Chest pain: is There an optimal test? When & Where

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Disclosures: None
No financial relationships
No commercial interests
No off-label or investigational use will be discussed

Case STUDY

42-year-old male, investment advisor is complaining of chest discomfort
20 pack-year smoker, non-insulin dependent diabetic

Januvia, Actos, metformin, Pravastatin, lisinopril

136/84, 5’6” 180# BMI 29

What is the likelihood?

Pretest Likelihood of CAD in Symptomatic Patients According to Age and Sex* (Combined Diamond/Forrester and CASS Data)

	Nonanginal Chest Pain		Atypical Angina		Typical Angina	
Age, y	Men	Women	Men	Women	Men	Women
30–39	4	2	34	12	76	26
=> 40–49	13	3	51	22	87	55
50–59	20	7	65	31	93	73
60–69	27	14	72	51	94	86

*Each value represents the percent with significant CAD on catheterization.

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Practice Guideline 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease: Executive Summary: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, JACC 18 December 2012: Vol. 60, No. 60, pp. 2564-2603

42 yo male with chest discomfort 13 to 87% of significant CAD

When and Where

Outpatient Office

- Echocardiogram for wall motion
- Stress testing with or without imaging study
- Coronary calcium score with cardiac CT
- Coronary angiography

Test	Exercise Status		ECG Interpretable		Pretest Probability of IHD			COR	LOE
	Able	Unable	Yes	No	Low	Intermediate	High		
Patients able to exercise*									
=> Exercise ECG	X		X			X		I	A
=> Exercise with nuclear MPI or Echo	X			X		X	X	I	B
Exercise ECG	X		X		X			IIa	C
Exercise with nuclear MPI or Echo	X		X			X	X	IIa	B
Pharmacological stress CMR	X			X		X	X	IIa	B
CCTA	X		Any			X		IIb	B
Exercise Echo	X		X			X		IIb	C
=> Pharmacological stress with nuclear MPI, Echo, or CMR	X		X		Any			III: No Benefit	C
=> Exercise stress with nuclear MPI	X		X		X			III: No Benefit	C
Patients unable to exercise									
=> Pharmacological stress with nuclear MPI or Echo		X	Any			X	X	I	B
Pharmacological stress Echo		X	Any		X			IIa	C
CCTA		X	Any		X	X		IIa	B
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Other									
CCTA If patient has any of the following: a) Continued symptoms with prior normal test, or b) Inconclusive exercise or pharmacological stress, or c) Unable to undergo stress with MPI or Echo	Any		Any			X		IIa	C
=> CAC score	Any		Any		X			IIb	C

2012 ACCF/AHA Guideline for the Diagnosis and Management with Stable Ischemic Heart Disease

Case STUDY

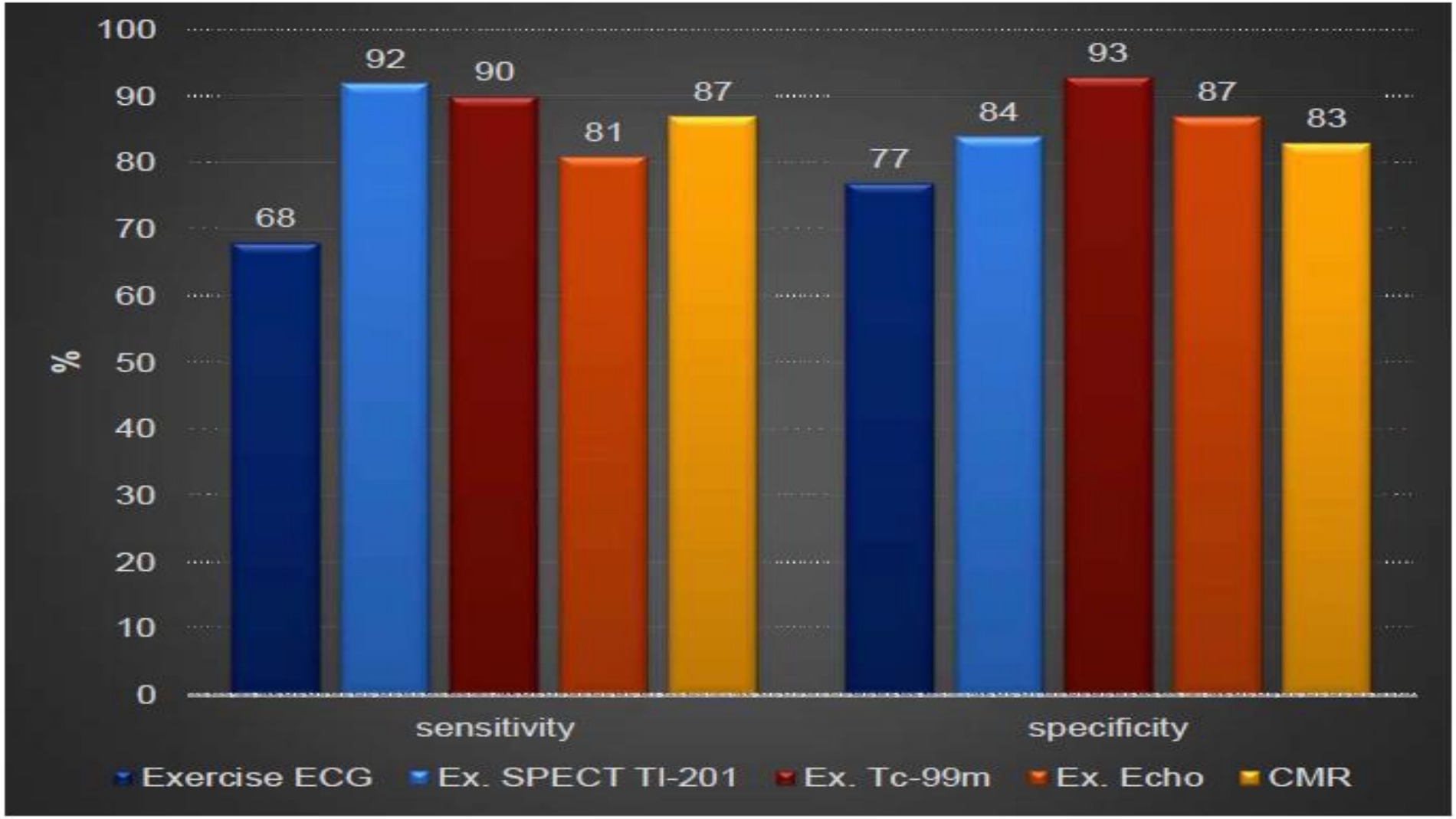
42-year-old male, investment advisor is complaining of chest discomfort
20 pack-year smoker, non-insulin dependent diabetic

Januvia, Actos, metformin, Pravastatin, lisinopril

136/84, 5’6” 180# BMI 29 Intermediate Risk 13 (non cardiac) – 87 (angina)

Additional information: stable chest pain exacerbated by exercise, relieved with rest, EKG interpretable, able to walk

Sensitivity & Specificity of Stress Studies



Lee TH, et al. *N Engl J Med*. 2001;344:1840-1845
Jahnke C, et al., *Circulation*, 2007; 115(13):1769-1776.

Treadmill exercise without imaging study Class I

Treadmill + MPI or Echo if EKG uninterpretable Class I

Treadmill + MPI or Echo if EKG OK Class Iia

Pharm stress + CMR if EKG uninterpretable Class Iia

CCTA Class IIb

Pharm Stress with MPI, echo or CMR CLASS III

Cannot exercise:

Pharm stress + MPI or Echo Class I

Pharm stress + CMR Class IIa

CCTA Class IIa

Request to perform multiple modalities at same time

When and Where

Coronary Calcium Score

Calcium Scoring (AU)	Severity
0	No identifiable disease
1-99	Mild Disease
100-399	Moderate Disease
≥ 400	Severe Disease

INTERMEDIATE RISK PATIENT (10-year Framingham Risk Score between 10-20%)

"It may be reasonable to consider use of CAC measurement in such patients based on available evidence that demonstrates incremental risk prediction information in this selected patient group. This conclusion is based on the possibility that such patients might be reclassified to a higher risk status based on high CAC score, and subsequent management strategies may be modified".

ACCF/AHA 2007 Clinical Expert Consensus Document on CAC

Case STUDY not in the Outpatient Office but the ER

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Troponins

What happens in the Emergency Room

Triage starts the IV, gives the aspirin, DRAWS THE LABS, before the physician sees the patient

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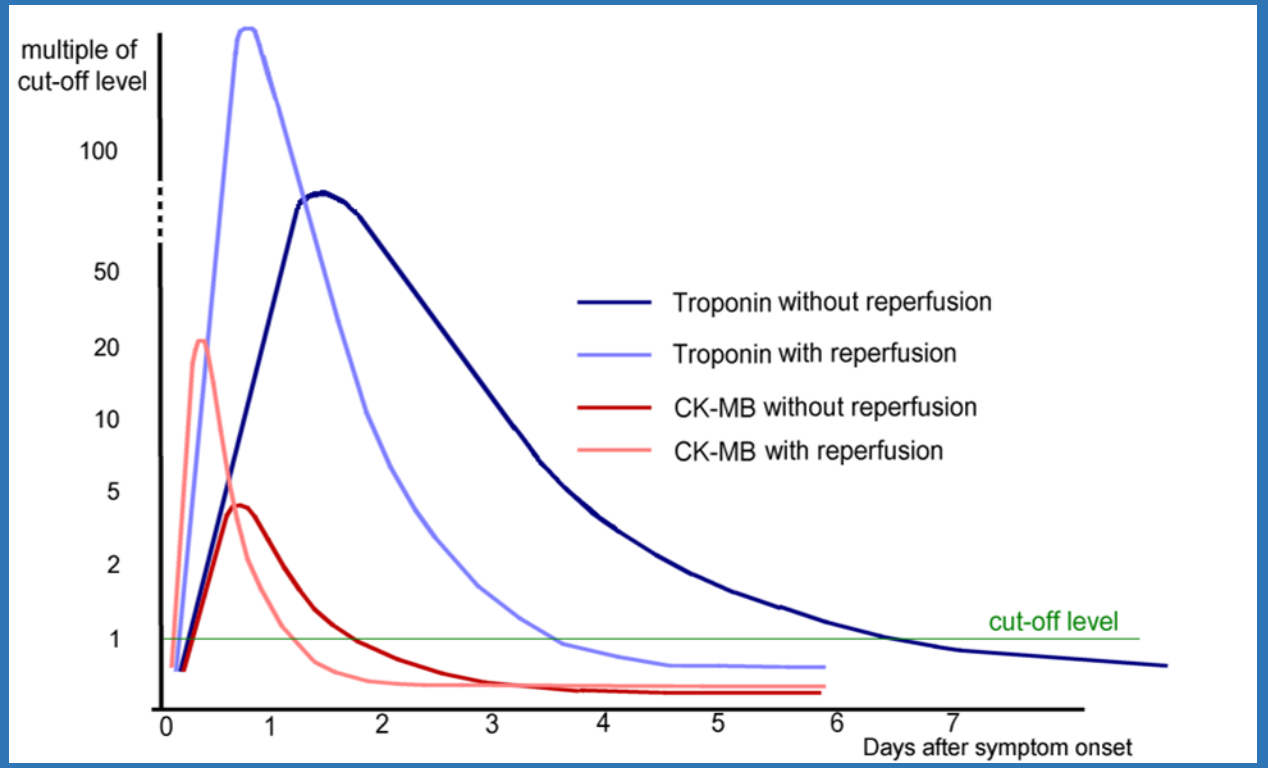
Troponins

TABLE 5 **Summary of Recommendations for Cardiac Biomarkers and the Universal Definition of MI**

Recommendations	COR	LOE
Diagnosis		
Measure cardiac-specific troponin (troponin I or T) at presentation and 3–6 h after symptom onset in all patients with suspected ACS to identify pattern of values	I	A
Obtain additional troponin levels beyond 6 h in patients with initial normal serial troponins with electrocardiographic changes and/or intermediate/high risk clinical features	I	A
Consider time of presentation the time of onset with ambiguous symptom onset for assessing troponin values	I	A
With contemporary troponin assays, CK-MB and myoglobin are not useful for diagnosis of ACS	III: No Benefit	A
Prognosis		
Troponin elevations are useful for short- and long-term prognosis	I	B
Remeasurement of troponin value once on d 3 or 4 in patients with MI may be reasonable as an index of infarct size and dynamics of necrosis	IIb	B
BNP may be reasonable for additional prognostic information	IIb	B

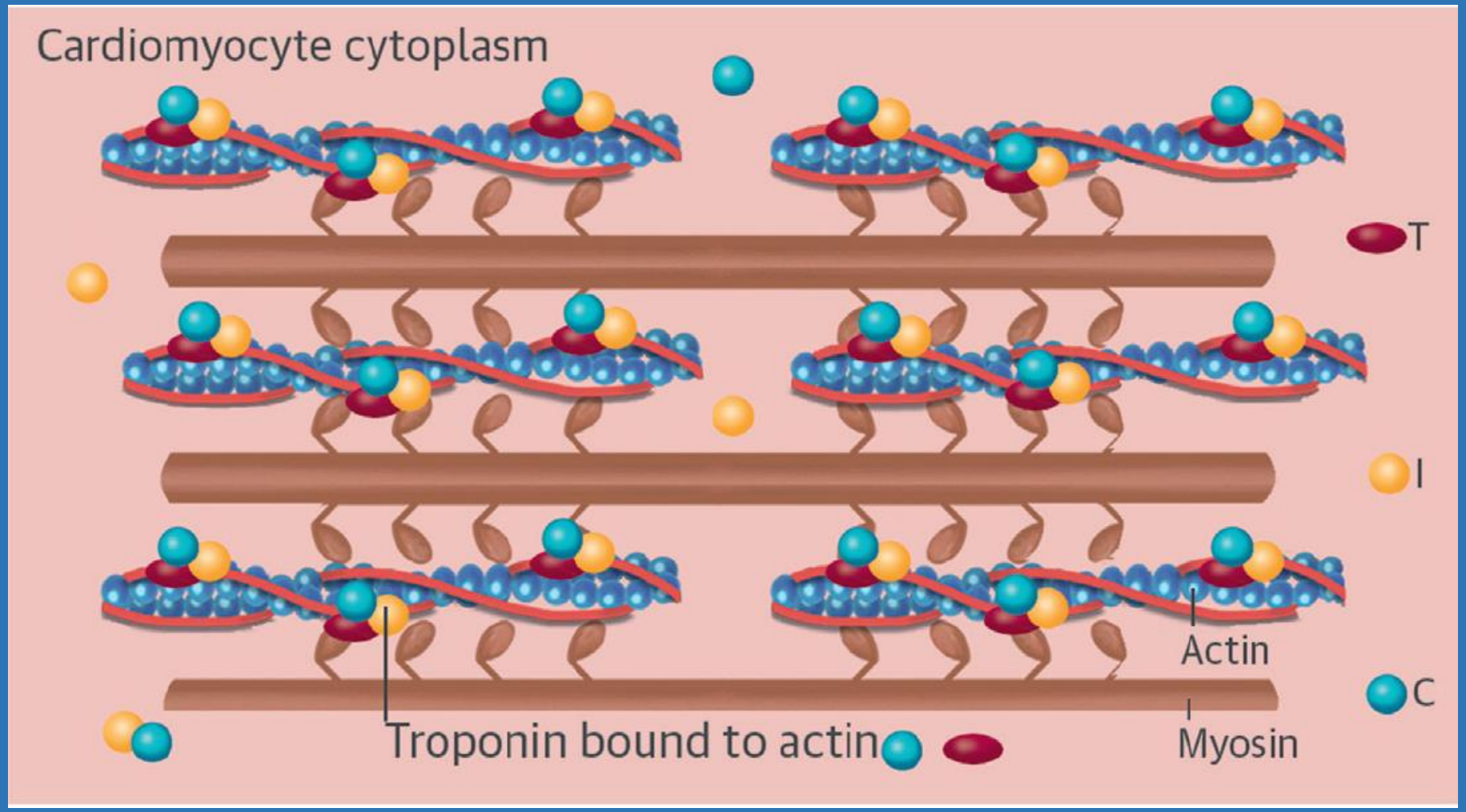
2014 AHA/ACC Guideline for the Management of Patients with Non-ST Elevation Acute Coronary Syndromes

Biomarkers (where we came from)



J. Heuser modified from ACC/AHA Practice Guidelines 2005 p E32

Troponins



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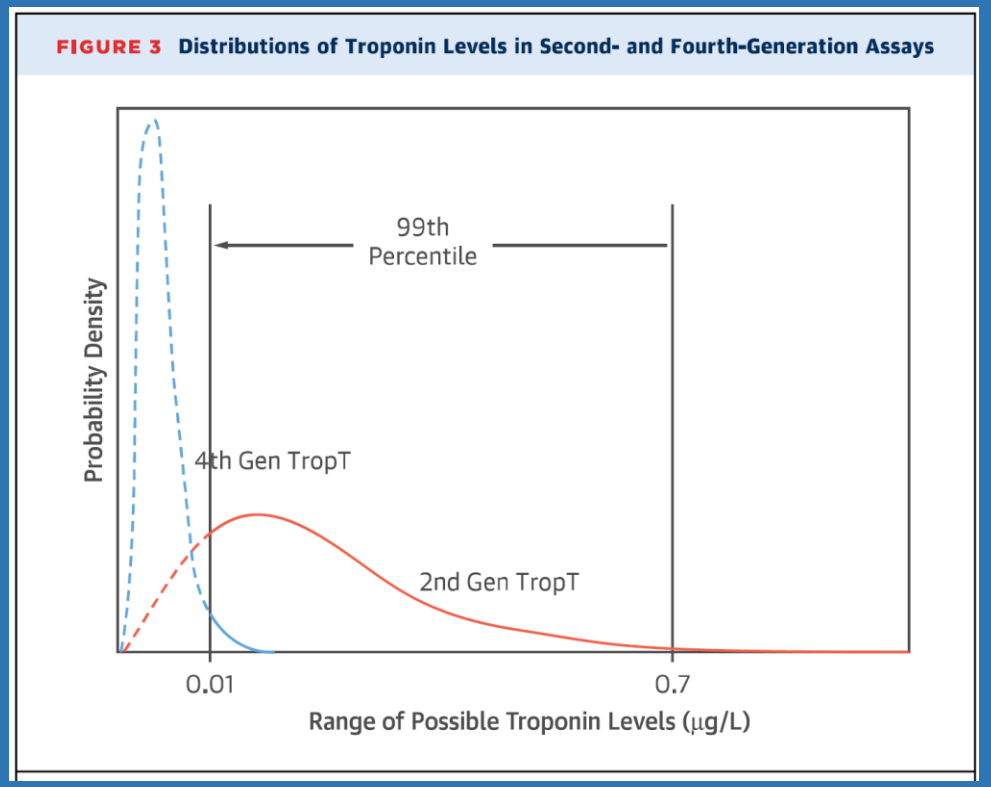
Troponins

Tests have been available since the late 1980s

One commercially available test for Troponin T

Many commercially available test for Troponin I

Most Troponin tests are on the fourth generation test



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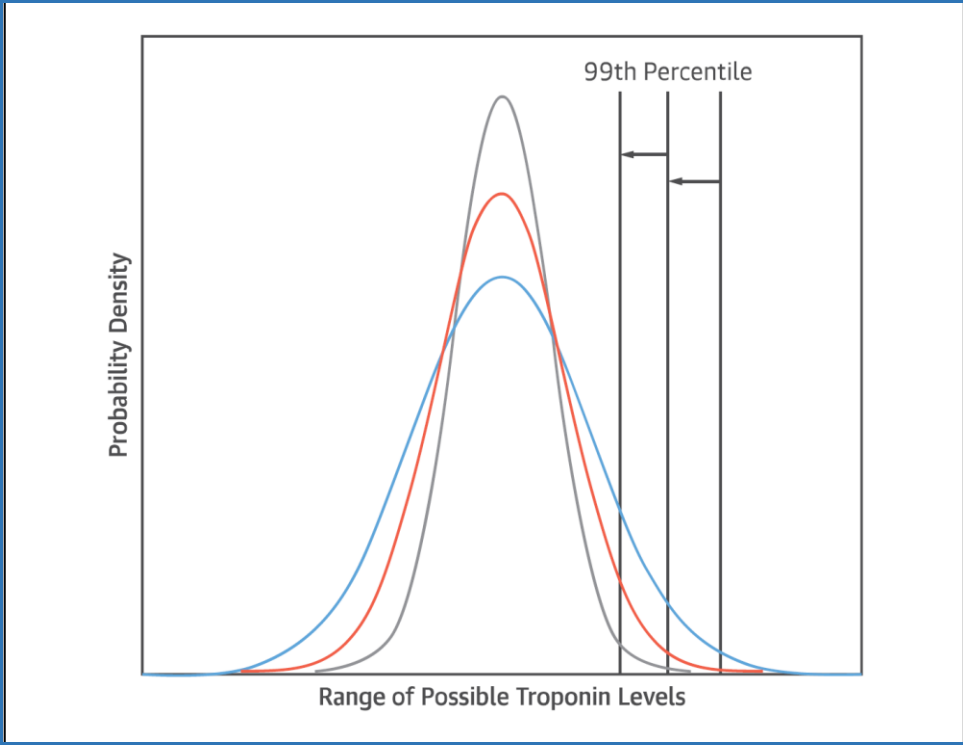
Troponins

High-sensitivity narrows the 4th generation curve significantly



Brush, Troponins Testing for Clinicians JACC 2016: 2365-75
Katus Circulation 1991

High-Sensitivity Troponins (hs-TnT or hs-TnI)

Accuracy in acute myocardial infarction

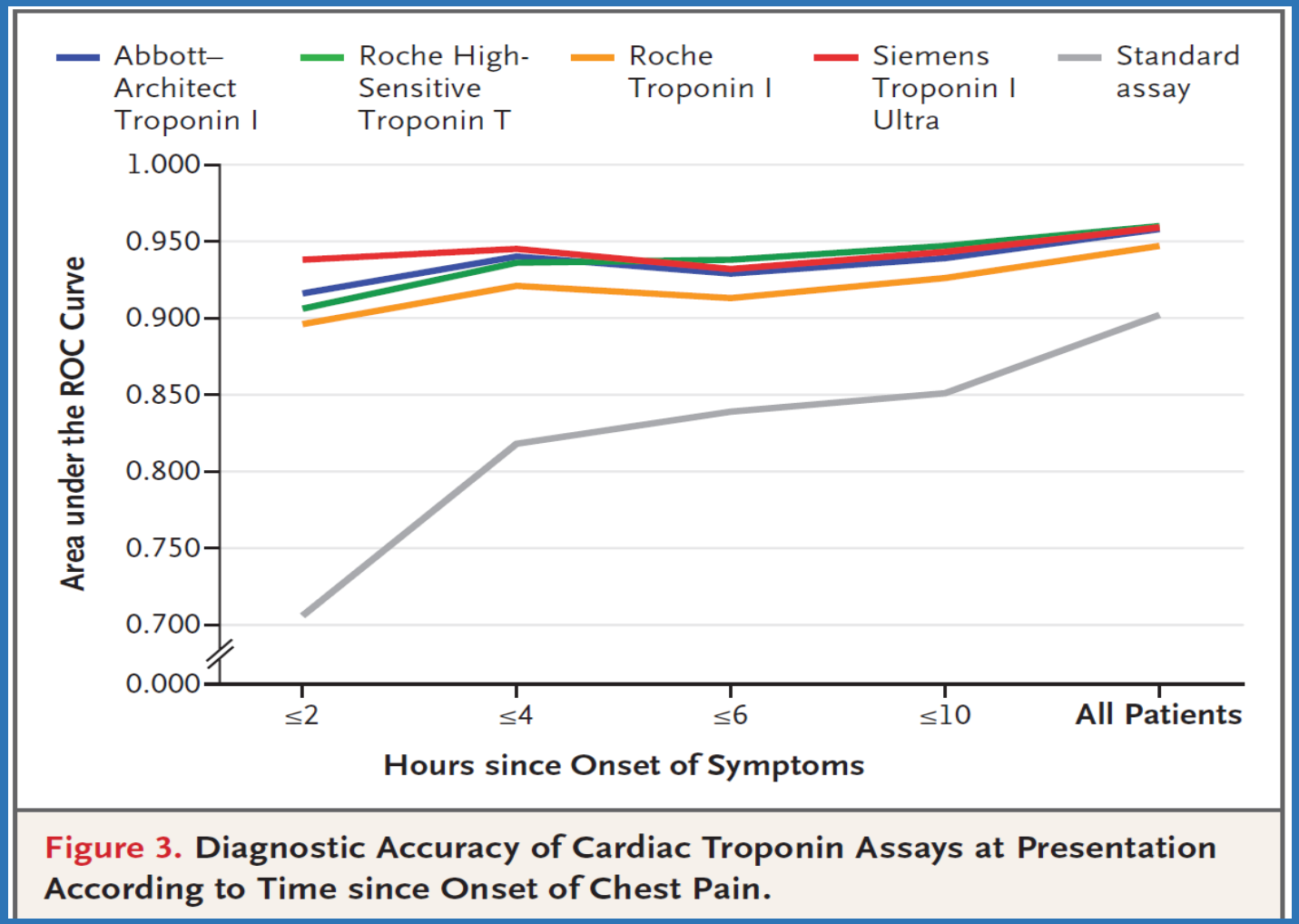


Figure 3. Diagnostic Accuracy of Cardiac Troponin Assays at Presentation According to Time since Onset of Chest Pain.

Troponins

High-sensitivity refers to the test's ability to detect troponin

Troponins have diagnostic and prognostic utility

Troponin elevation can be reflective of other conditions

- HFrEF, Sepsis, Aortic Dissection, Hypovolemia, Tachycardia
- Pulmonary Embolism, Pulmonary Hypertension
- CAD or Diabetes

Community-dwelling adults $\geq$ 65 without HF hs-cTnT detectable in 66.2%

General population age 30-65 years hs-cTnT detectable in 25% & is a marker for structural heart disease, eg. LVH, hypertension, CKD, (possibly diastolic dysfunction)

Reichlin, NEJM 2009 Aug 27;361 (9):858-67

Troponins

What would the Rev Bayes think about this

TABLE 1 Test Results in Patients With Suspected Acute Myocardial Infarction

Test Result	Disease	No Disease	Total
Positive Test	162	166	328
Negative Test	8	664	672
Total	170	830	1,000

The table shows the results of a test with 95% sensitivity (true positive rate) and 80% specificity (true negative rate) in 1,000 patients with a disease prevalence of 17%.

TABLE 2 Test Results in Unselected ED Patients

Test Result	Disease	No Disease	Total
Positive test	108	416	524
Negative test	8	468	476
Total	116	884	1,000

The table shows the test results in 1,000 patients after adding 250 patients with elevated troponin due to diagnoses other than AMI to the 166 patients with false positive test results, yielding a new total of 416 patients with false positive test results. This has reduced prevalence of disease to 12% and specificity of the test to 53% (468 of 884) but only slightly reducing the sensitivity of the test to 93% (108 of 116).

AMI = acute myocardial infarction; ED = emergency department.

In patients with suspected ACS the High-sensitivity (true positive is 95% and the specificity of 80% (true negative)

But in the general population the sensitivity drops to 93% and the specificity to 53%

It is all about context and what is the pre-test incidence prior to the test

Brush, Troponins Testing for Clinicians JACC 2016: 2365-75

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What is the likelihood of HFrEF?

Demographics and risk factors based on NHANES data 2013–2014.

	CHF	Non-CHF	*p*-Value
Total number of estimated population	182	5579	
Age at screening – mean	**66.29**	**48.52**	**<0.0001**
Female – no.%	95 (52.19%)	2913 (52.21%)	0.9966
Black – no.%	44 (24.18%)	1129 (20.24%)	0.1940
Less than high school education – no.%	51 (28.02%)	1189 (21.31%)	0.0302
Current cigarette smoking (everyday/some days) – no. %	31 (17.03%)	1161 (20.81%)	0.2158
Abnormal alcohol consumption – no.%			
Female: two or more drinks everyday	17 (17.89%)	896 (30.76%)	0.0073
Male: three or more drinks everyday	8 (9.20%)	816 (30.61%)	<0.0001
NOT participate in moderate physical activity – no.%	142 (78.02%)	3753 (67.27%)	0.0023
Hypertension – no. %	**149 (81.87%)**	**1989 (35.65%)**	**<0.0001**
High cholesterol level – no.%	**120 (65.93%)**	**1884 (33.77%)**	**<0.0001**
BMI (Body mass index), means ±SD	**32.75 (9.83)**	**28.99 (7.03)**	**<0.0001**
Overweight (BMI 15–29.9) – no.%	39 (21.43%)	1727 (30.96%)	0.0061
Obese (BMI ≥30) – no.%	89 (48.90%)	1991 (35.69%)	0.0003
Self-reported diabetes, %	**73 (40.11%)**	**645 (11.56%)**	**<0.0001**
Coronary artery disease, %	**70 (38.46%)**	**161 (2.89%)**	<0.0001

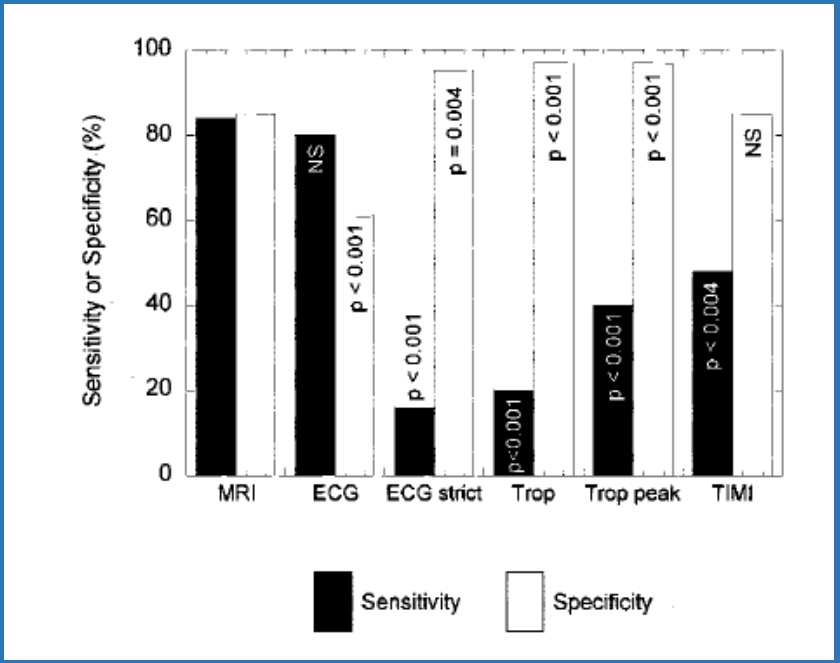
What is the likelihood of HFrEF?

Pulmonary hypertension by mechanism of disease

Due to left heart failure (increased back pressure in the pulmonary vessels)
• Left ventricular pump failure (heart attack, cardiomyopathy)
• Left ventricular stiffness (hypertension, diabetes, metabolic syndrome)
• Valve disease (mitral or aortic stenosis or regurgitation)
Diseases affecting the whole lung (lung diseases obliterate blood vessels)
• Chronic bronchitis and emphysema (combination of loss of lung plus hypoxia)
• Interstitial lung diseases (destructive diseases that obliterate vessels, such as pulmonary fibrosis, sarcoidosis, and many others)
Hypoxia related (decreased oxygen constricts pulmonary blood vessels)
• High-altitude dwelling
• Sleep apnea and other hypoventilation syndromes
• Hypoxia of chronic bronchitis and emphysema (chronic obstructive pulmonary disease, or COPD)
Pulmonary arterial hypertension (changes in the structure and function of the pulmonary arteries)
• Idiopathic (formerly primary pulmonary hypertension)
• Heritable (formerly familial, due to BMPR2 or Alk-1 mutations)
• Drug- and toxin-induced (stimulants)
• Connective tissue diseases (especially scleroderma)
• HIV infection (rare occurrence <1%)
• Portal hypertension (cirrhosis and other advanced liver diseases)
• Congenital heart disease that allows blood to shunt around the lungs
• Pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis (rare)
Primarily obstructing diseases of the pulmonary vessels
• Pulmonary thromboembolism
• Schistosomiasis
• Sickle cell anemia
• Tumor emboli
• Fibrosing mediastinitis (obstruction by fibrosis related to histoplasmosis)

https://www.thoracic.org/patients/patient-resources/breathing-in-america/resources/chapter-17-pulmonary-hypertension.pdf

Cardiac MR in the ER

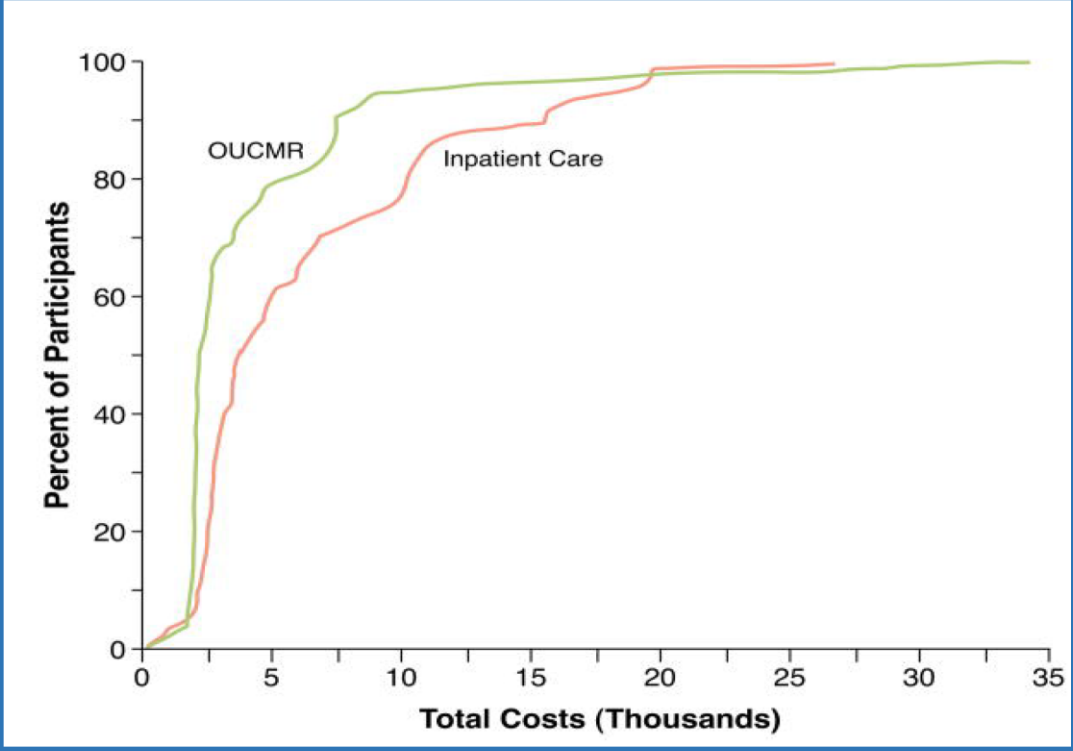


Sensitivity 84%; specificity 85%

Kwong, etal, Detecting Acute Coronary Syndrome in the Emergency Department With Cardiac Magnetic Resonance Imaging, Circulation. 2003;107:531-537.

Cardiac MR in the ER

"An OU-CMR strategy reduces cardiac-related cost of medical care during the index visit and over the first year subsequent to discharge, without an observed increase in major cardiac events."



Miller et al. Stress CMR imaging observation unit in the emergency department reduces 1-year medical care costs in patients with acute chest pain: a randomized study for comparison with inpatient care. JACC Cardiovasc Imaging. 2011;4(8):862–870.

Cardiac MR in the ER

391 patients

CMRI was read as normal for CAD-related findings in 285 (72.9%) patients

106 patients with CAD-related abnormalities, 42 (39.6%) had ischemia on stress perfusion imaging

64 (60.4%) patients had MI without ischemia 54.7% had no known history of prior MI

20 (5.1%) previously undiagnosed moderate to severe valvular disease in cases

4 (1.0%) new cases of hypertrophic cardiomyopathy

1 (0.3%) new case of non-ischemic cardiomyopathy

Other diagnoses; 1 aortic aneurysm, 1 aortic dissection, 1 acute myocarditis,

3 pericarditis, 1 myxoma, 2 moderate pericardial effusions.

Miller et al. Stress CMR imaging observation unit in the emergency department reduces 1-year medical care costs in patients with acute chest pain: a randomized study for comparison with inpatient care. JACC Cardiovasc Imaging. 2011;4(8):862–870.

Cardiac MR in the ER

Position Paper: Cardiac MRI in the Emergency Room

Cardiovascular and Pulmonary Branch, National Heart, Lung and Blood Institute, National Institutes of Health

“Cardiac MRI is capable of diagnosing and triaging patients with possible or probable ACS. It has substantial advantages in terms of the lack of radiation compared with CT or nuclear imaging (SPECT). However, there are substantial infrastructure hurdles to overcome. Even though MRI is already used in ~600,000 emergency room patients per year, handling some significant fraction of the ~6 million US patients with chest pain each year will require a major deployment in scanners and cardiac MRI specific expertise.”

Aria, A., Cardiac MRI in the Emergency Room, Proc. Intl. Soc. Mag. Reson. Med. 19 (2011)

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	Able	Unable	Yes	No	Low	Intermediate	High		
Patients able to exercise*									
Exercise ECG	X		X			X		I	A
Exercise with nuclear MPI or Echo	X			X		X	X	I	B
Exercise ECG	X		X		X			IIa	C
Exercise with nuclear MPI or Echo	X		X			X	X	IIa	B
=> Pharmacological stress CMR	X			X		X	X	IIa	B
CCTA	X		Any			X		IIb	B
Exercise Echo	X		X			X		IIb	C
Pharmacological stress with nuclear MPI, Echo, or CMR	X		X		Any			III: No Benefit	C
Exercise stress with nuclear MPI	X		X		X			III: No Benefit	C
Patients unable to exercise									
Pharmacological stress with nuclear MPI or Echo		X	Any			X	X	I	B
Pharmacological stress Echo		X	Any		X			IIa	C
CCTA		X	Any		X	X		IIa	B
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Other									
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CAC score	Any		Any		X			IIb	C

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Cardiac CT Angiograms in the ER

Outcome	CCTA-Based Strategy (N=908)	Traditional Care (N=462)	Difference, CCTA-Based Strategy – Traditional Care (95% CI)
			percentage points
Disposition — no. (%)			
Discharge	450 (50)	105 (23)	26.8 (21.4 to 32.2)
Admission or observation	458 (50)	357 (77)	
Length of stay — hr			
Overall*			
Median	18.0	24.8	
Interquartile range	7.6 to 27.2	19.2 to 30.5	
Cardiovascular events — no. (%)			
Death	0	0	0
Acute myocardial infarction	9 (1)	4 (1)	0.1 (–5.5 to 5.7)
Acute coronary syndrome without acute myocardial infarction	28 (3)	7 (2)	1.6 (–4.0 to 7.2)
Diagnosis of coronary disease	82 (9)	16 (3)	5.6 (0 to 11.2)
Revascularization	23 (3)	4 (1)	1.7 (–3.9 to 7.3)

49% v 22% discharged from the ER with no difference in 30-day outcomes (1% of AMI in both groups)
CAD diagnosed in 9% in CCTA group v 3% in traditional treatment group

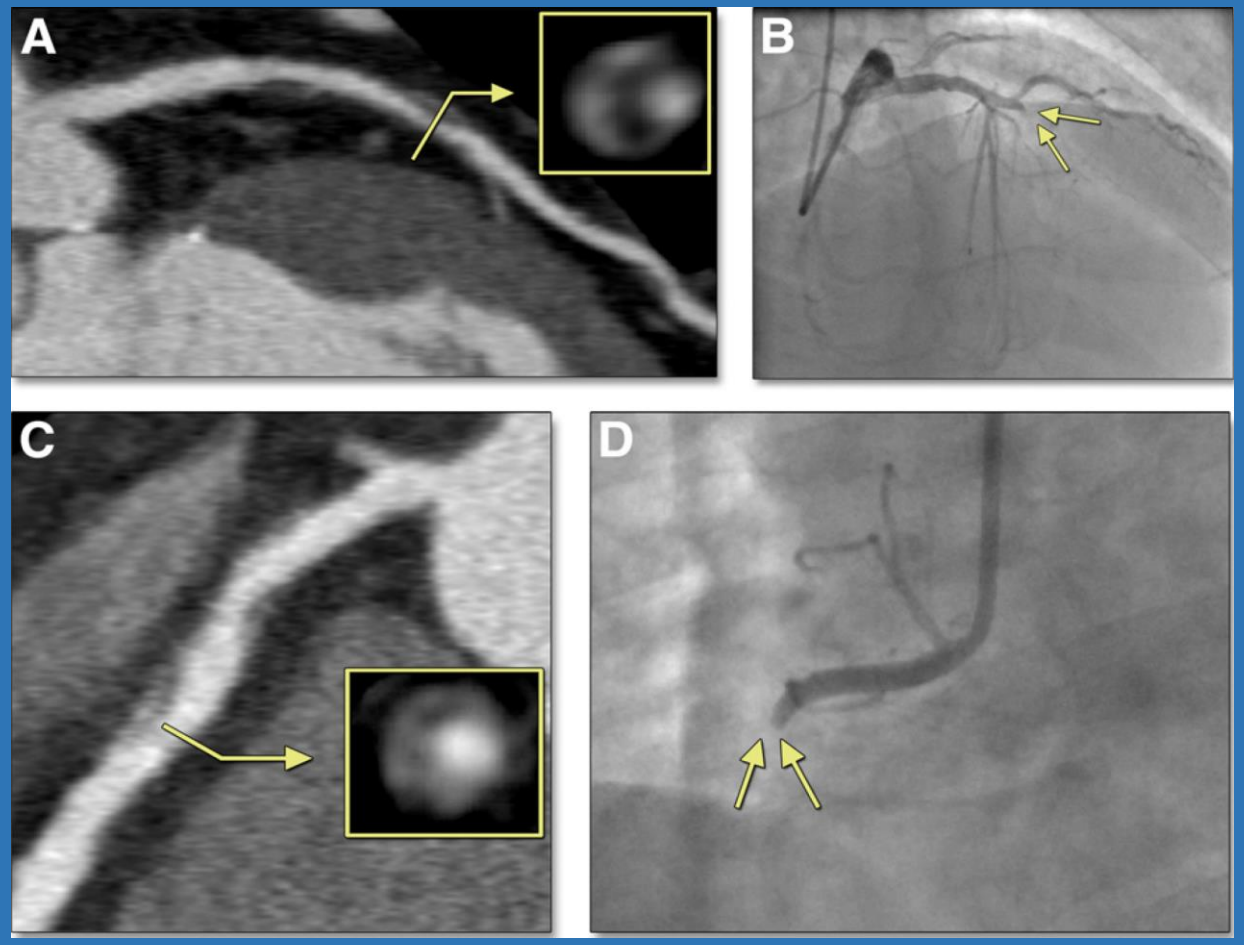
Litt, etal, CT Angiography for Safe Discharge of Patients with Possible Acute Coronary Syndromes, NEJM 366;393-403

Cardiac CT Angiograms in the ER

End Point	CCTA (N=501)	Standard Evaluation (N=499)	P Value
Length of hospital stay — hr			
All patients in intention-to-treat analysis			<0.001
Mean	23.2±37.0	30.8±28.0	
Median	8.6	26.7	
Interquartile range	6.4–27.6	21.4–30.6	
Patients with final diagnosis other than acute coronary syndrome			<0.001
Mean	17.2±24.6	27.2±19.5	
Median	8.1	26.3	
Patients with final diagnosis of acute coronary syndrome			0.87
Mean	86.3±72.3	83.8±61.3	
Median	56.9	71.8	
Time to diagnosis — hr			
All patients in intention-to-treat analysis			<0.001
Mean	10.4±12.6	18.7±11.8	
Median	5.8	21.0	
Discharge status — no. (%)			<0.001
Direct discharge from emergency department	233 (47)	62 (12)	
Admission to observation unit	153 (30)	301 (60)	
Admission to hospital	107 (21)	125 (25)	
Left against medical advice	8 (2)	11 (2)	
Follow-up for recurrent chest pain within 28 days — no.			
Repeat visit to emergency department	14	19	0.38
Repeat hospitalization	7	7	

Hoffman, etal, Coronary CT Angiography versus Standard Evaluation in Acute Chest Pain, NEJM 367;299-308

Cardiac CT Angiograms in the ER



Napkin-ring sign suggests lesions are one of the vulnerable plaque lesions in ACS

Otsuka, etal., Napkin-Ring Sign on Coronary CT Angiography for the Prediction of Acute Coronary Syndrome, JACC CARDIOVASCULAR IMAGING, VOL. 6, NO. 4, 2013, APRIL 2013:448 –57

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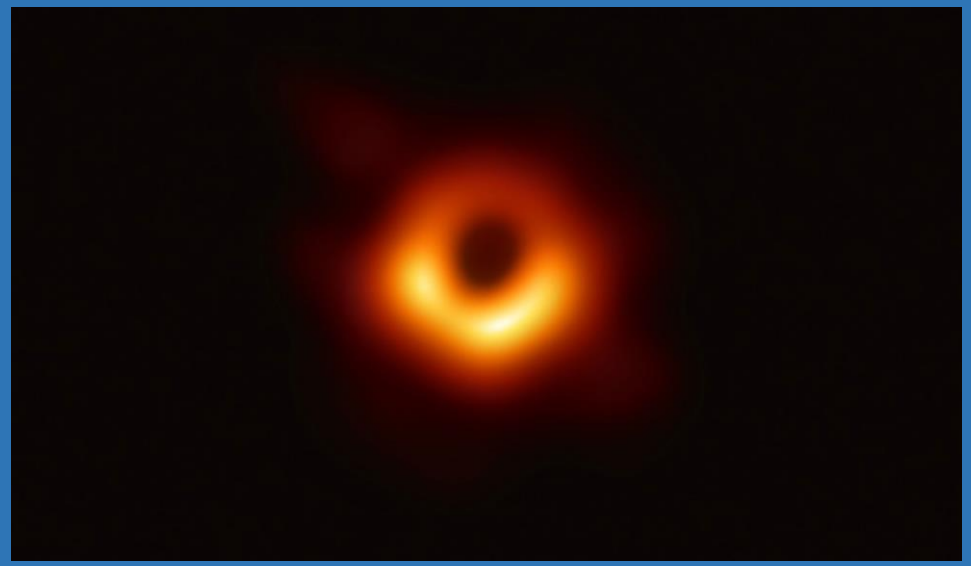
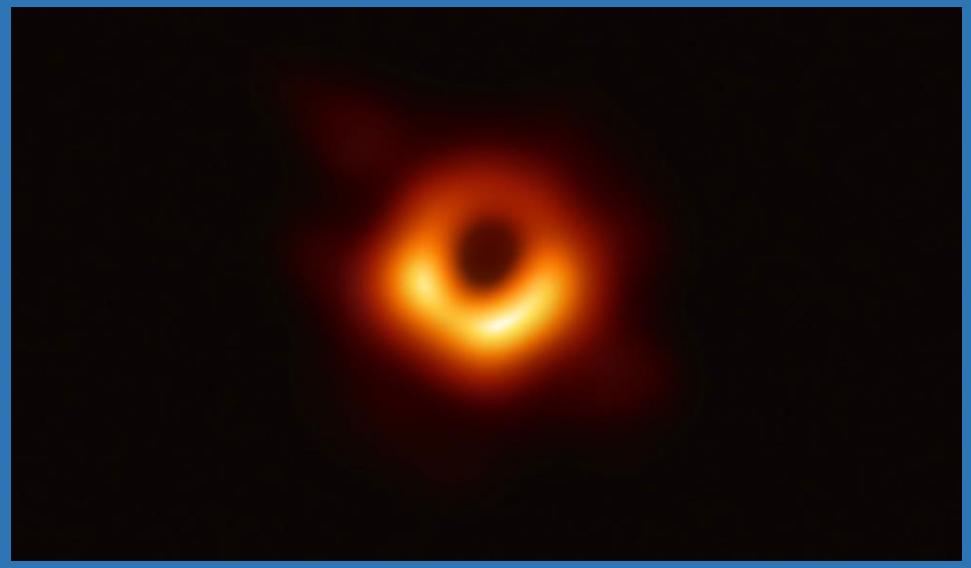
Equally important is “In what context?”



Chest pain: is There an optimal test? When & Where

Context is everything!



The Event Horizon Telescope has captured a photo of a supermassive black hole at the center of M87, a galaxy 54 million light years away.

https://www.wired.com/story/scientists-reveal-the-first-picture-of-a-black-hole/

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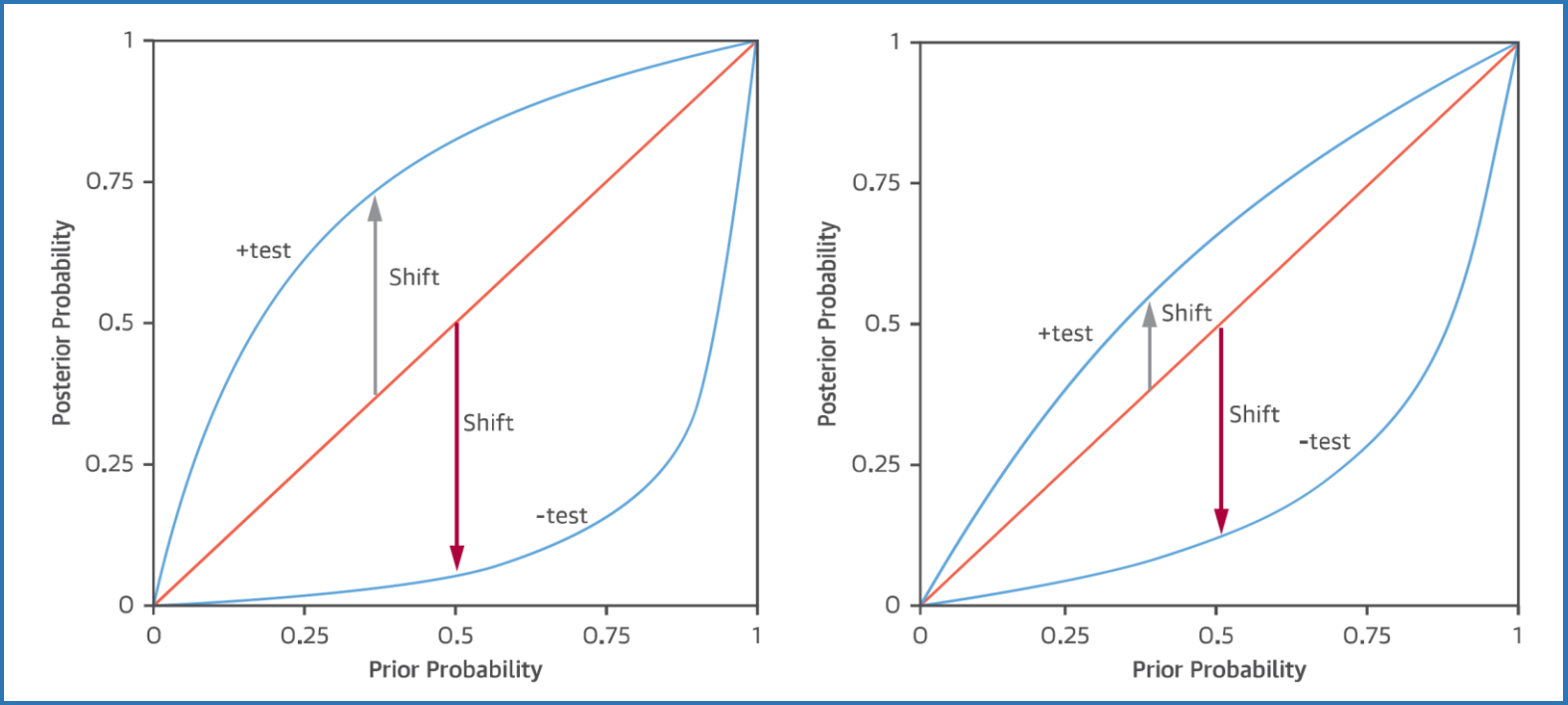
Interpreting the results must always occur in light of what is the pre-test probability of disease.



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