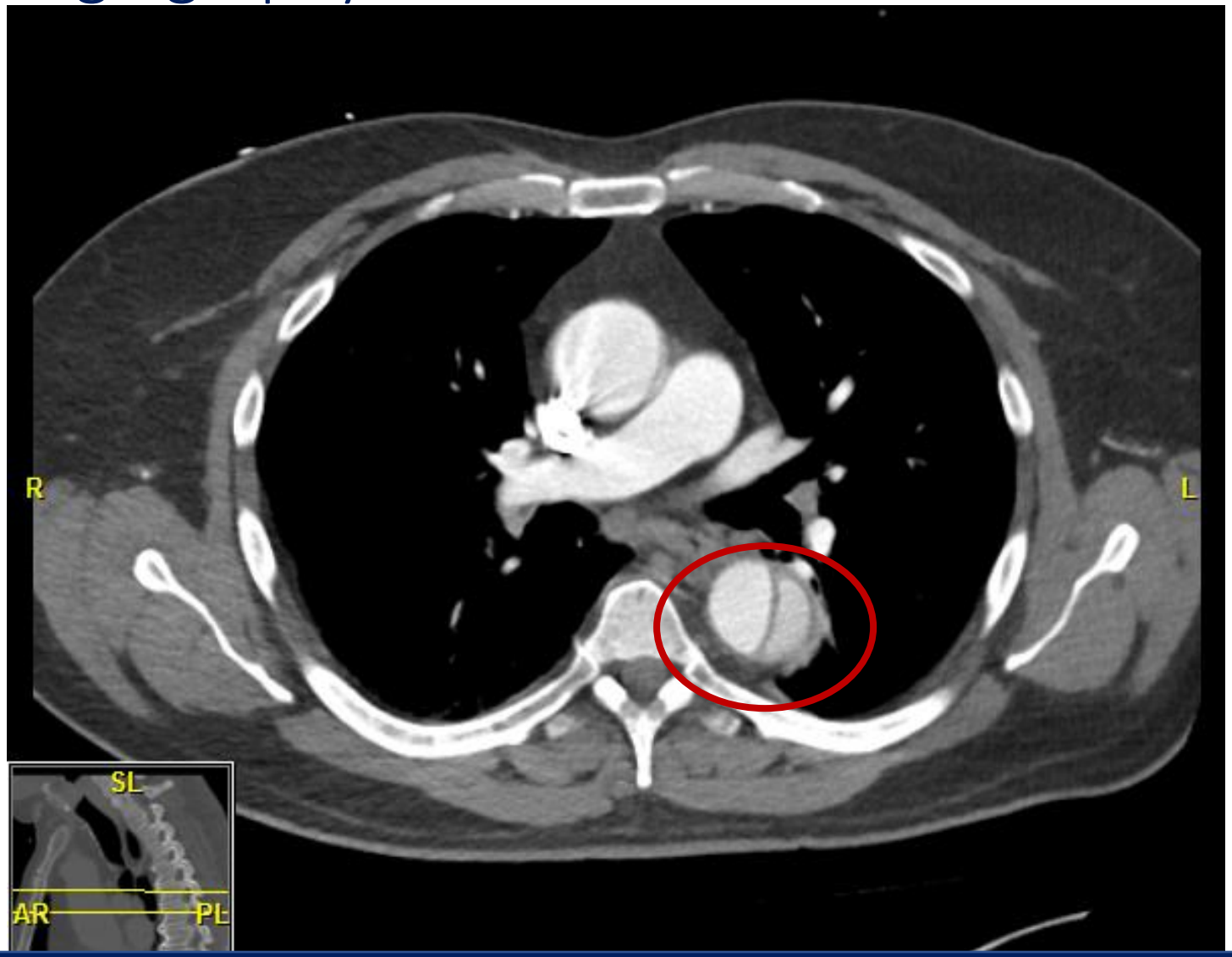
- **Score 0-3** based on the presence of any positives in each of the categories
  - low risk = 0
  - intermediate risk = 1
  - high risk = 2-3

D-Dimer in Acute Aortic Dissection

- **[ADD-RS score 0 or 1 + D-dimer < 500 ng/mL]** is a *possible* rule out diagnostic strategy [21]
  - If ADD-RS >1 should proceed to CT Angiography regardless of D-dimer
- Likely most useful in first 24 hours, for low-risk patients


Low Risk
Intermediate Risk
High Risk
Proceed with diagnostic testing as clinically indicated
ECG consistent with STEMI?
Immediate surgical consult and expedited imaging
NO
YES
Alternative diagnosis identified?
CXR, history, or physical strongly suggestive of alternate diagnosis?
Strongly consider immediate coronary reperfusion
NO
NO
Expedited aortic imaging
Unexplained hypotension or widened mediastinum on CXR?
Culprit lesion identified?
NO
Consider aortic imaging
YES
Treat for ACS
YES
NO
Expedited aortic imaging
Expedited aortic imaging

CT Angiography Chest



Mr. S

CT Angio Chest

CONCLUSION:
1. Type B aortic dissection in the mid descending thoracic aorta with slow flow in the false lumen and intramural hematoma extending into the abdominal aorta. Please see dedicated abdominal CT for detailed intra-abdominal findings.

CT Angio Abd+Pelvis

CONCLUSION:
1. Partially imaged type B aortic dissection without extension of the dissection flap into the abdominal aorta described in detail below and on the concurrent chest CT. There is intramural hematoma within the abdominal aorta extending into the left common iliac artery. No abdominal aortic aneurysm or evidence of rupture.

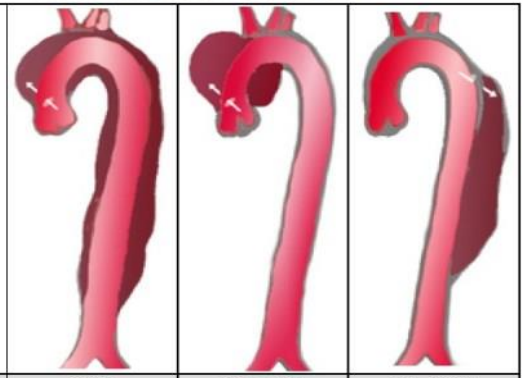
Management of Aortic Dissection

- **If hypotension or shock**:
  - IVF bolus +/- vasopressors
  - Surgical consultation
  - Review/additional imaging studies
    - Severe AR? Cardiac tamponade?

- **If stable**, IV labetalol preferred
  - Maintain HR <60, SBP <120 mmHg
- Pain control is essential
  - IV morphine reduces force of cardiac contraction

- Dissections involving the **ascending thoracic aorta (Type A)** should have urgent operative or interventional management if able
  - Some type B dissections may also have indications for urgent surgery

Classification of aortic dissection



Percentage	60%	10–15%	25–30%
Type	DeBakey I	DeBakey II	DeBakey III
	Stanford A (Proximal)		Stanford B (Distal)

Back to Mr. S

- Admitted to the ICU, started on esmolol drip + nicardipine drip
- **Vascular Surgery consult**: recommended conservative management and serial imaging studies

- Complicated hospital course, eventually discharged hospital day 5 on the following regimen:
  - labetalol 400mg TID
  - lisinopril 40mg QD
  - amlodipine 10mg QD
  - chlorthalidone 25mg QD

In Summary…

- Have a high index of suspicion for potentially deadly causes of chest pain
- Cardiac chest pain not always typical
- Risk stratification helpful in undifferentiated CP
  - Always couple with clinical judgement
- Assessment of severity and risk important in optimal management of PE
- Acute aortic dissection often under-recognized
  - D-dimer helpful rule out, ADD-RS

References

1. Swap CJ, Nagurney JT. Value and Limitations of Chest Pain History in the Evaluation of Patients With Suspected Acute Coronary Syndromes. J*AMA*.2005;294(20):2623-2629.
2. Long B, Oliver J, Streitz M, et al. An End User's Guide to the HEART Score and Pathway. *Am Journ Emerg Med*. 2017;35(9):1350-1355.
3. Arbab-Zadeh A. Stress testing and non-invasive coronary angiography in patients with suspected coronary artery disease: time for a new paradigm. *Heart International*. 2012;7(1):e2.
4. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. *J Am Coll Cardiol.* 2010;56(25):e50-e103
5. Nieman K, Hoffmann U. Cardiac computed tomography in patients with acute chest pain. Eur Heart J. 2015 Apr 14; 36(15): 906–914
6. Hoffmann U, Truong QA, Schoenfeld DA, et al. Coronary CT angiography versus standard evaluation in acute chest pain. N Engl J Med. 2012;367:299-308.
7. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol. 2008;52(21):1724–32. doi: 10.1016/j.jacc.2008.07.031.
8. Tweet MS, Arruda-Olson AM, Anavekar NS, et al. Stress Echocardiography: What Is New and How Does It Compare with Myocardial Perfusion Imaging and Other Modalities? Current Cardiology Reports. 2015;17:43.
9. Litt HI, Gatsonis C, Snyder B, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. N Engl J Med. 2012;366:1393-403.
10. Hoffmann U, Bamberg F, Chae CU, et al. Coronary computed tomography angiography for early triage of patients with acute chest pain: the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial. J Am Coll Cardiol. 2009;53:1642-50.
11. Pickering J, Than M, Young J, et al. Rapid Rule-out of Acute Myocardial Infarction With a Single High-Sensitivity Cardiac Troponin T Measurement Below the Limit of Detection: A Collaborative Meta-analysis. *Annals Of Internal Medicine* [serial online]. April 18, 2017;Available from: MEDLINE Complete, Ipswich, MA.
12. Garg P, Morris P, Fazlanie AL, et al. Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin. Intern Emerg Med. 2017; 12(2): 147–155. doi: 10.1007/s11739-017-1612-1

References

13. Hofmann R, James SK, Jernberg T, et al. Oxygen Therapy in Suspected Acute Myocardial Infarction. *N Engl J Med*. 2017;377(13):1240.
14. Moradkhan R, Sinoway LI. Revisiting the role of oxygen therapy in cardiac patients. *J Am Coll Cardiol*. 2010;56(13):1013.
15. Meine TJ, Roe MT, Chen AY, Patel MR, et al. Association of intravenous morphine use and outcomes in acute coronary syndromes: results from the CRUSADE Quality Improvement Initiative. *Am Heart J*. 2005 Jun;149(6):1043-9.
16. Kubica J, Adamski P, Ostrowska M, et al. Morphine delays and attenuates ticagrelor exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial. *Eur Heart J.* 2016;37(3):245.
17. Freund Y, Cachanado M, Aubry A. Effect of the Pulmonary Embolism Rule-Out Criteria on Subsequent Thromboembolic Events Among Low-Risk Emergency Department Patients: The PROPER Randomized Clinical Trial. JAMA. 2018;319(6):559.
18. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014;129:479–486.
19. Piazza G, Hohlfelder B, Jaff MR, et al. A prospective, single-arm, multicenter trial of ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: The SEATTLE II study. JACC Cardiovasc Interv. 2015;8:1382–1392.
20. Mangi MA, Rehman H, Bansal V. Ultrasound Assisted Catheter-Directed Thrombolysis of Acute Pulmonary Embolism: A Review of Current Literature. Cureus. 2017 Jul; 9(7): e1492. doi: 10.7759/cureus.1492
21. Nazerian P, Mueller C, Soeiro AM, et al. Diagnostic Accuracy of the Aortic Dissection Detection Risk Score Plus D-Dimer for Acute Aortic Syndromes: The ADvISED Prospective Multicenter Study. Circulation. 2018;137(3):250.
22. Hiratzka LF, Bakris GL, Beckman JA, et al. Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease: ACC/AHA Pocket Guideline: March 2010. Accessed July 26, 2018.
23. Poldervaart JM, et al. Comparison of the GRACE, HEART and TIMI score to predict major adverse cardiac events in chest pain patients at the emergency department. International Journal of Cardiology. 2017; 227: 656-661.
24. Thygesen K, et al. Fourth Universal Definition of Myocardial Infarction (2018). Journal of American College of Cardiology. DOI: 10.1016/j.jacc.2018.08.1038. Accessed July 2019.
25. Body R, et al. The Value of Symptoms and Signs in the Emergent Diagnosis of Patients with Acute Coronary Syndromes. *Resuscitation.* 2010; 81:281-286.
26. Bonello L, Lemesle G, Laine M. Ticagrelor is the Best Antiplatelet Agent for Pretreatment in Patients with ACS. American College of Cardiology. 2016. https://www.acc.org/latest-in-cardiology/articles/2016/06/13/10/01/ticagrelor-is-the-best-antiplatelet-agent-for-pretreatment-in-patients-with-acs. . Accessed August 2019.
27. Lim et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. *Blood Advances* 2018 2:3226-3256; doi: https://doi.org/10.1182/bloodadvances.2018024828.

References

28. Alley W, Mahler SA. Clinical decision aids for chest pain in the emergency department: identifying low-risk patients. *Open Access Emerg Med*. 2015; 7:85-92. doi: 10.2147/OAEM.S71282

29. The SCOT-HEART Investigators. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. *N Engl J Med* 2018; 379:924-933. DOI: 10.1056/NEJMoa1805971

30. Sharma A, Coles A, Sekaran NK, et al. Stress Testing Versus CT Angiography in Patients With Diabetes and Suspected Coronary Artery Disease. *JACC* 2019; 78(8). DOI: 10.1016/j.jacc.2018.11.056

31. Gimbel M, Qaderdan K, Willemsen L. Clopidogrel versus ticagrelor or prasugrel in patients aged 70 years or older with non-ST-elevation acute coronary syndrome (POPular AGE): the randomised, open-label, non-inferiority trial. Lancet. 2020;395(10233):1374

32. Welsford M, Nikolaou NI, Beygui F, et al. for the Acute Coronary Syndrome Chapter Collaborators. Part 5: Acute coronary syndromes:. 2015 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Circulation 2015; 132(6): S146-76

33. Navarese EP, Khan SU, Kolodziejczak M, et al. Comparative Efficacy and Safety of Oral P2Y12 Inhibitors in Acute Coronary Syndrome: Network Meta-Analysis of 52816 Patients From 12 Randomized Trials. *Circulation* 2020; 142(2): 150-160. https://doi.org/10.1161/CIRCULATIONAHA.120.046786

34. Duarte GS, Nunes-Ferreira A, Rodrigues FB, Pinto FJ, Ferreira JJ, Costa J, Caldeira D. Morphine in acute coronary syndrome: systematic review and meta-analysis. BMJ Open 2019; 9(3): e025232. doi: 10.1136/bmjopen-2018-025232

35. Ghadban R, Enezate T, Payne J, Allaham H, Halawa A, Fong HK, Abdullah O, Aggarwal K. The safety of morphine use in acute coronary syndrome: a meta-analysis. Heart Asia 2019; 11(1): e011142.

36. Furtado RH, Nicolau JC, Guo J, et al. Morphine in Non-ST-Segment Elevation ACS. J Am Coll Cardiol 2020;75:289-300.

37. Koskinas KC, Windecker S, Pedrazzini G, et al. Evolucumab for Early Reduction of LDL Cholesterol Levels in Patients With Acute Coronary Syndromes (EVOPACS). J Am Coll Cardiol 2019;74(20):2452-2462. https://doi.org/10.1016/j.jacc.2019.08.010

References

38. Key NS, Khorana AA, Kudere NM, et al. Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update. *Journal of Clinical Oncology* 2020; 38(5): 496-520.

39. Agnelli G, Becattini C, Meyer G, et al. Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer. *N Engl J Med* 2020; 382:1599-1607. DOI: 10.1056/NEJMoa1915103

40. Laureano-Phillips J, Robinson RD, Aryal S, et al. HEART Score Risk Stratification of Low-Risk Chest Pain Patients in the Emergency Department: A Systematic Review and Meta-Analysis. *Annals of Emergency Medicine* 2019;74(2):187-203. https://doi.org/10.1016/j.annemergmed.2018.12.010

41. Januzzi JL, Mahler SA, Christenson RH, et al. Recommendations for Institutions Transitioning to High-Sensitivity Troponin Testing: JACC Scientific Expert Panel. *J Am Coll Cardiol* 2019;73(2):1059-1077.

42. Stopyra J, Snavely AC, Hiestand B, et al. Comparison of accelerated diagnostic pathways for acute chest pain risk stratification. *Heart* 2020;106:977-984. DOI: 10.1136/heartjnl-2019-316426

43. Farge D, Frere C, Connors JM, et al. 2019 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. *Lancet Oncol* 2019;20(10):e566-e581. doi: 10.1016/S1470-2045(19)30336-5.

44. Streiff MB, Holmstrom B, Angelini D, et al. NCCN Guidelines Insights: Cancer-Associated Venous Thromboembolic Disease, Version 2.2018. *J Natl Compr Canc Netw* 2018;16(11):1289-1303. https://doi.org/10.6004/jnccn.2018.0084.

45. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolisms developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart Journ* 2020;41(4):543-603. https://doi.org/10.1093/eurheartj/ehz405

46. Moores LK, Tristschler T, Brosnahan S, et al. Prevention, Diagnosis, and Treatment of VTE in Patients With Coronavirus Disease 2019: CHEST Guideline and Expert Panel Report. *Ches*t 2020; S0012-3692(20)31625-1. doi: 10.1016/j.chest.2020.05.559. Online ahead of print.

47. Rivera-Lebron B, McDaniel M, Ahrar K, et al. Diagnosis, Treatment and Follow Up of Acute Pulmonary Embolism: Consensus Practice from the PERT Consortium. *Clin Appl Thromb Hemost* 2019; 25: 1076029619853037. Published online 2019 Jun 11. doi: 10.1177/1076029619853037

48. Van der Hulle T, Cheung WY, Kooji S, et al. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. *Lancet* 2017; Published online May 23, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30885-1.

49. Evangelista A, Isselbacher EM, Bossone E, et al. Insights From the International Registry of Acute Aortic Dissection: A 20-Year Experience of Collaborative Clinical Research. *Circulation* 2018;137:1846-1860. https://doi.org/10.1161/CIRCULATIONAHA.117.031264

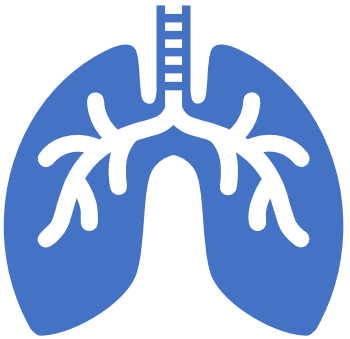
50. Fukui T. Management of acute aortic dissection and thoracic aortic rupture. *J Intensive Care* 2018; 6(15). https://doi.org/10.1186/s40560-018-0287-7

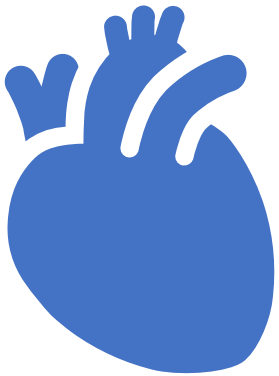
51. Hammer Y, Eisen A, Hasdai D, et al. Comparison of Outcomes in Patients With Acute Coronary Syndrome Presenting With Typical Versus Atypical Symptoms. *Am J Cardiol* 2019;124(12):1851-1856. doi: 10.1016/j.amjcard.2019.09.007.

References

52. Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. *Blood Adv.* 2020 Oct 13;4(19):4693-4738.

53. Stevens SM, Woller SC, Baumann Kreuziger L, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. *Chest.* 2021 Dec;160(6):e545-e608. doi: 10.1016/j.chest.2021.07.055.





Questions?

jalabast@msu.edu
anderson.adrijana@mayo.edu