Brigham and Women's Hospital
Founding Member, Mass General Brigham

Stress Testing 101

Sanjay Divakaran, MD, MPH
Associate Chief and Clinical Director
Division of Cardiovascular Medicine
Brigham and Women's Hospital
Assistant Professor of Medicine
Harvard Medical School

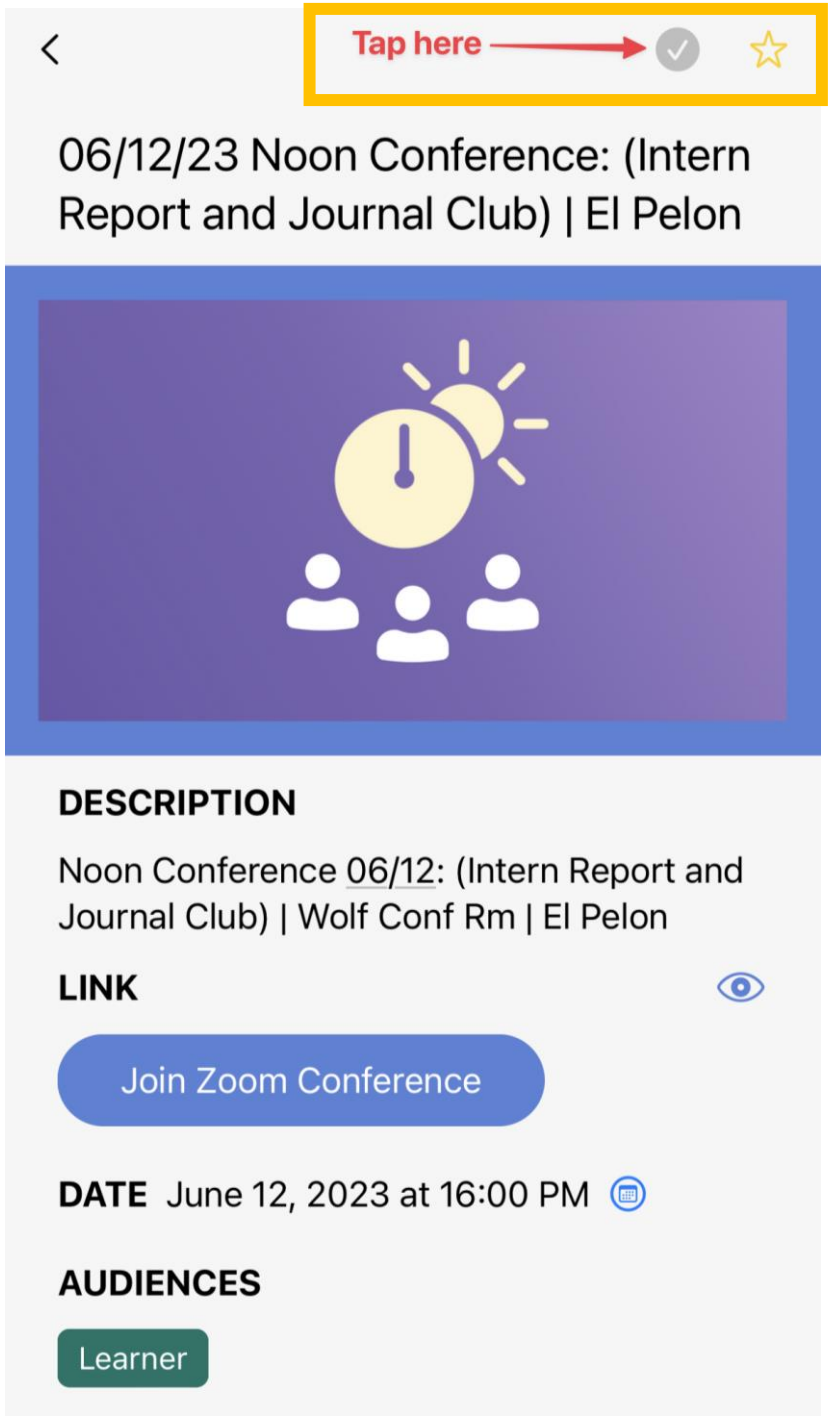
@sanjaydivakaran
sdivakaran@bwh.harvard.edu

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

No Disclosures

Residents– keep track of your noon conference progress with Sparkle

For more information on Sparkle: https://bei.brighamandwomens.org/essential-apps



Learning Objectives

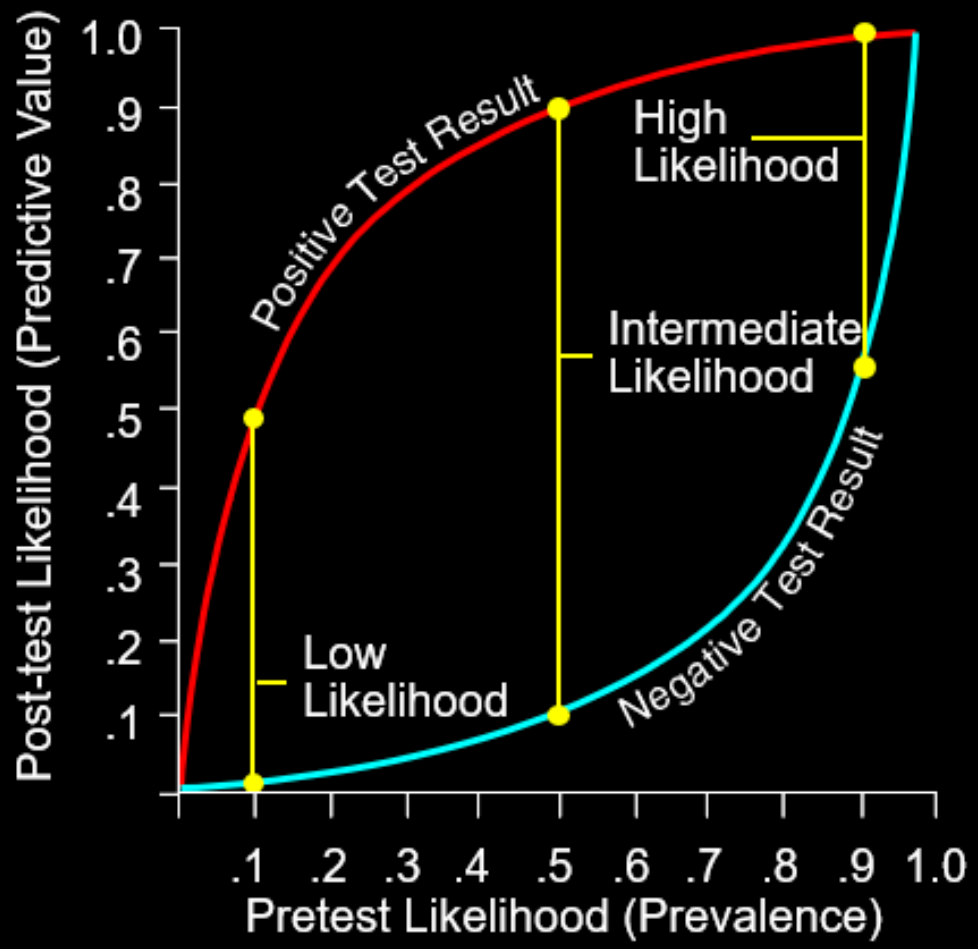
By the end of this presentation, BWH Internal Medicine residents should be able to:

1. Review the reasons why we refer patients to the stress lab
2. Describe the data we obtain via exercise stress testing
3. Develop a framework for how to provide patient-centered care with regards to stress testing

Key #1 to Ordering a Diagnostic Test: Bayes' Theorem

- Testing is best used in patients with intermediate pre-test probability of disease

(Hypothetical Test with 90% Sensitivity and Specificity)



Gibson and Watson. Progr Cardiol 1983;12:67

Table A. Diamond and Forrester Pre-Test Probability of Coronary Artery Disease by Age, Sex, and Symptoms*

Age (years)	Sex	Typical/Definite Angina Pectoris	Atypical/Probable Angina Pectoris	Nonanginal Chest Pain
≤39	Men	Intermediate	Intermediate	Low
	Women	Intermediate	Very low	Very low
40–49	Men	High	Intermediate	Intermediate
	Women	Intermediate	Low	Very low
50–59	Men	High	Intermediate	Intermediate
	Women	Intermediate	Intermediate	Low
≥60	Men	High	Intermediate	Intermediate
	Women	High	Intermediate	Intermediate

High: >90% pre-test probability. **Intermediate:** between 10% and 90% pre-test probability. **Low:** between 5% and 10% pre-test probability. **Very low:** <5% pre-test probability. *Modified from the ACC/AHA 2002 Guideline Update for Exercise Testing (30a).

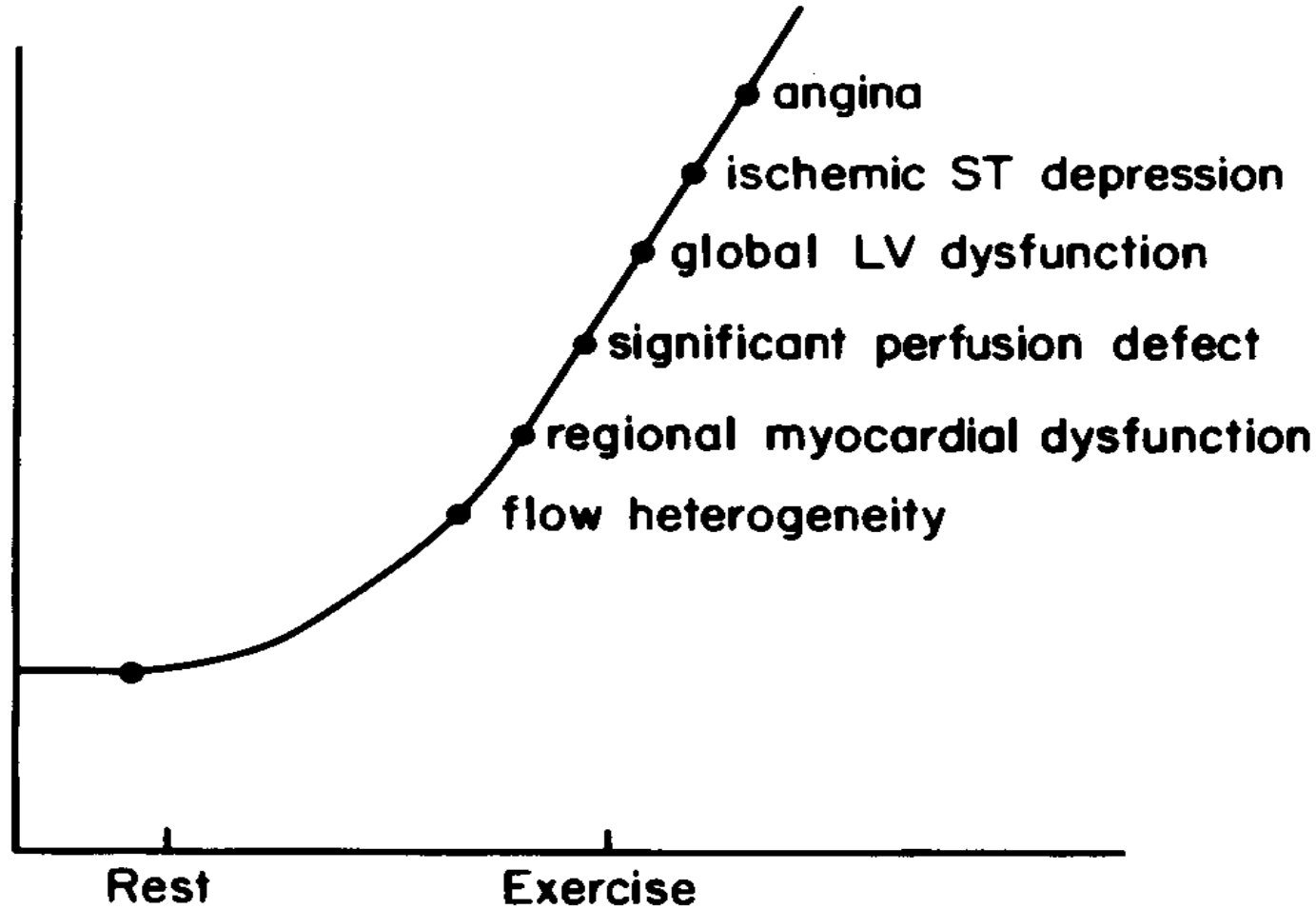
	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

Wolk MJ et al. J Am Col Cardiol. 2014:380–406.
Knuuti J et al. EHJ 2020. 407-477.

Key #2 to Ordering a Diagnostic Test: Know Your Question

- **Are my patient's symptoms from flow-limiting epicardial coronary artery disease?**
- Are my patient's symptoms from new ischemia from his/her known coronary artery disease?
- Is my patient truly asymptomatic, or does he/she not do enough activity at home to be symptomatic?
- Is the medical regimen I have provided adequate for my patient with known coronary artery disease and chronic angina?
- Should I start a statin for my patient who is at borderline, intermediate risk for a cardiovascular event over the next 10 years?

Ischemic Cascade



Diagnostic Testing for CAD

Anatomic

Functional

Diagnostic Testing for CAD

Anatomic

- Coronary artery calcium score
- Coronary computed tomography angiography (CTA)
- Invasive coronary angiography

Diagnostic Testing for CAD

Functional

- Electrocardiogram Exercise Treadmill Testing (ECG-ETT)
- Single-Photon Emission Computed Tomography (SPECT)
- Positron Emission Tomography
- Stress Echocardiography
- Stress Cardiac Magnetic Resonance Imaging (CMR)

Exercise Treadmill Testing (ETT)

Contraindications to ETT

Contraindications

- Acute MI (2 days)
- High risk unstable angina
- Uncontrolled arrhythmias (symptoms, hemodynamic compromise)
- Symptomatic severe aortic stenosis
- Acute pulmonary embolism, myocarditis, or pericarditis
- Acute aortic dissection

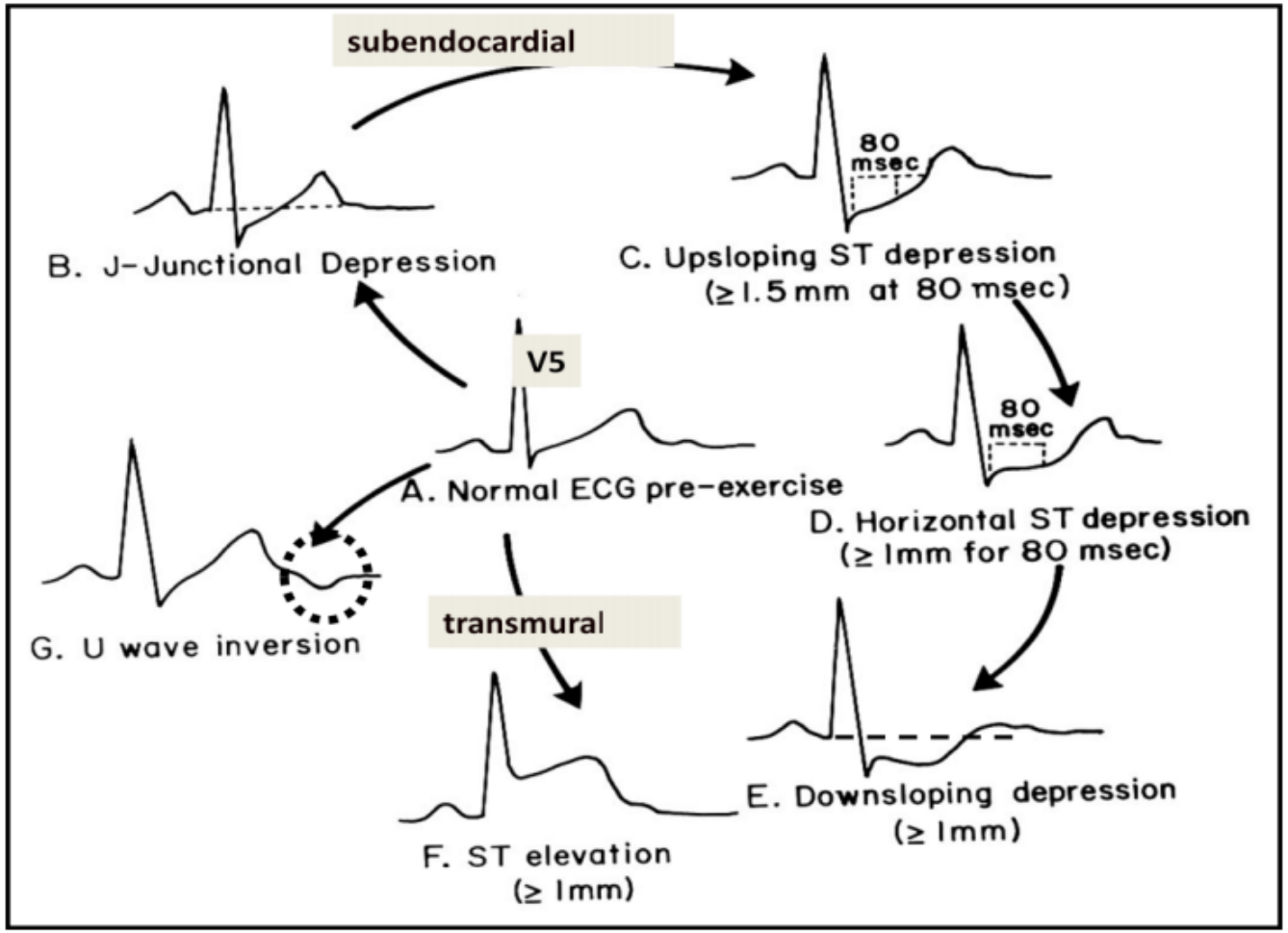
Relative Contraindications

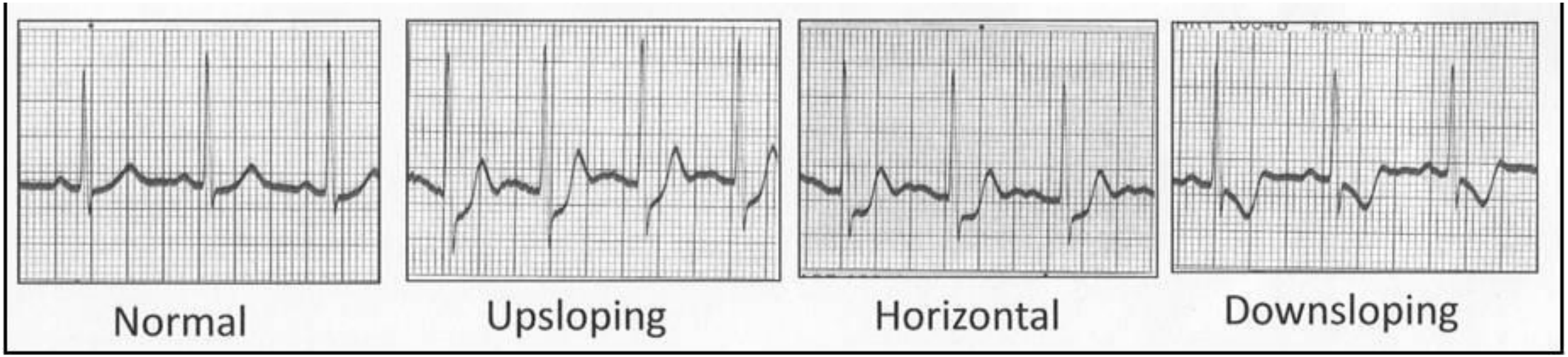
- Known left main disease
- Moderate valvular stenosis
- Electrolytes abnormalities (potassium)
- Severe hypertension (200/110 mmHg)
- Hypertrophic cardiomyopathy
- Mental or physical impairment
- High-degree AV block

Baseline ECG Abnormalities

- ST-T abnormalities, LVH (>1mm)
- LBBB
- V-pacing
- Pre-excitation
- Changes associated with digoxin Rx

- *Baseline ECG abnormalities do not contraindicate ECG exercise testing to assess function, arrhythmia, or other clinical endpoints*


subendocardial
80 msec
B. J-Junctional Depression
C. Upsloping ST depression (≥1.5 mm at 80 msec)
V5
80 msec
A. Normal ECG pre-exercise
D. Horizontal ST depression (≥ 1mm for 80 msec)
G. U wave inversion
transmural
E. Downsloping depression (≥ 1mm)
F. ST elevation (≥ 1mm)


Normal
Upsloping
Horizontal
Downsloping

ETT – What to Look For

- Symptoms: timing, quality, and duration
- Blood pressure response: normal/blunted/hypotensive/hypertensive
- ECG changes:
  - Depth and morphology of ST segment changes
  - Timing of ECG changes
  - Duration
- Arrhythmias: atrial arrhythmias, ventricular arrhythmias, AV nodal disease

ETT – What to Look For

- Functional capacity
- Chronotropic response
- HR recovery
- BP response
- Duke treadmill score

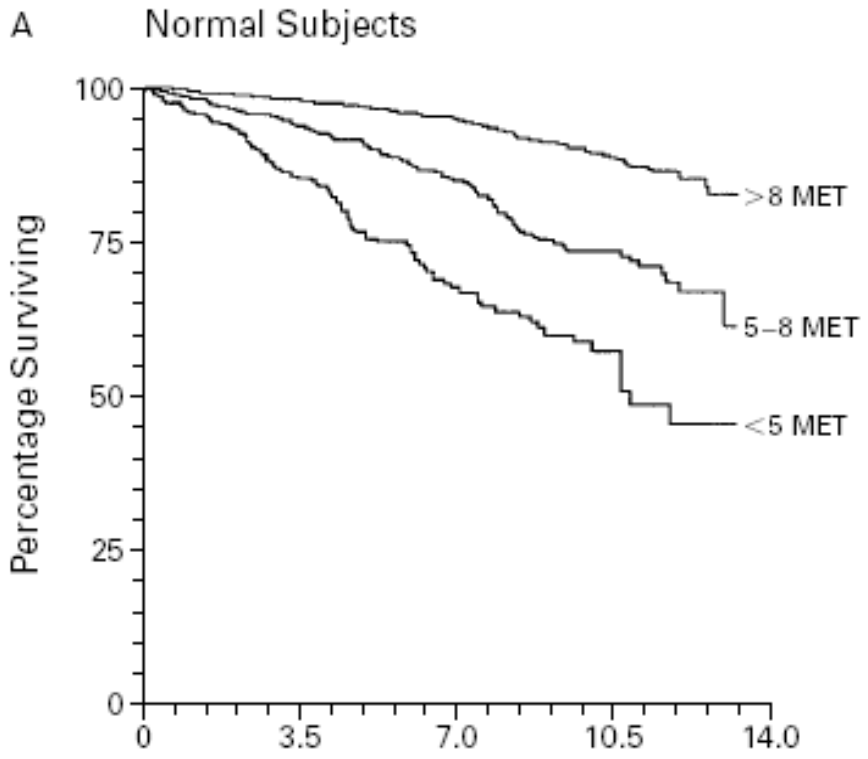
Bruce Protocol

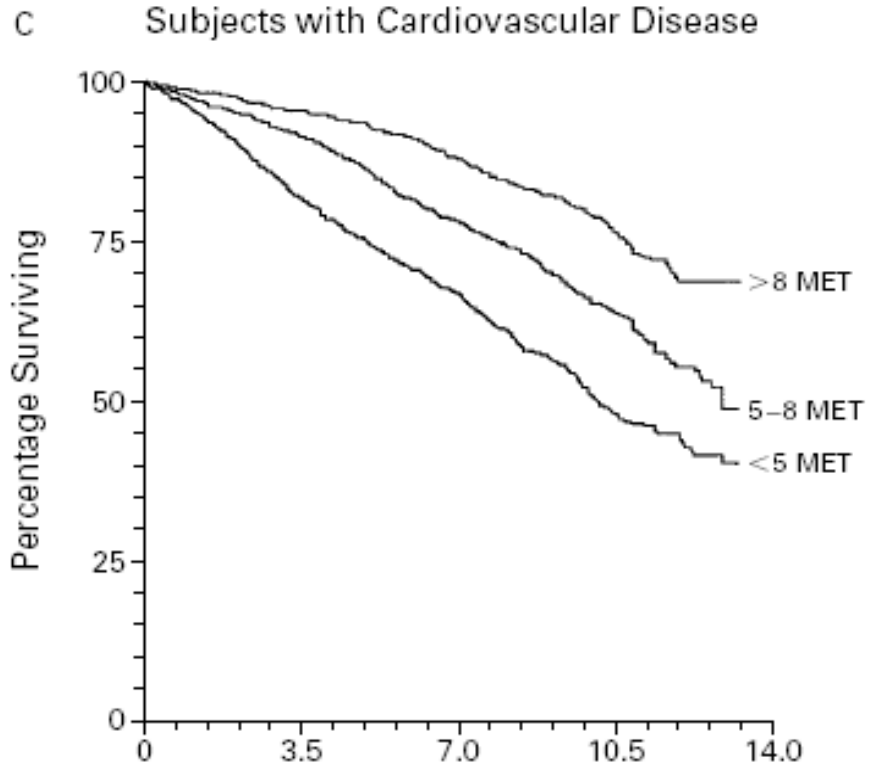
Stage	Minutes	% grade	km/h	MPH	METS
1	3	10	2.7	1.7	5
2	6	12	4.0	2.5	7
3	9	14	5.4	3.4	10
4	12	16	6.7	4.2	13
5	15	18	8.0	5.0	15
6	18	20	8.8	5.5	18
7	21	22	9.6	6.0	20

Estimated functional capacity (METs)

Age	Poor	Fair	Average	Good	High
Women					
<29	<7.5	8 - 10	10 - 13	13 - 16	>16
30 - 39	<7	7 - 9	9 - 11	11 - 15	>15
40 - 49	<6	6 - 8	8 - 10	10 - 14	>14
50 - 59	<5.0	5 - 7	7 - 9	9 - 13	>13
60 - 69	<4.5	4.5 - 6	6 - 8	8 - 11.5	>11.5
70 - 79	<3.5	3.5 - 4.5	4.5 - 6.5	6.5 - 8	>8
>80	<2.5	2.4 - 4.0	4 - 5. 5	5.5 - 7	>7
Men					
<29	<8	8 - 11	11 - 14	14 - 17	>17
30 - 39	<7.5	7.5 - 10	10 - 12.5	12.5 - 16	>16
40 - 49	<7	7 - 8.5	8.5 - 11.5	11.5 - 15	>15
50 - 59	<6	6 - 8	8 - 11	11 - 14	>14
60 - 69	<5.5	5.5 - 7	7 - 9.5	9.5 - 13	>13
70 - 79	<4.5	4.5 - 5.5	5.5 - 8	8 - 9.5	>9.5
>80	<3.5	3.5 - 4.5	4.5 - 6.5	6.5 - 7.5	>7.5

One MET increase in exercise capacity reduces mortality 12-18%





J. Myers, et al. NEJM. 2002; 346:793-801

Duke Treadmill Score

DTS = exercise time (min) – (5 *ST deviation (mm)) – (4 *angina score)

Angina Score:
0 if none
1 if not test terminating
2 if test terminating

Risk	Score	Annual Mortality
Low	≥ 5	1%
Intermediate	-10 to 4	2-3%
High	≤ -11	>5%

Mark DB et al. NEJM 1991;325:849-853

ETT: Sensitivity and Specificity

Froelicher VF et al. Ann Intern Med. 1998 Jun 15;128(12 Pt 1):965-74.

ETT: Sensitivity and Specificity

Sensitivity – 45%

Specificity – 85%

Froelicher VF et al. Ann Intern Med. 1998 Jun 15;128(12 Pt 1):965-74.

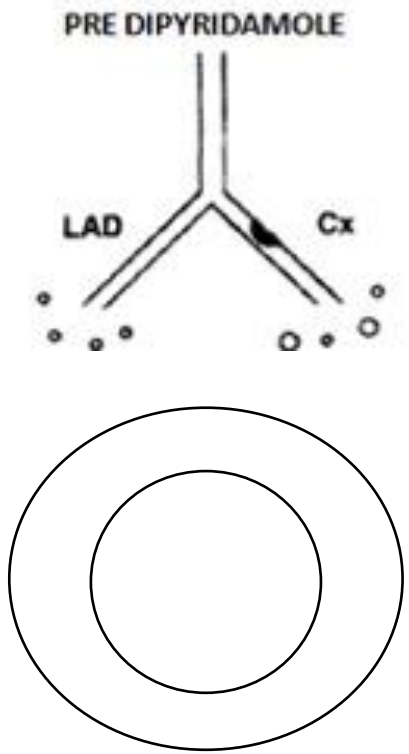
Functional Testing for CAD – Stress Options

- Exercise
- Pharmacologic

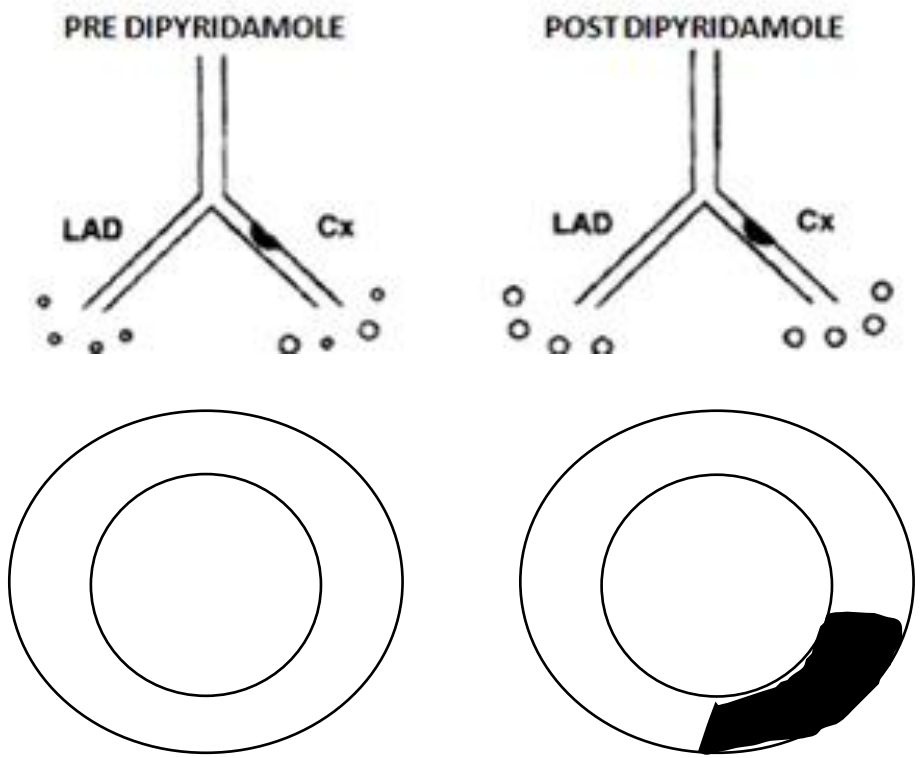
Functional Testing for CAD – Stress Options

Exercise
- Treadmill
- Bike
- Arm ergometry

Pharmacologic
- Vasodilator
- Inodilator



Picano E. *Stress Echocardiography*. 5th edition 2009]



Picano E. *Stress Echocardiography*. 5th edition 2009]

Functional Testing for CAD

- Electrocardiogram Exercise Treadmill Testing (ECG-ETT)
- Single-Photon Emission Computed Tomography (SPECT)
- Positron Emission Tomography
- Stress Echocardiography
- Stress Cardiac Magnetic Resonance Imaging (CMR)

Functional Testing for CAD

- Electrocardiogram Exercise Treadmill Testing (ECG-ETT)
  - Exercise only
- Single-Photon Emission Computed Tomography (SPECT)
  - Exercise or pharmacologic
- Positron Emission Tomography
  - Pharmacologic only
  - (can exercise, but cannot obtain myocardial blood flows)
- Stress Echocardiography
  - Exercise or pharmacologic
- Stress Cardiac Magnetic Resonance Imaging (CMR)
  - Pharmacologic only

SD's General Algorithm

Disclaimers:

1. These are my personal practices, and not recommendations per any guideline document, consensus statement, etc.

2. Please email or page me anytime re: finding the best test for your patient. Our CV Imaging Program strives to provide patient-centered care, and there are often nuances we can help with after discussing the clinical question you are looking to answer and reviewing the patient's existing data with you

SD's General Algorithm

ECG Treadmill Test

- Patients without known CAD, can exercise, and have a normal ECG at rest (no LBBB, no LVH, no pre-excitation, no baseline ST changes > 1mm)

Coronary CTA

- Low-to-intermediate risk patients without known CAD particularly if I can find a chest CT that shows no or mild coronary artery calcium.
- I especially like to use it in young people with typical symptoms as it can
    - 1. Identify an anomalous coronary artery (which, though rare, can be a more likely cause of obstructive disease than atherosclerosis in a very young patient)
    - 2. Identify non-obstructive atherosclerosis which can open up a conversation re: primary prevention (statin Rx, for example).
- Coronary CTA is not great if someone has significant coronary artery calcifications on chest CT (though we have a new scanner that makes this less of an issue), is obese, or has a fast HR that we may not be able to get down to the 60-70s with oral metoprolol at the time of imaging.

SD's General Algorithm

Stress SPECT

- Patients with known CAD, particularly those who can exercise
- Known CAD because it's important to not only identify ischemia (like an ECG-ETT can) but also identify where it is (which an ECG-ETT cannot)
- Of note, if patients do not meet target HR/workload, we can switch an exercise study to a pharmacologic study at that time, which is a nice feature (we tell all patients (whether ordered for an exercise or pharmacologic study) to bring sneakers and to not have caffeine for 24h prior to the test)

Stress PET/CT

- Patients with known CAD who can't exercise (if you already know they can't exercise, then might as well get a pharmacologic stress PET as opposed to a pharmacologic stress SPECT as image quality is superior and we will also obtain myocardial blow flows and CT calcium scoring which can help identify coronary microvascular disease, multivessel obstructive disease, etc.)
- I also use stress PET for patients with suspected coronary microvascular disease (large body of literature on this (including from Marcelo Di Carli's laboratory))

SD's General Algorithm

Stress cardiac MRI

- My practice is to use this modality in cases of suspected non-ischemic cardiomyopathy: stress portion rules out epicardial CAD, and the remainder of the study is helpful re: identifying cause of the cardiomyopathy.

Exercise stress echo

- Patients who may have a valvular or pHTN component to their symptoms
- Nice to have exercise data, inducible wall motion abnormalities, and ECG changes, but also data on rest and exercise-induced/worsening MR, TR, RSVP
- We also use stress echo in patients with HCM to look for dynamic LVOT obstruction, worsening MR, etc.
- I also use it for some patients with an abnormal baseline ECG and therefore require imaging, but I am trying to avoid radiation

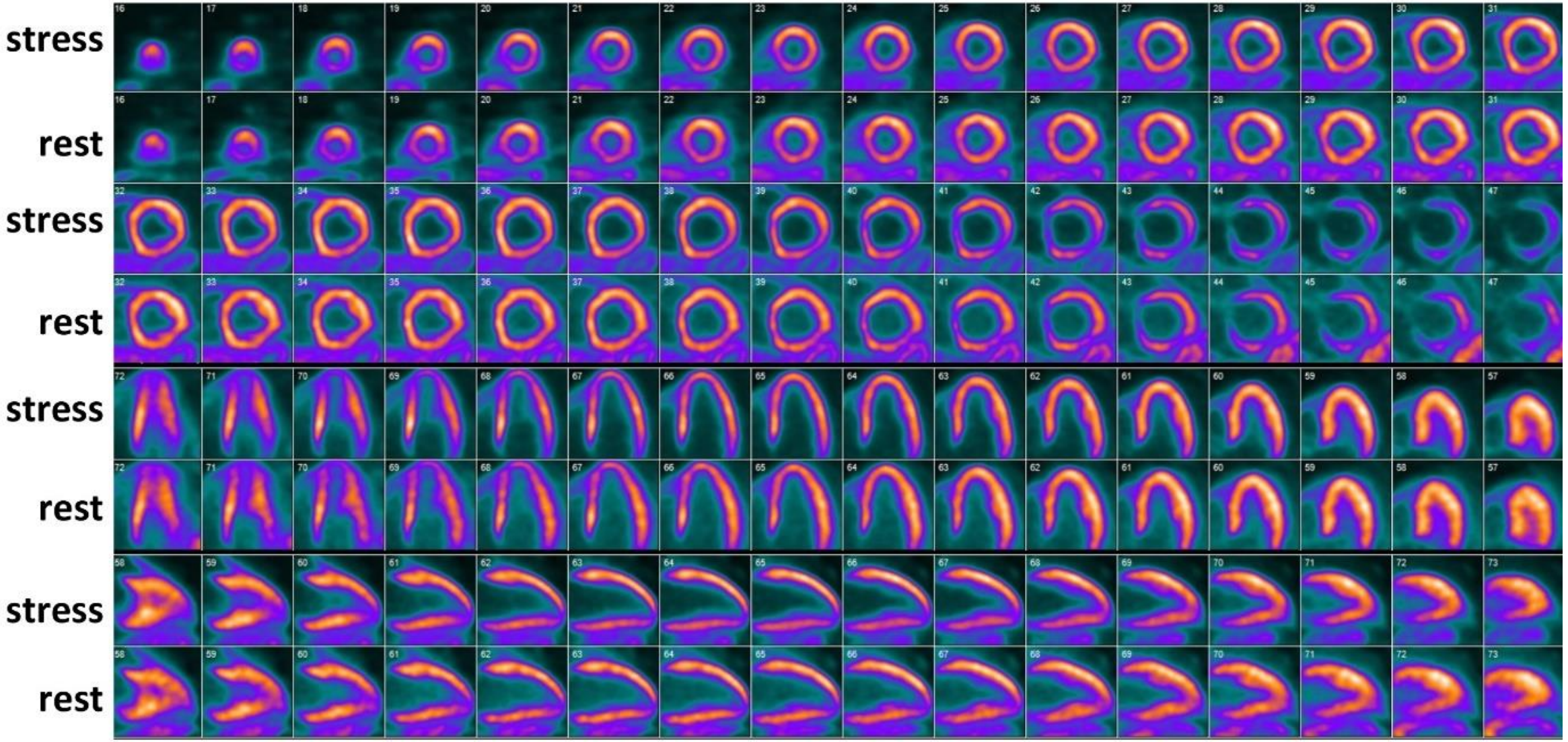
Dobutamine stress echo

- I use very rarely for CAD. I typically only refer for AS assessment in low LVEF to delineate true severe AS vs pseudosevere AS

Cases

Case 1

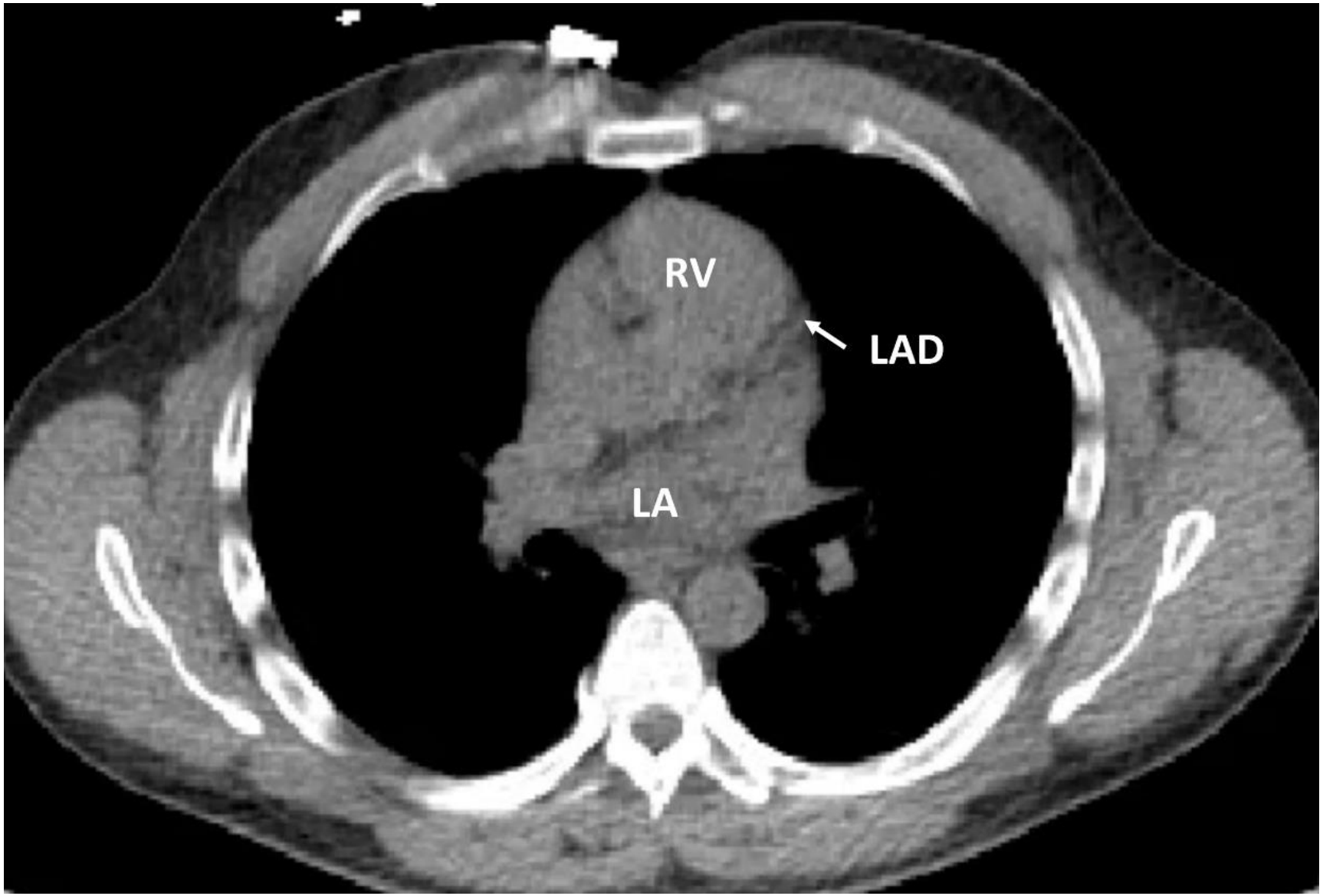
A 52-year-old obese female (BMI 35) with a history of hypertension referred for evaluation for atypical angina and dyspnea. She was referred for a PET at BWH after an equivocal stress SPECT at an outside facility


stress
rest
stress
rest
stress
rest
stress
rest

	Rest (ml/min/g)	Stress (ml/min/g)	MFR (stress/rest)
LAD	1.15	1.96	1.70
LCX	1.27	2.04	1.61
RCA	1.17	2.00	1.71
Global LV	1.19	2.00	1.68

Differential diagnosis?

- Multivessel coronary artery disease (balanced ischemia)
- Coronary microvascular dysfunction


RV
LAD
LA

Case 1

- Normal rest and stress myocardial perfusion
- Normal stress myocardial blood flow, but reduced myocardial flow reserve in all coronary territories and globally
- No coronary artery calcium

The findings in sum are consistent with a diagnosis of coronary microvascular dysfunction

Case 1 – Teaching Points

Helpfulness of integration of perfusion imaging, dynamic blood flow analysis, and CT for CAC assessment via PET/CT

Abnormal myocardial flow reserve in the setting of normal perfusion and no CAC is likely due to coronary microvascular dysfunction

This diagnosis places the patient at intermediate clinical risk (1-3% cardiac death rate/year) despite the lack of obstructive CAD

- Aggressive risk factor modification indicated

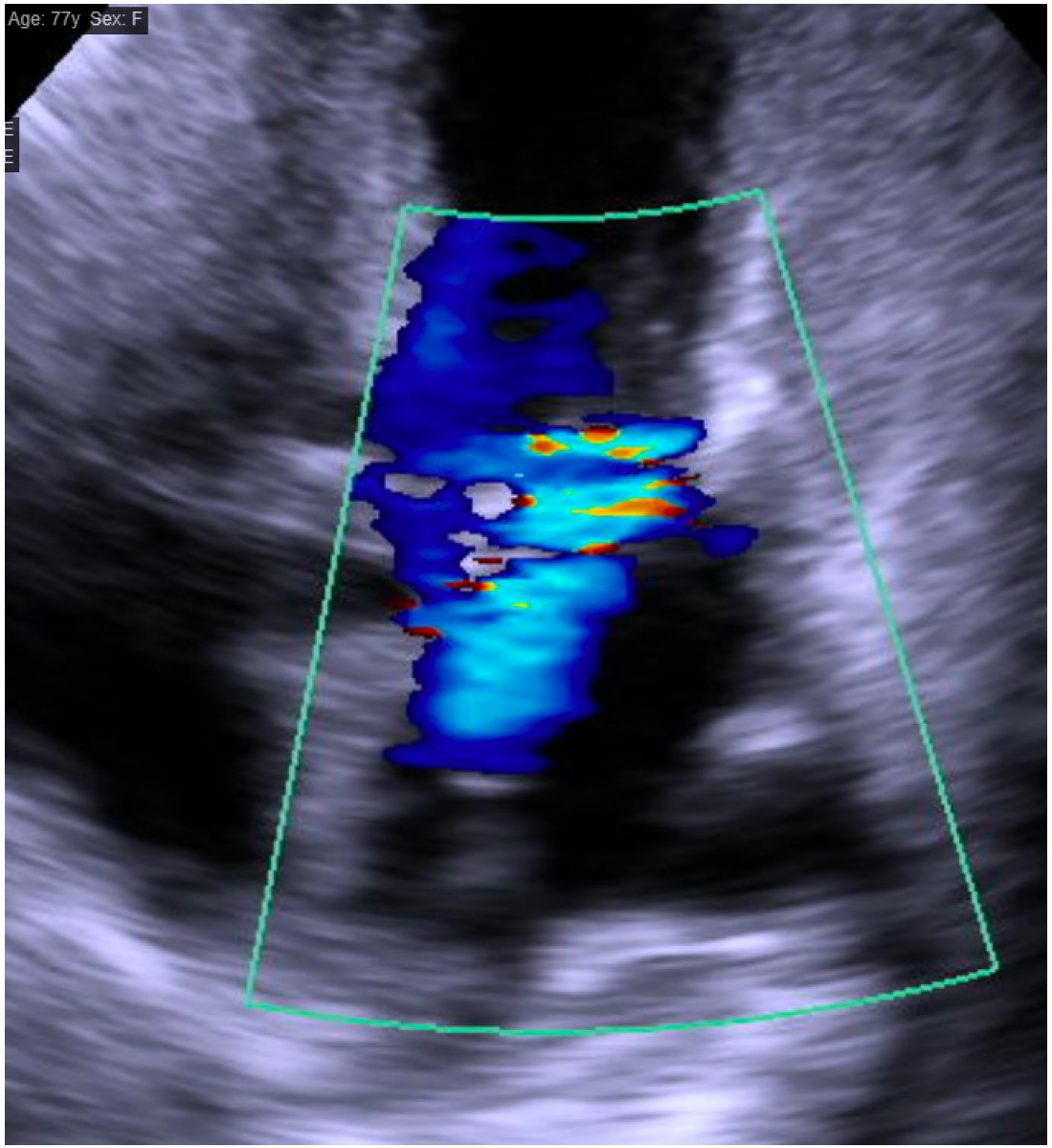
Gupta A…Di Carli MF. Circulation 2017.
Taqueti VR…Di Carli MF. Circulation 2017.
Murthy VL…Di Carli MF. Circulation 2014.

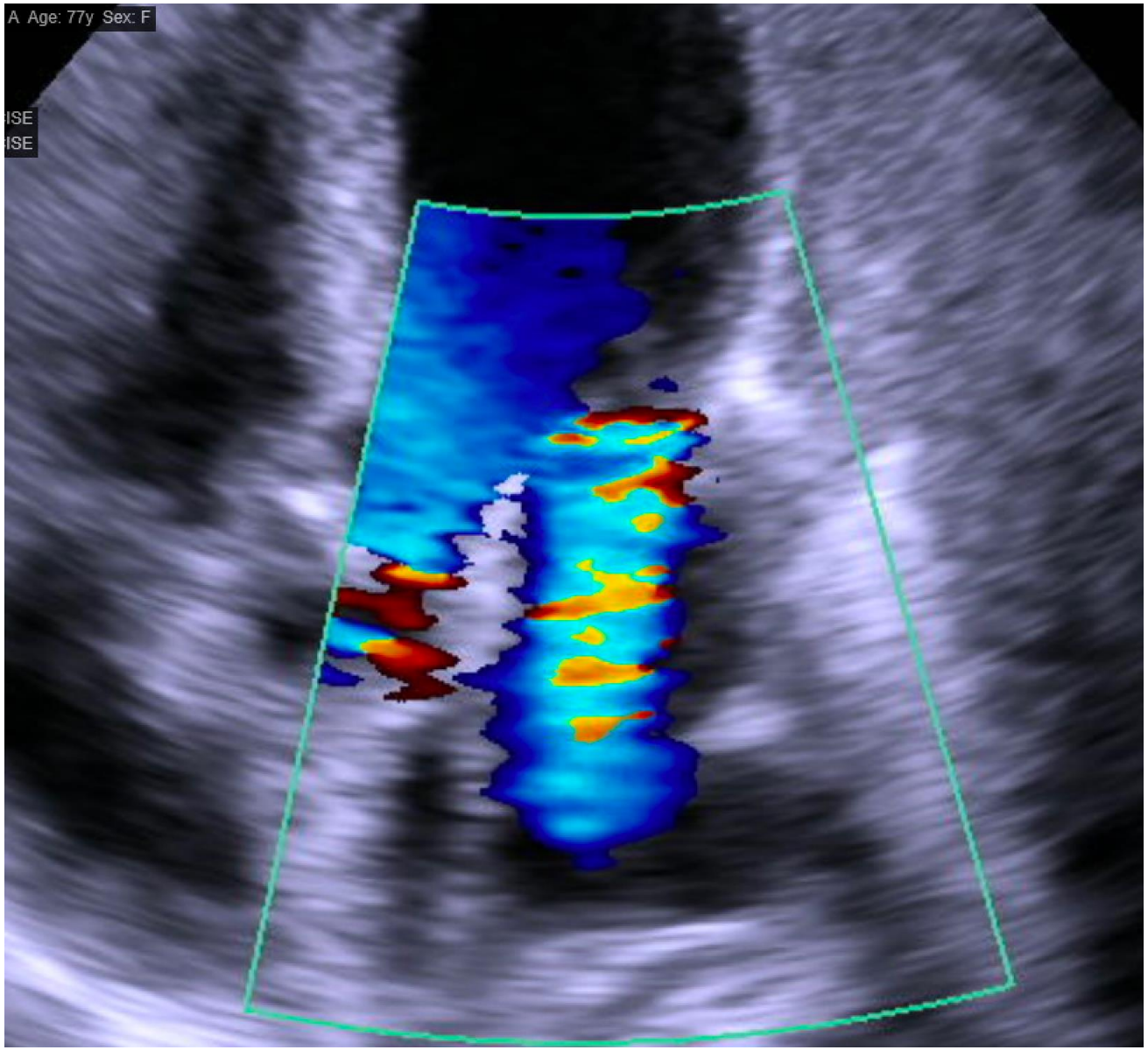
Case 2

77-year-old female with HTN and HLD who is referred to cardiovascular medicine due to exertional shortness of breath and reduction in exercise capacity

Examination notable for II/VI holosystolic murmur at apex

Referred for exercise stress echocardiogram


Age: 77y Sex: F


A Age: 77y Sex: F

Case 2

No resting wall motion abnormalities and no exercise-induced wall motion abnormalities.

Mild-to-moderate mitral regurgitation at rest that worsens to severe mitral regurgitation with exercise. Estimated RVSP increases from 31 mmHg to 60 mmHg with exercise.

Case 2 – Teaching Point

Consider stress echocardiography if there is clinical suspicion of exercise-induced valvular heart disease (+/- CAD) as the cause of symptoms

Case 3

37-year-old woman with no past medical history who is referred for an ECG-ETT due to recurrent exertional chest pain

Pain radiates to the left upper chest and lasts for 5 to 10 minutes with resolution with rest

ECG-ETT

Exercised for 6:10 minutes of a Bruce protocol (7.2 METS)

HR increased from 56 to 96 bpm (59% APHR)

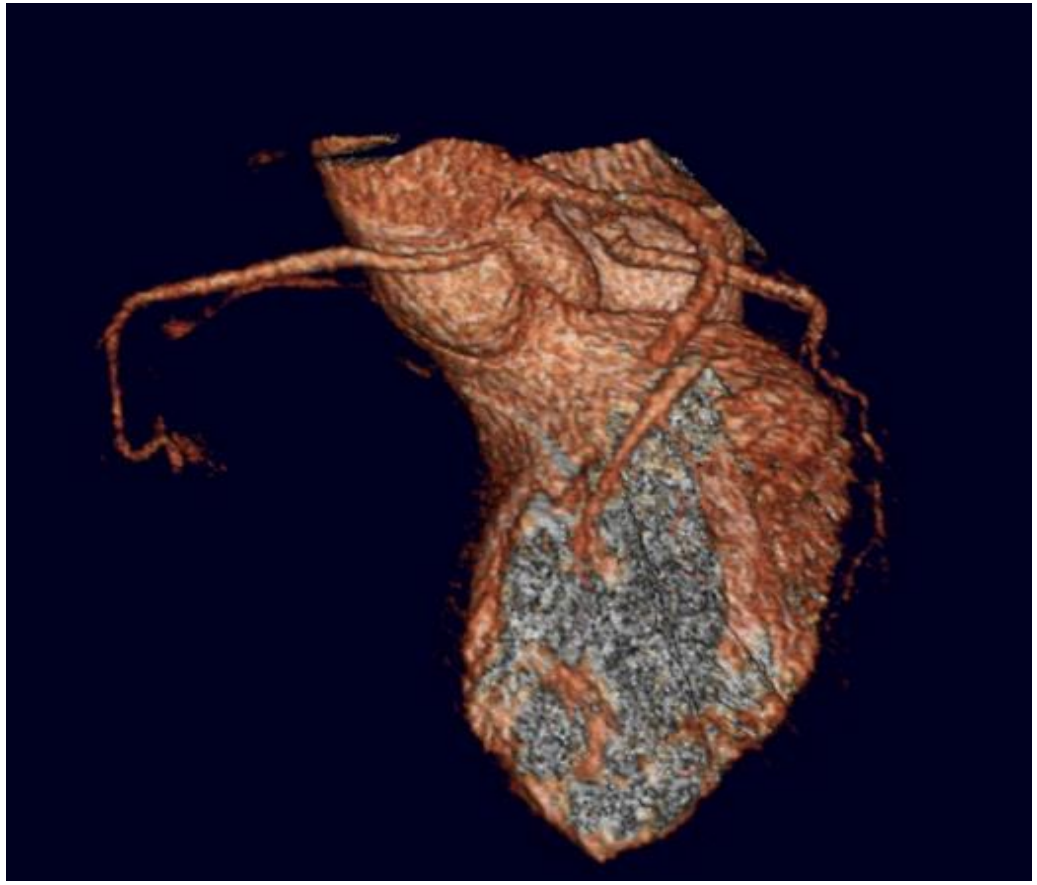
BP increased from 110/78 to 120/70 mmHg

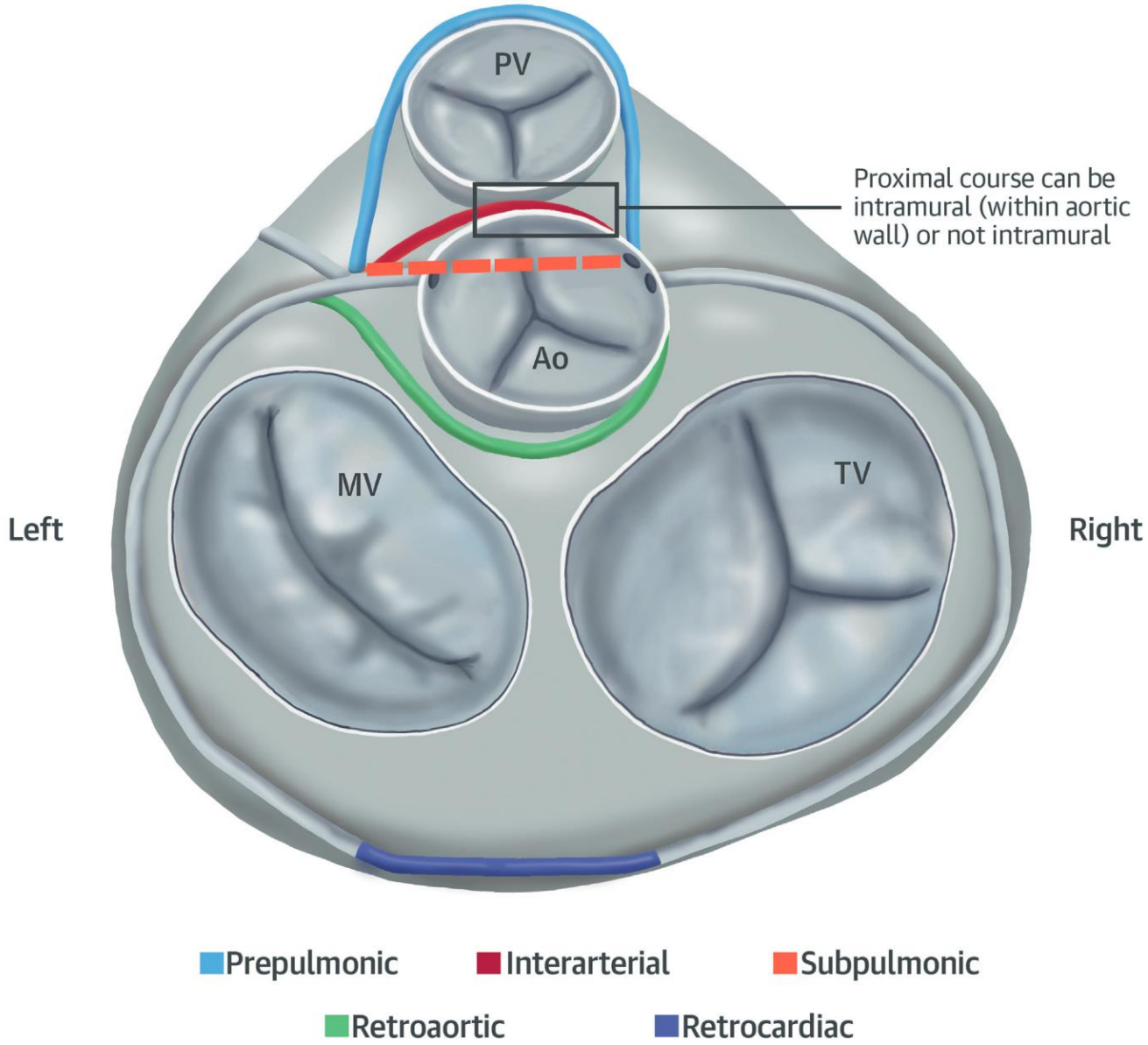
Severe chest pain, dyspnea and fatigue, started 3:00 minutes into the test and resolved 6:00 minutes into recovery

ECG response: non-ischemic


RCA


R
LAD





Cheezum, M.K. et al. J Am Coll Cardiol. 2017;69(12):1592-608.

Case 3 – Teaching Point

In young patients with typical angina despite lack of coronary risk factors, consider referral for coronary CTA (+/- ECG-ETT) for evaluation of traditional CAD, but also for a coronary artery anomaly

Thank You

Chaitu Madamanchi, MD
Ping Sun, MD
Allison Tsao, MD

BWH Cardiovascular Imaging Program: cvimaging.brighamandwomens.org

Learning Objectives

By the end of this presentation, BWH Internal Medicine residents should be able to:

1. Review the reasons why we refer patients to the stress lab
2. Describe the data we obtain via exercise stress testing
3. Develop a framework for how to provide patient-centered care with regards to stress testing

Summary

- Classic angina
  1. Central chest pain or chest pressure that
  2. Increases with exertion and is
  3. Relieved with rest or nitroglycerin
- Bayes' Theorem is key when ordering any diagnostic test, including stress testing
- Know your question as it will help you choose the best test
- Exercise everyone you can – a lot of data beyond the ST segments

@sanjaydivakaran
sdivakaran@bwh.harvard.edu