Stress Echocardiography Boot Camp Review

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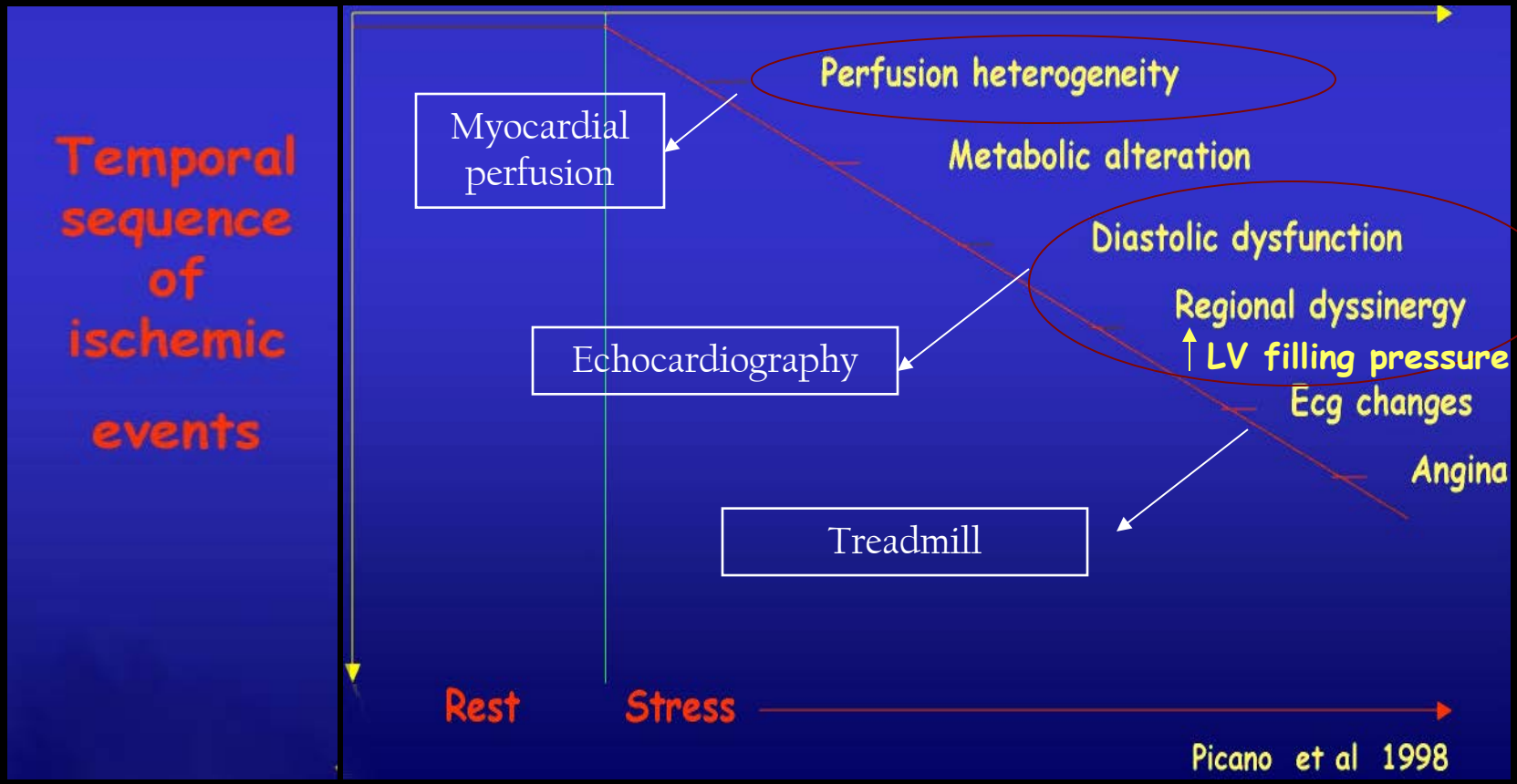
Definition of Stress Echocardiography

The use of echocardiography as an imaging modality to evaluate *wall motion* during stress for the purpose of diagnosing coronary artery disease

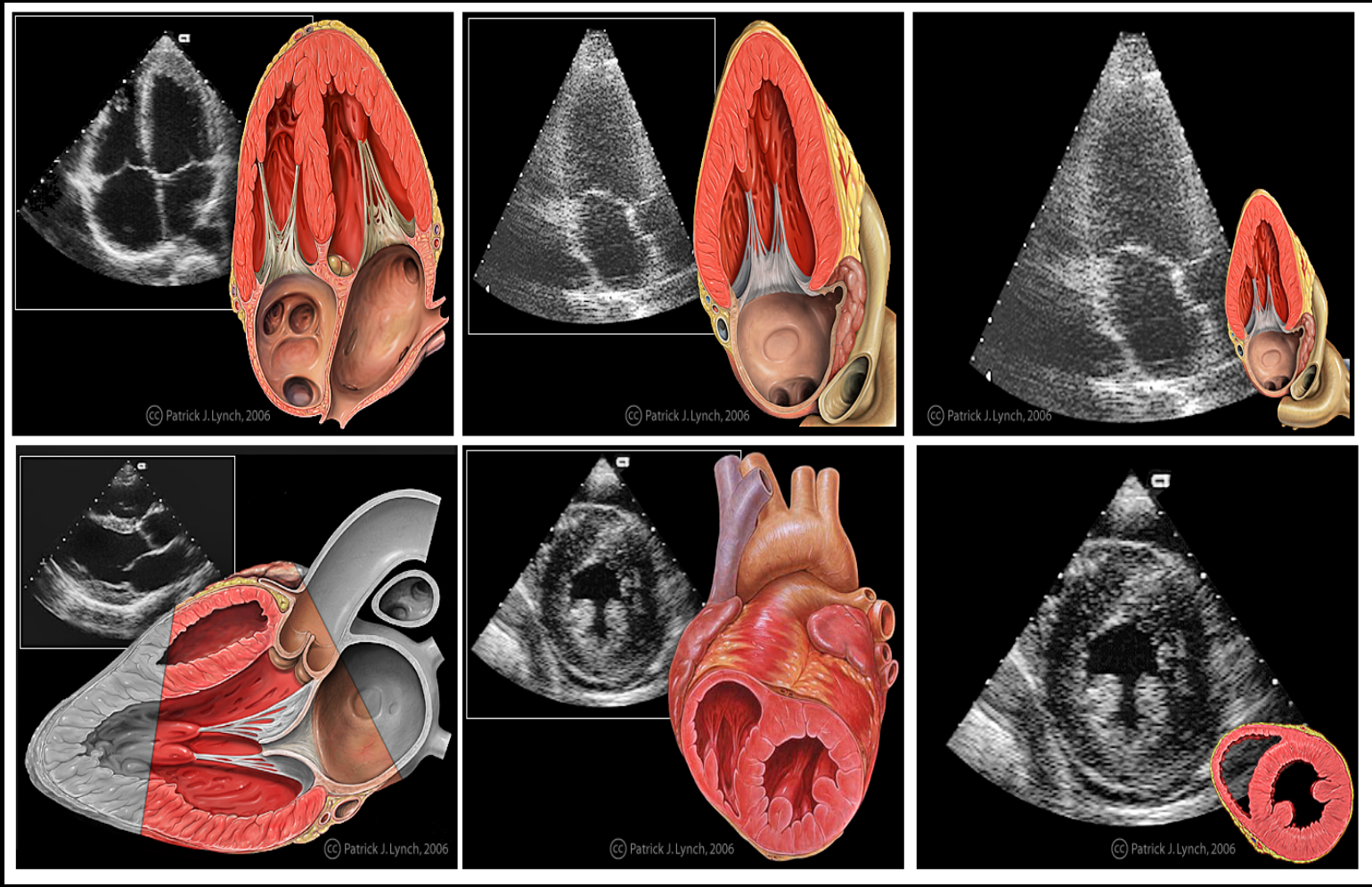
Indications for Stress Echo

- Diagnosis CAD in patients with chest pain
- Determination of the location and severity of inducible myocardial ischemia
- Risk stratification post-myocardial infarction and in stable CAD
- Assessment of viability prior to revascularization
- Preoperative evaluation in select patients

Ischemic Cascade



Cardiac Anatomy and Views



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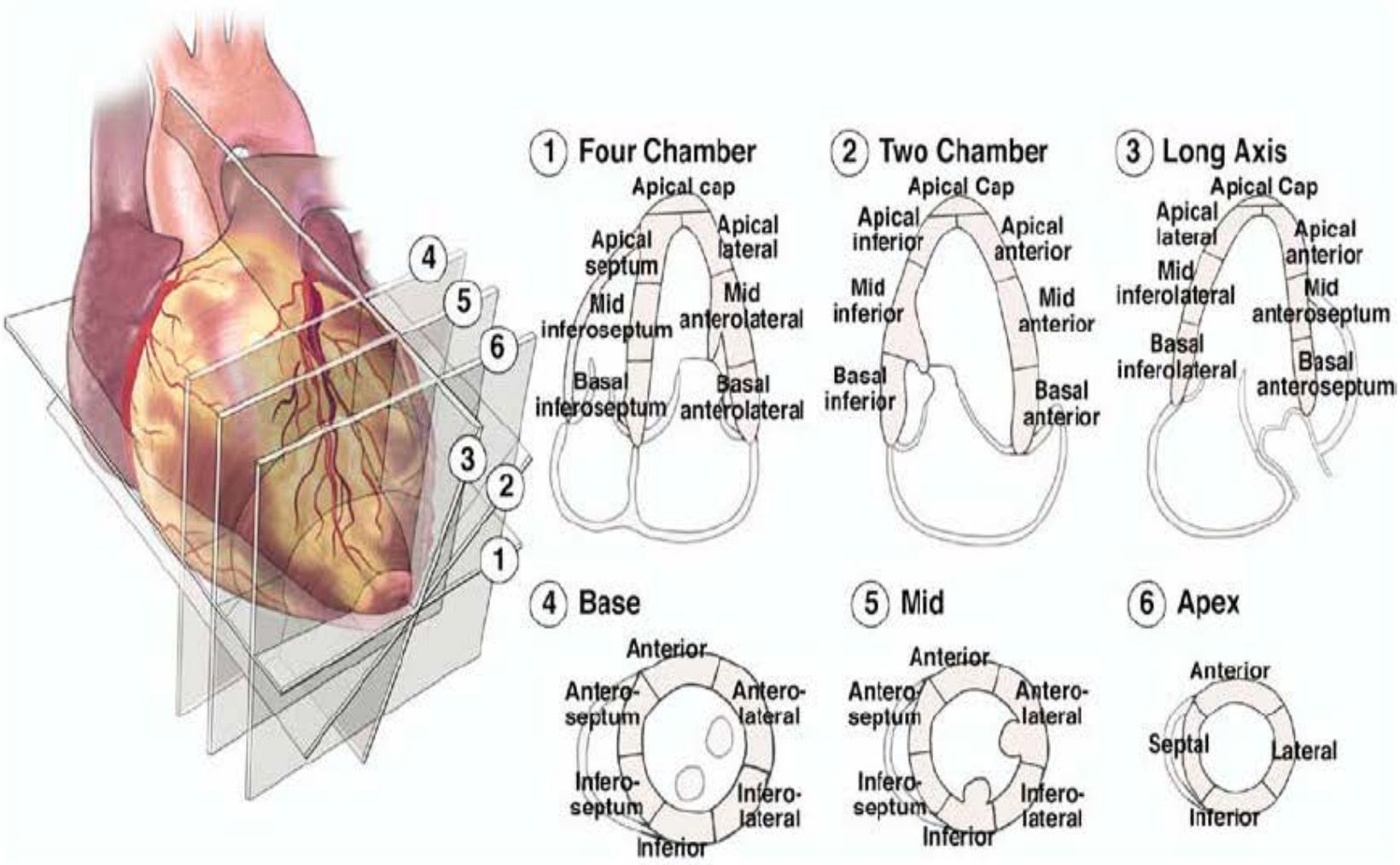
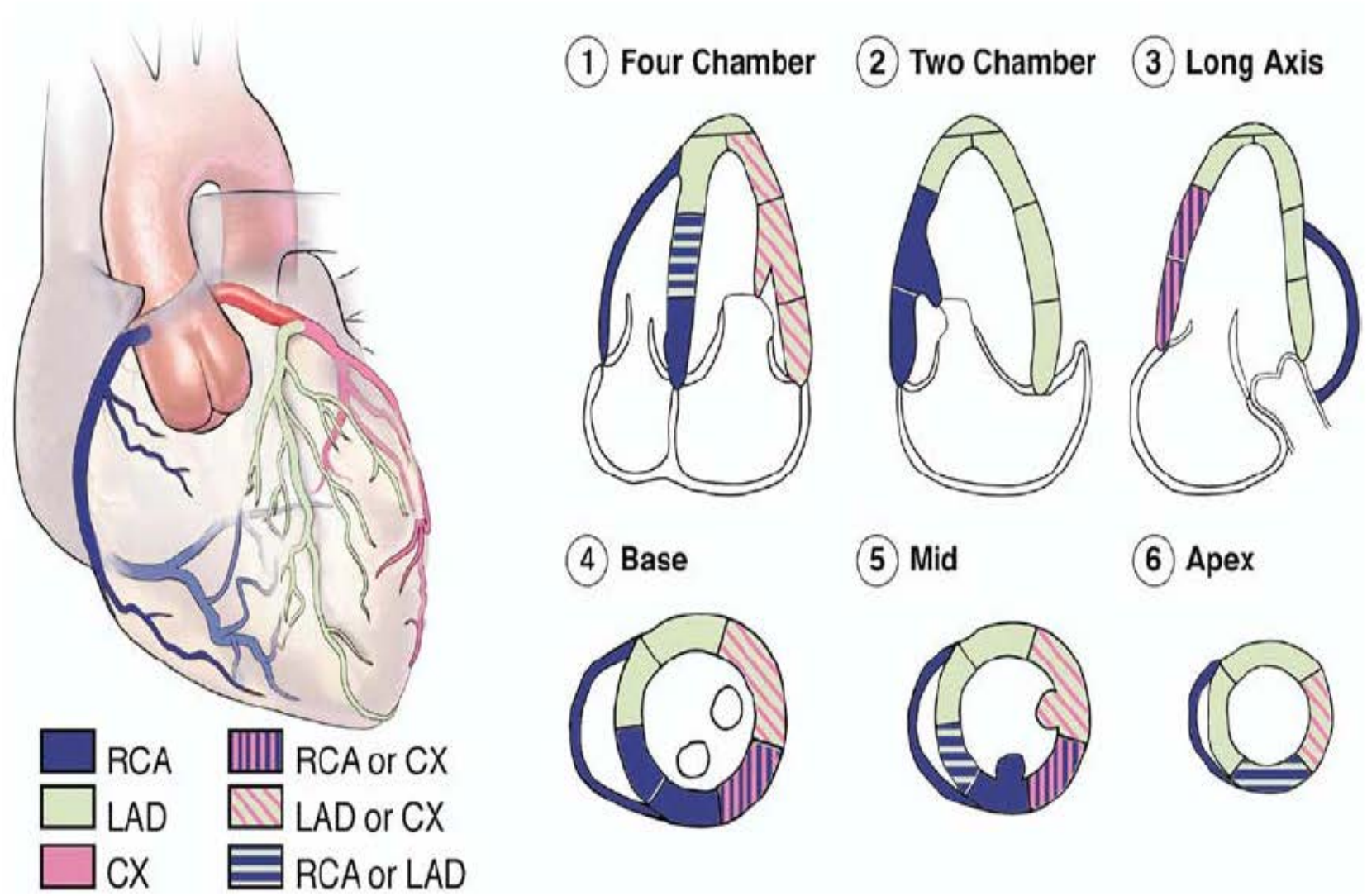


Lang JASE 2005



Lang JASE 2005

Imaging in Stress Echocardiography

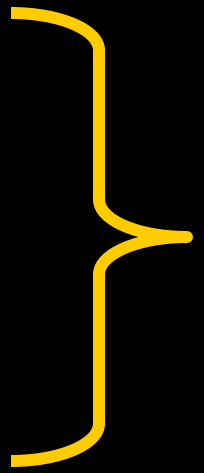
- Tissue harmonic imaging should always be used
  - Reduces near-field artifact
  - Improves resolution
  - Enhances myocardial definition
- Contrast should be used when two or more contiguous segments are not well visualized

Echocardiographic Views for Stress Echocardiography

- Parasternal long and short
- Apical 4 and 2 chamber
- Apical 3 chamber

Regional Wall Motion Scoring

- 0= Hyperkinetic
- 1= Normal
- 2= Hypokinesis
- 3= Akinesis
- 4= Dyskinesis
- 5= Aneurysmal



Baseline Scoring

Quantitation of Regional Function

- Centroid method: forming multiple radii, extending from a geometric center of mass (centroid) to the endocardial and epicardial surfaces
- Centerline methods: generation of chords to the endocardium and epicardium generated perpendicular to the LV long-axis

Centroid Method

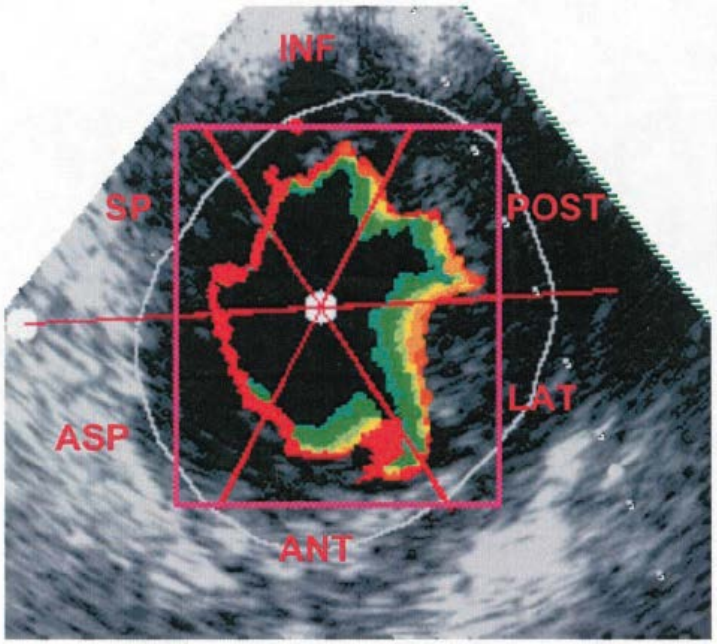
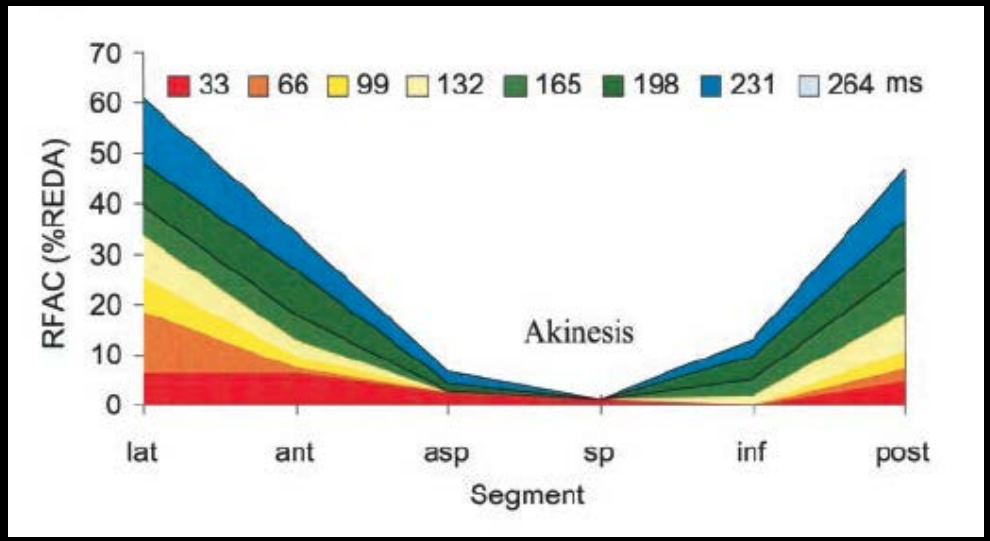
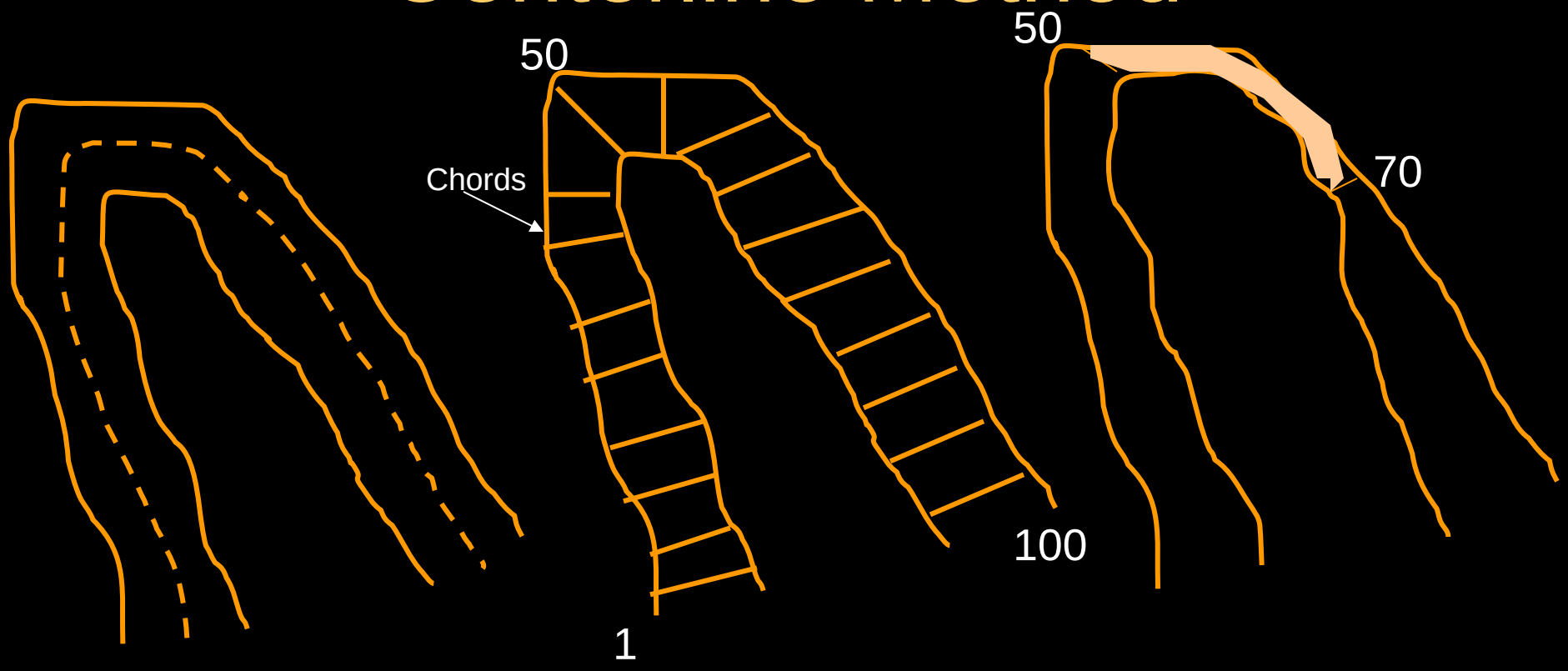


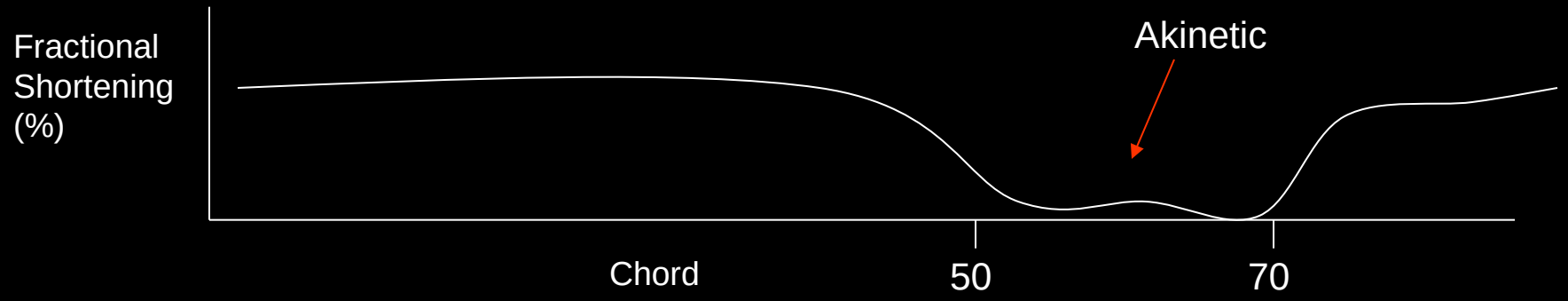
Figure 1. Example of an end-systolic color kinesis image of the left ventricle in transgastric short-axis view. The segmentation scheme used for analysis of endocardial motion is superimposed on the end-systolic color-encoded frame: ant = anterior; asp = anteroseptal; sp = septal; inf = inferior; post = posterior; lat = lateral.



ANESTH ANALG 2003;96:1294–300

Centerline Method





Methods of Assessing Wall Motion

	Endocardial Excursion	Wall Thickening
Advantages	Relies on readily defined interface	Independent of a center of reference
	More readily measured around entire circumference of ventricle	Unaffected by shape changes
Disadvantages	Centroid-dependent	Difficult to measure around entire circumference due to poor epicardial definition
	Affected by translation and rotation	Difficult to correlate with results of radionuclide or contrast ventriculograms

Mann et al: Prog Cardiovasc Dis, 1986

Methods to Correct for Cardiac Motion

- Fixed or floating reference point to assess endocardial excursion or myocardial thickening
- Fixed point does not realign with cardiac motion
- Floating point realigns with translational and/or rotational motion

Fixed and Floating Reference

- Fixed reference system: may cause artifactual hypokinesis in a normal heart
- Floating reference may present a dysfunctional segment as normal
- Parisi, et al found that both fixed and floating methods yield similar accuracy in assessing wall motion abnormalities, but fixed method may be better to localize the abnormality

Problems with Quantitation

- Problems with rotation and translation confer some degree of ambiguity on segmental localization (false positive)
- Tethering of ischemic segments to intact myocardium may result in underestimation of ischemic severity
- Endocardial excursion of nonischemic segments may be limited if they are adjacent to ischemic segments that move poorly resulting overestimation of ischemic severity (false positive)
- Overall, centroid methods do NOT improve sensitivity of stress echo

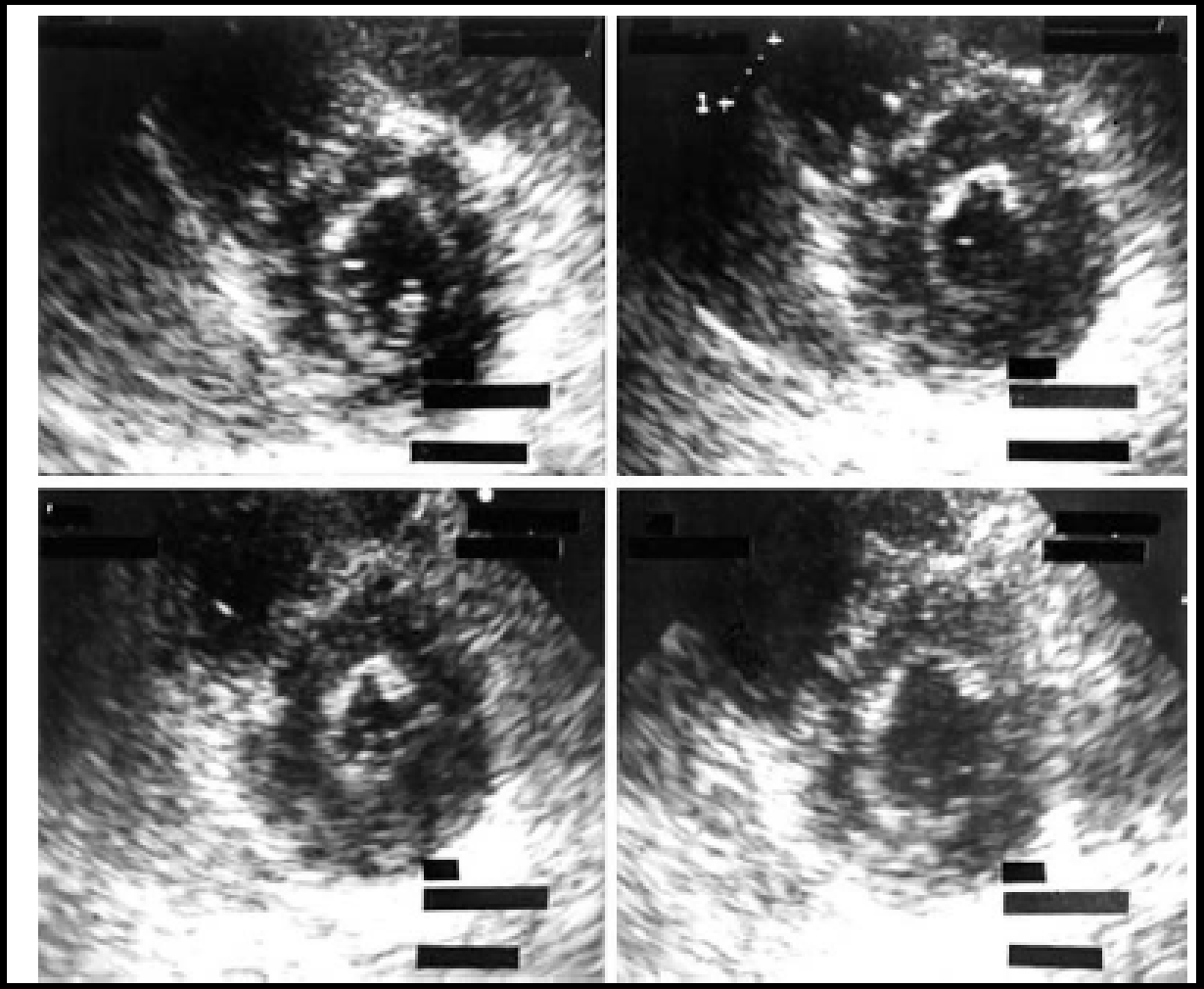
Wall Motion and Severity of Stenosis

- At rest, wall motion may be normal with stenosis of < 85% (when flow at rest is still within normal)
  - Hypokinesis can be seen in a reduction of blood flow by 10-20%
  - Akinesis is observed when there is an 80% reduction in flow
- With stress, a stenosis of ≥ 50% can cause regional wall motion abnormality
- The decrease in wall thickening is more closely coupled to subendocardial rather than subepicardial blood flow, i.e. can be affected by amount of stress, wall thickness, collaterals, diffuse disease

Normal Responses to Stress

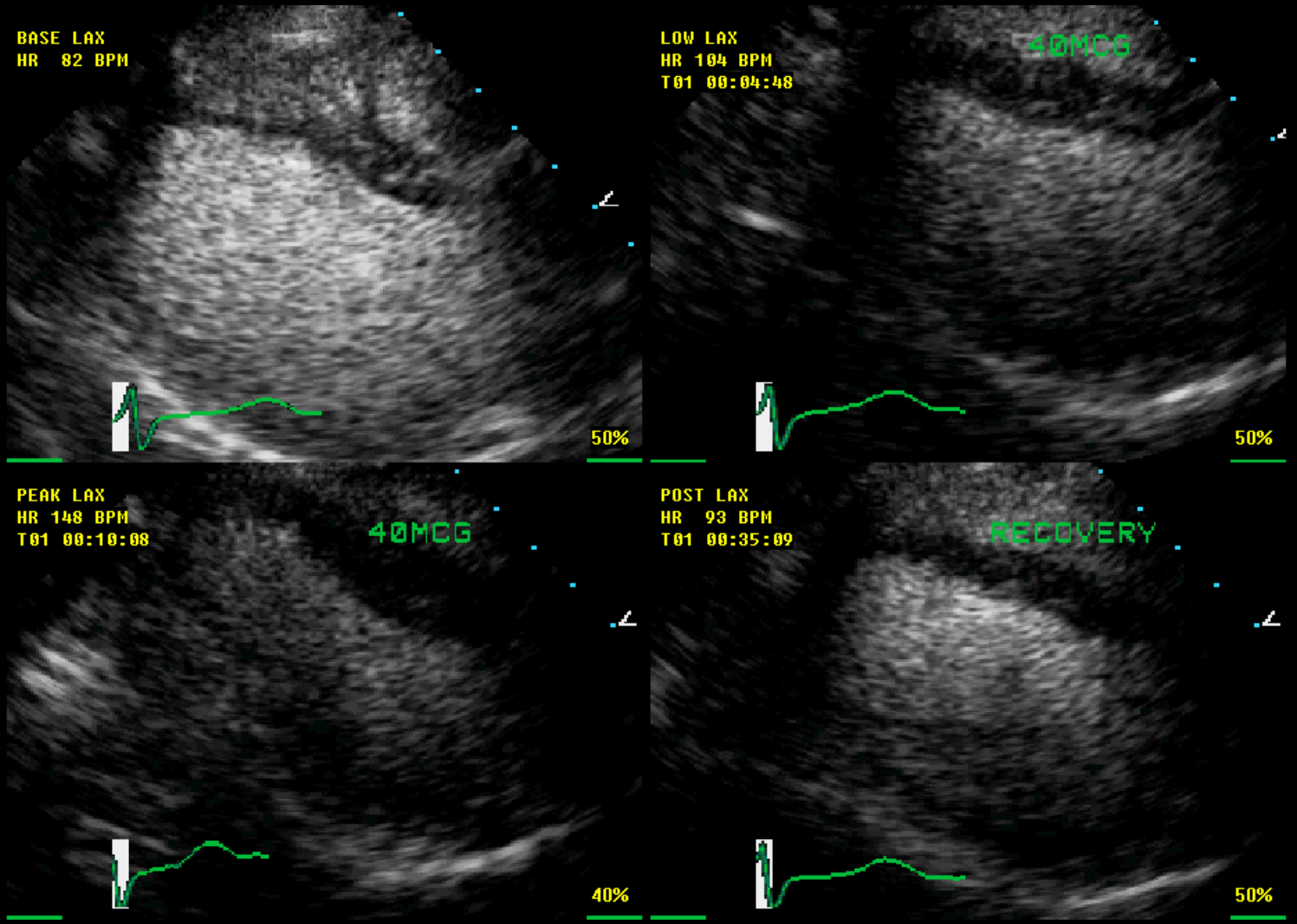
- Hypercontractile wall motion
- Wall thickening, normal is >50%
- Improved endocardial excursion
- Smaller LV chamber size in systole *and* diastole
- Flat response is *not* specific for ischemia

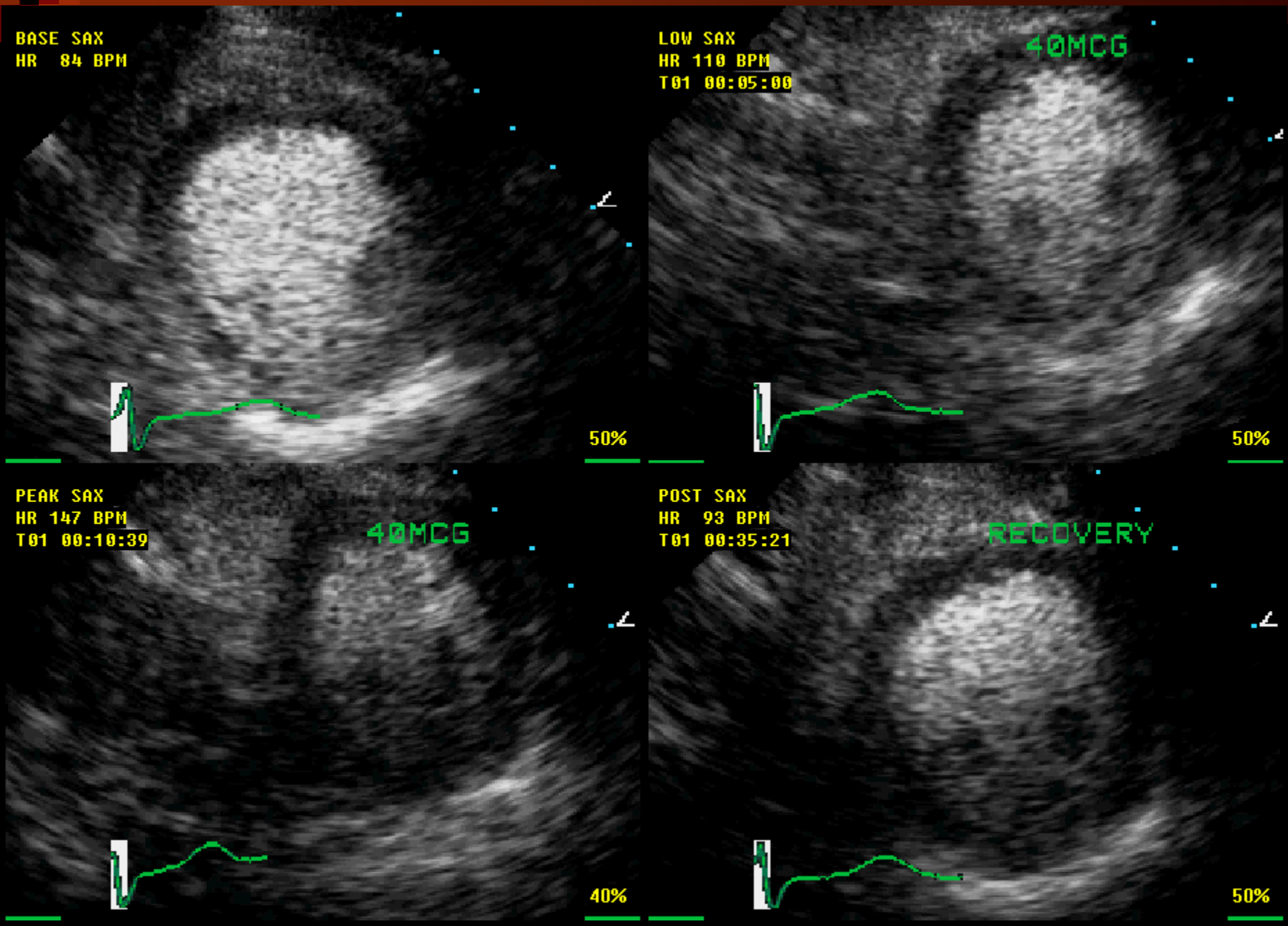
Normal Response to Stress



Senior, et al *Heart* 2005

Normal Stress Echo

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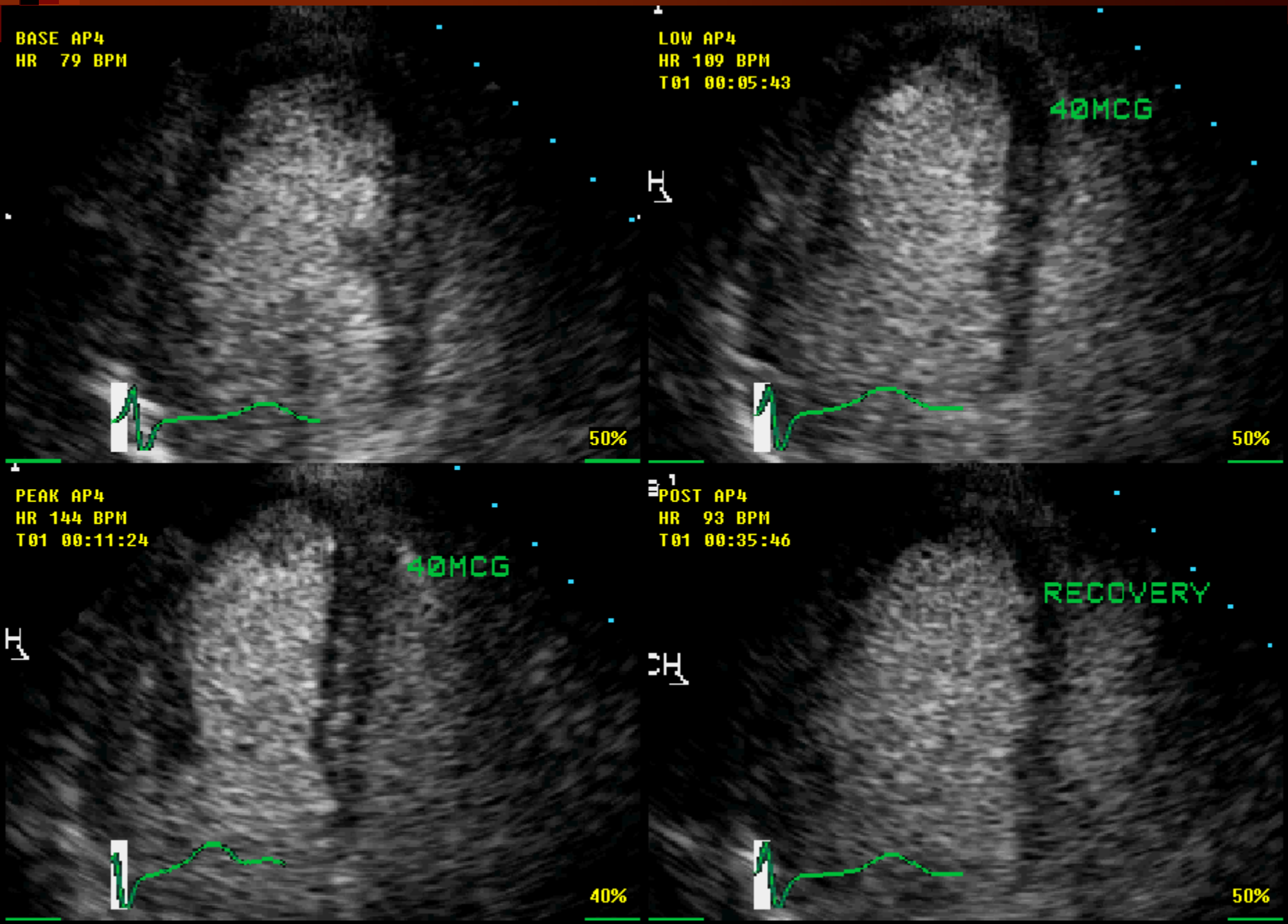
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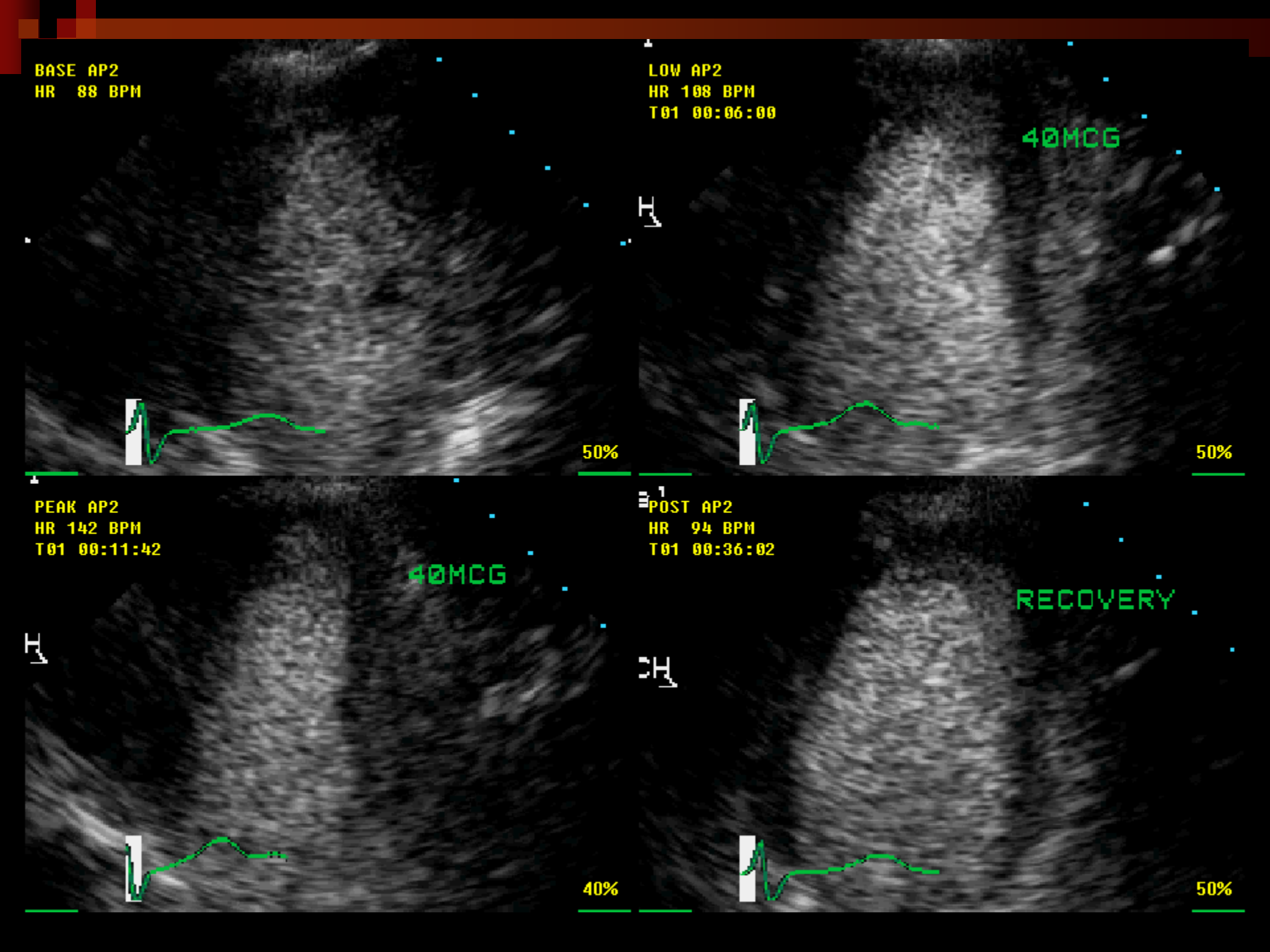
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RECOVERY
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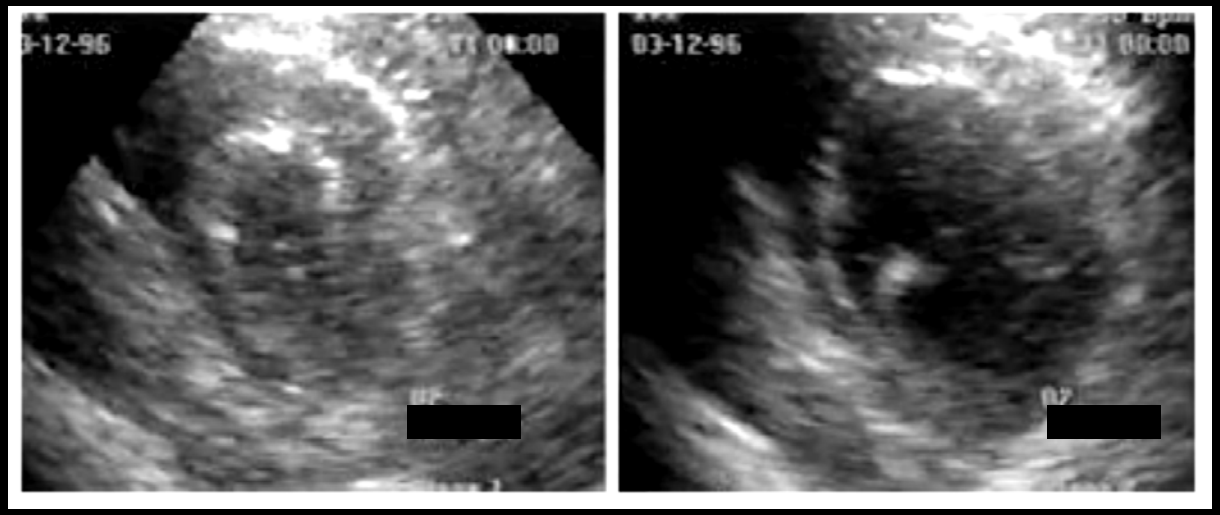
Abnormal Response to Stress

- Hypokinesia: less than normal (5 mm) degree of inward myocardial excursion or thickening (40%)
- Akinesia: complete lack of inward motion and thickening (<10%)
- Dyskinesia: paradoxical (outward motion during systole)
- Aneurysm: thinning and bulging during systole and diastole

Otto, *The Practice of Clinical Echocardiography*

Abnormal Response to Stress

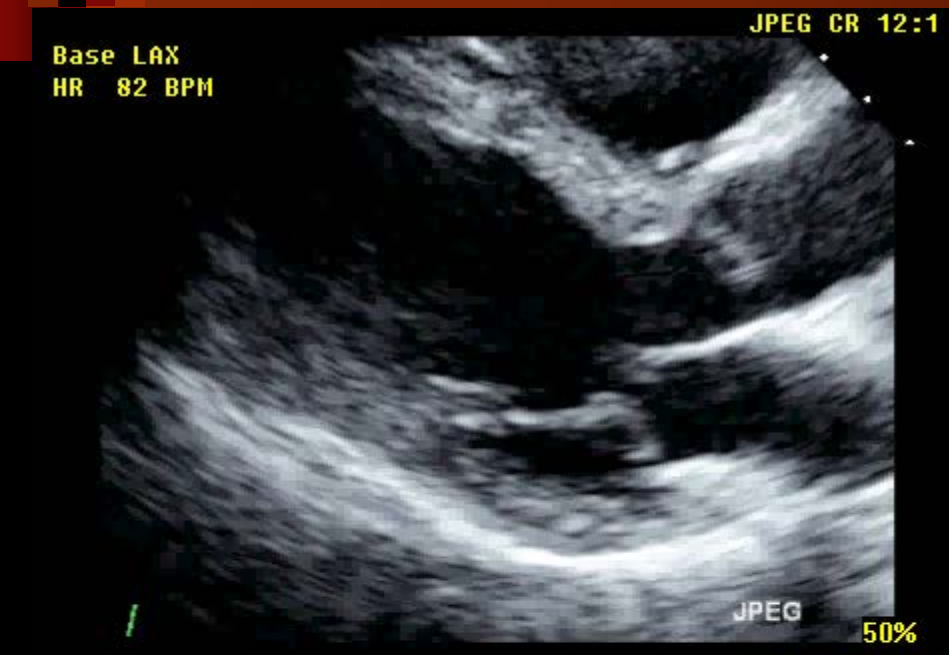


Extreme example of myocardial stunning due to multivessel disease

Senior, et al *Heart* 2005

Case 1

58 yo man with history of hyperlipidemia, gastroesophageal reflux disease, and atypical chest pain with a treadmill ECG test that revealed ischemic ST changes in the absence of chest pain at 10 METs of exercise on a Bruce protocol. Duke treadmill score was -1 (intermediate risk). He, therefore, was sent for dobutamine stress echo for further risk stratification.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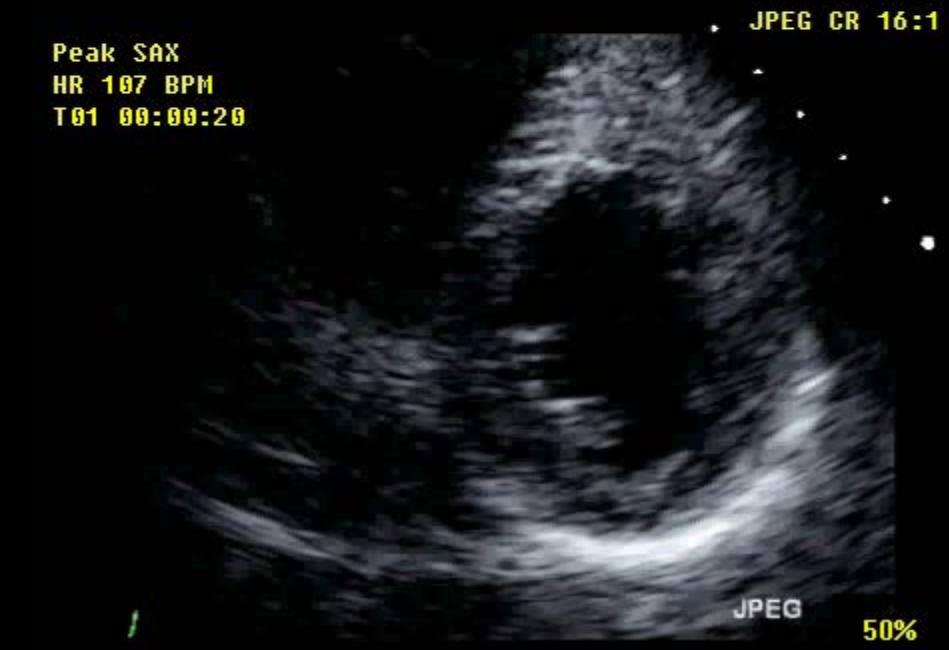
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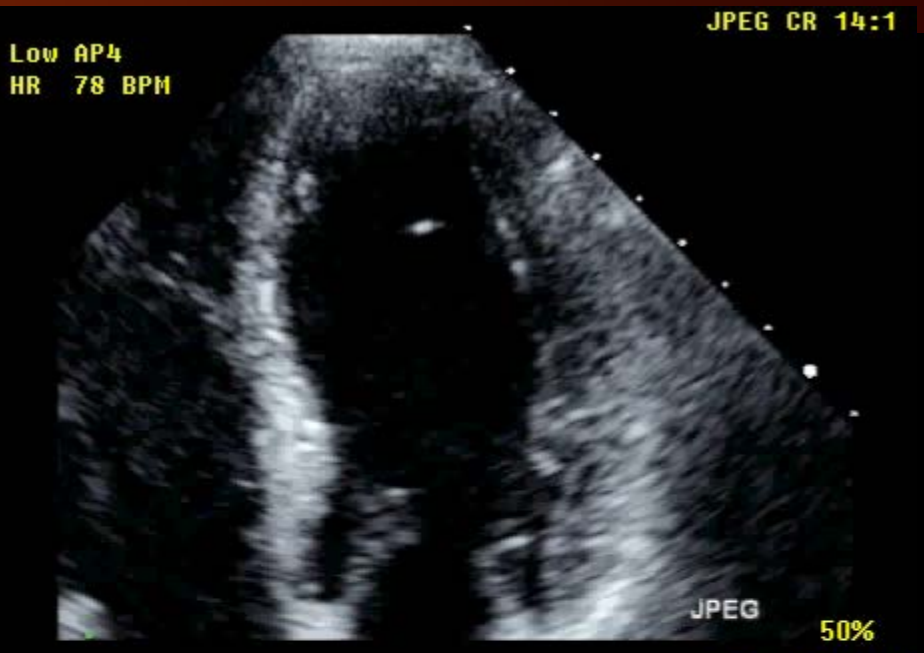
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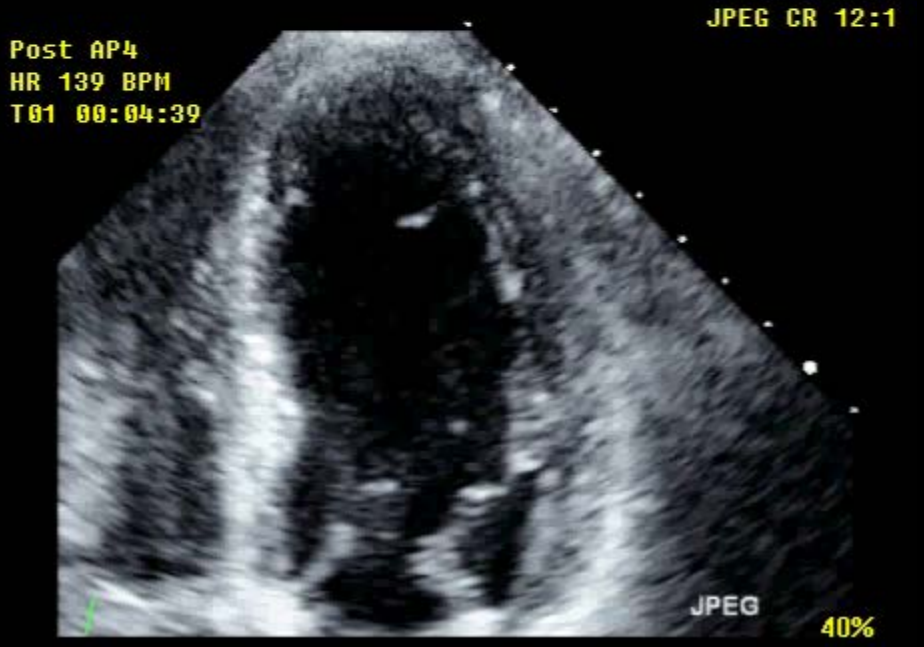
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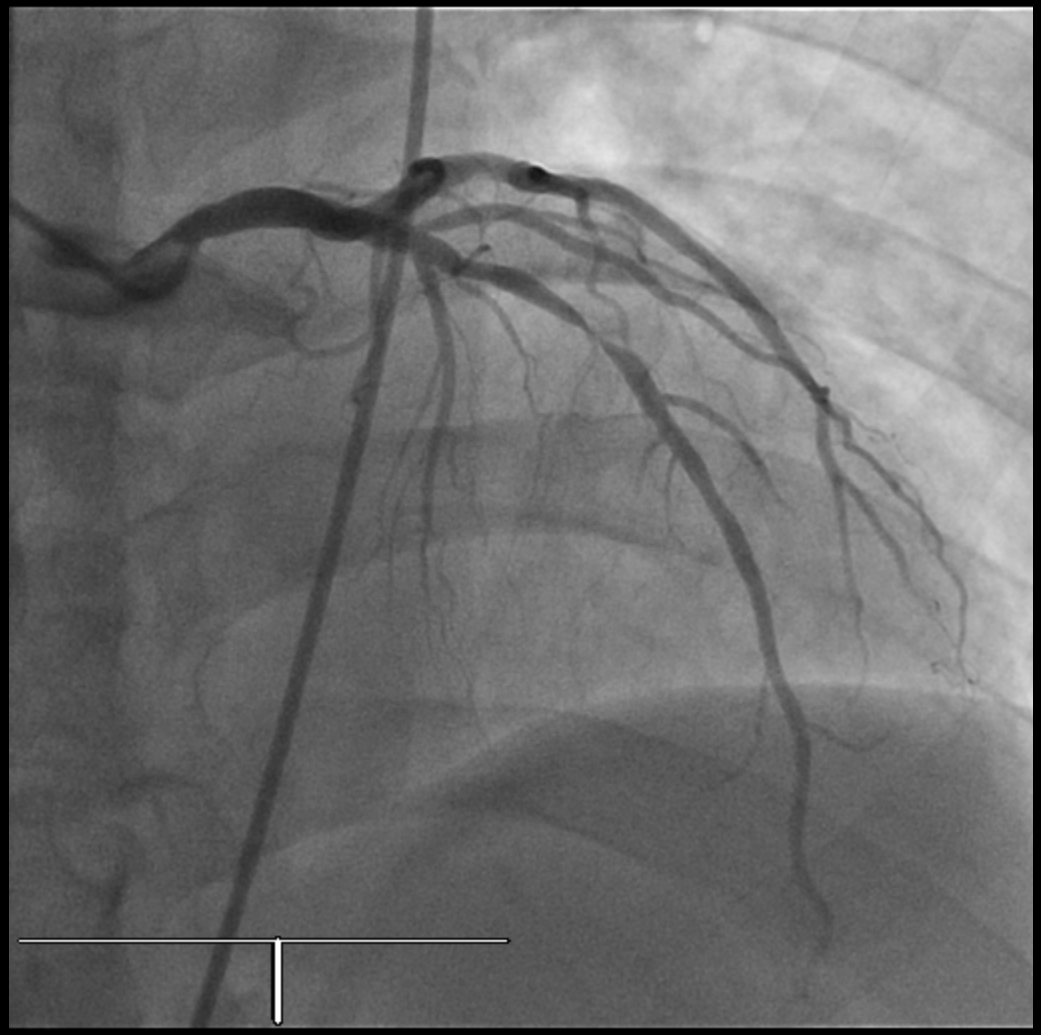
Catheterization Results



Interpretation of Stress Echo

- Can be interpreted qualitatively with a descriptive summary of the myocardial response: for example, normal hyperdynamic response, decrease in cavity size, no new wall motion abnormalities
- Can be interpreted quantitatively using the standardized segments with numeric descriptions

Qualitative Interpretation:
Classification and Clinical Implications of Stress Echo Responses

		Rest	Stress	Implication	Clinical situation
I	Normal	Normal	Hyperdynamic	No CAD, no ischemia	No CAD
II	Ischemic	Normal	Abnormal	CAD present, ischemia induced	CAD, no prior MI
III	Fixed	Abnormal	Stable	CAD present, no inducible ischemia	CAD, prior MI
IV	Mixed	Abnormal	New abnormality	CAD present, additional areas of ischemia	CAD, prior MI and multivessel disease

J Am Soc Echocardiogr 1998; 11:97-104

16 or 17 Segment Model

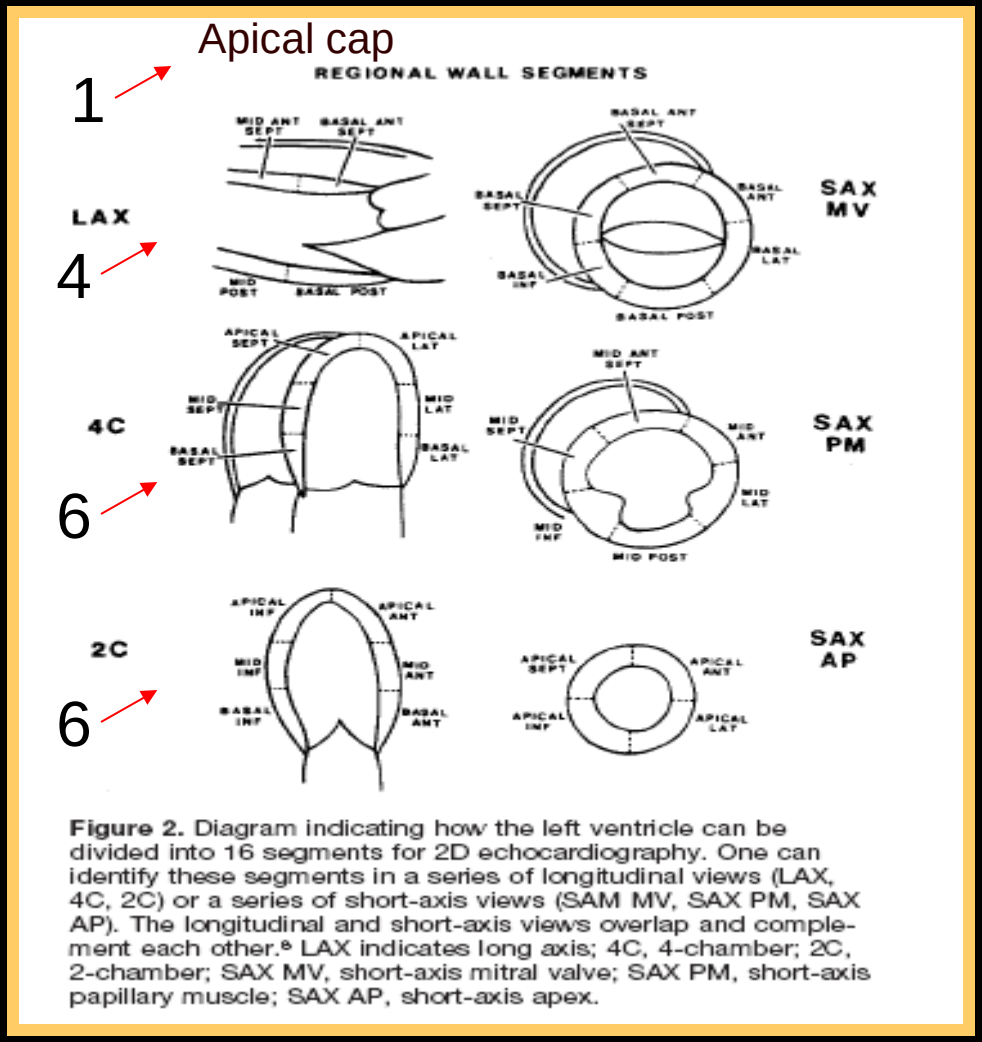


Figure 2. Diagram indicating how the left ventricle can be divided into 16 segments for 2D echocardiography. One can identify these segments in a series of longitudinal views (LAX, 4C, 2C) or a series of short-axis views (SAM MV, SAX PM, SAX AP). The longitudinal and short-axis views overlap and complement each other.[5] LAX indicates long axis; 4C, 4-chamber; 2C, 2-chamber; SAX MV, short-axis mitral valve; SAX PM, short-axis papillary muscle; SAX AP, short-axis apex.

- Comparison among imaging modalities is done using the 17 segment model
- Apical cap is the thinnest portion of LV and does not contract or thicken

Quantitative Interpretation:
ASE Guidelines for Calculating Summed Stress Score

For each of the segments: Scoring from 1-5

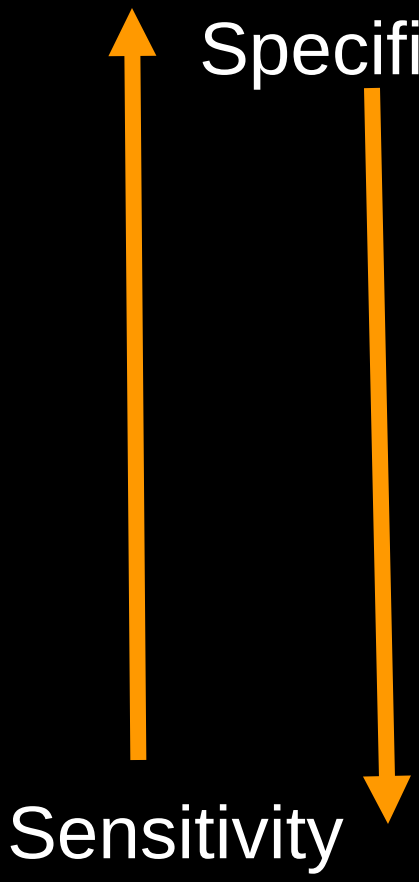
REGIONAL WALL MOTION SCORE INDEX (RWMSI) =sum of scores/number of segments visualized

RWMSI=1 is normal

RWMSI >1 is abnormal

J Am Soc Echocardiogr 1989;2:358

Changes in Sensitivity and Specificity with Abnormal Findings



- Flat response
- Single segment new WMA
- ≥2 segments new WMA
- Extensive new WMA
- LV dilation

Protocols for Stress Echo

- Exercise:
  - Bruce protocol
  - Supine bicycle (25-100 watts in 4 stages)
  - Upright bicycle
- Dobutamine: 10-40 mcg/kg every 3 min
- Dipyridamole: 0.56 mg/kg to 0.84mg/kg
- Adenosine: 140 mg/kg per min
- Atropine can be added to the pharmacologic agents if target heart rate is not reached

Protocols for Stress Echo

- Exercise
  - Treadmill
  - Bicycle
- Pharmacologic:
  - Dobutamine
  - Dipyridamole or Adenosine
- Other
  - Atrial pacing
  - Programmed pacing
  - Handgrip

Exercise or Non-exercise Stress

- Exercise capacity adds prognostic information to the stress data
- It is independent of any demonstration of ischemia
- Generally use treadmill or bicycle
- Can be symptom limited or until target heart rate is achieved

Exercise Stress Protocol

- Treadmill: Imaging done at rest and immediately *after* exercise
  - Bruce protocol to achieve 85% of MPHR
- Bicycle: Imaging done at rest, initial workload of 25W, peak stress and recovery (4 stages)
  - In young pts, initial workload maybe higher

Pharmacologic Stress

- Dobutamine
- Adenosine or dipyridamole
- Atropine (usually added to dobutamine when target heart rate not achieved)

Pharmacology of Dobutamine

- Beta 1 agonist
- Increases myocardial oxygen demand by increased inotropy and chronotropy
- Half-life is 2 minutes

Dobutamine Stress Protocol

- Dobutamine to assess regional wall motion abnormalities
  - Start at 5 mcg/kg/min, increasing every 3min to 10, 20, 30 and maximum of 40 mcg/kg/min
  - In some instances can give up to 50 mcg/kg/min
- Atropine can be given in divided doses of 0.25 to 0.5 mg for maximum of 2.0 mg to achieve target heart rate
  - helps in those who are on beta blocker therapy
  - Increases sensitivity by 5% in single vessel CAD and in those on beta blockers

Contraindications to DSE

- Uncontrolled hypertension
- Uncontrolled dysrhythmia
- Unstable angina (as with any stress test)

- For atropine: untreated narrow angle glaucoma and severe urinary retention

Side Effects to Dobutamine

- Palpitations
- Chest pain
- Tremor
- Headache
- Dizziness
- Urinary urgency
- Nausea
- Dyspnea
- Hypertension
- Hypotension
- Arrhythmias

Endpoints to DSE

- Peak dose with atropine
- Target heart rate reached
- Moderate or extensive wall motion abnormalities
- Significant arrhythmias
- Hypotension or severe hypertension
- Intolerable symptoms (pt request)

Adenosine or Dipyridamole

- Vasodilators
- Increase adenosine (directly or indirectly with dipyridamole which increases endogenous levels)
- Usually response is mild hypotension with some reflex tachycardia
- Wall thickening is related to endocardial blood flow reserve rather than increase in oxygen demand

Side Effects of Vasodilator Stress

- Minor and greater with adenosine than dipyridamole
- Adenosine with much shorter half-life, less than 10 seconds (difficult for stress echo imaging)
- Flushing, AV block, headache, chest pain, nausea, bronchospasm, coughing

Vasodilator Stress Contraindications

- Adenosine
  - Severe bronchospasm
  - Theophylline
  - 2nd or 3rd degree heart block
- Dipyridamole
  - As above
  - Hypotension
  - Unstable carotid disease

Comparisons of Patient Factors and Choice of Stressors

	Medications for Pharmacologic Stress Testing		
Patient-Related Factors	**Dobutamine**	**Adenosine***	**Dipyridamole***
Associated Medical Conditions addressed in detail following this table			
a) Severe COPD or asthma	Indicated	Contraindicated	Contraindicated
b) Heart block (2° or 3°)	Indicated	Contraindicated	Contraindicated
c) Poorly controlled HTN	Contraindicated**	Indicated	Indicated
d) Relative hypotension	Contraindicated**	Indicated	Contraindicated
e) Unstable carotid cerebrovascular**** disease	Contraindicated**	Indicated	Contraindicated
f) Significant vent ectopy	Contraindicated**	Indicated	Indicated
g) Glaucoma***	Contraindicated	Indicated	Indicated
Medical Therapies			
h) Theophylline	Indicated	Contraindicated	Contraindicated
i) Dipyridamole by mouth	Indicated	Contraindicated	Indicated
j) Beta-blocker†	Indicated	Indicated	Indicated

Pharmacologic Reversal Agents

- Dobutamine: IV esmolol or metoprolol
- Dipyridamole: IV aminophylline
- Adenosine: usually not necessary due to short half life, can use IV aminophylline

Pacemaker Stress Protocol

- Patient with permanent pacemaker: can achieve MPHR by increasing pacing rate
- Can be done with or without dobutamine
- Transesophageal pacing can also be done in pts who are not able to exercise
  - Can increase heart rate every 2 min until 85% MPHR is achieved

Comparison of Stress Modalities

Bicycle	Treadmill	Dobutamine	Dipyridamole
Improved sensitivity	Easier protocol	Cumbersome protocol	Easier protocol
Decreased specificity	Improved image quality	Better image quality	Less sensitive
Lower workload	Higher workload	Easier to reach required workload	Not as much data
Leg fatigue	Better tolerated by patients	More side effects and risk	More side effects

Bicycle stress echo may be more sensitive than treadmill exercise

Validation

- Sensitivity
  - True positives/All positives
- Specificity
  - True negatives/All negatives
- Accuracy
  - True positives + True negatives/All tests

Sensitivity and Specificity of Stress Echo

	Sensitivity	Specificity	Accuracy
Exercise	85%	77%	85%
Dobutamine	80%	86%	83%
Dipyridamole (Not well studied)	74%	94%	77%

Modified from *Heart* 2003 and Beleslin Circ 1994

ECHO VERSUS SPECT

	ECHO	SPECT
ACCURACY	85%	~85%
HYPERTENSION/ LVH	Better specificity	Better sensitivity
WOMEN	Better accuracy	Decreased accuracy
COST	<$500	>$500

Why Stress Echo

- Global LV and RV function
- Chamber sizes
- Wall thickness
- Valve structure and function
- Pericardium
- Aorta
- Hemodynamics

Appropriateness Guidelines 2013

- Multiple societies in collaboration published appropriateness guidelines for multimodality imaging for ischemic heart disease
- Tables are too numerous to display but cover diagnoses including stable chest pain, ACS, post-revascularization, pre-op and others

Indications for Stress Testing in Symptomatic Patients

	Indication Text	Exercise ECG	Stress RNI	Stress Echo	Stress CMR	Calcium Scoring	CCTA	Invasive Coronary Angiography
1.	• Low pre-test probability of CAD • ECG interpretable AND able to exercise	A	R	M	R	R	R	R
2.	• Low pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	M	R	M	R
3.	• Intermediate pre-test probability of CAD • ECG interpretable AND able to exercise	A	A	A	M	R	M	R
4.	• Intermediate pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	A	R	A	M
5.	• High pre-test probability of CAD ECG interpretable AND able to exercise	M	A	A	A	R	M	A
6.	• High pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	A	R	M	A

Testing in Asymptomatic Patients

Indication Text		Exercise ECG	Stress RNI	Stress Echo	Stress CMR	Calcium Scoring	CCTA	Invasive Coronary Angiography
7.	• Low global CHD risk • Regardless of ECG interpretability and ability to exercise	R	R	R	R	R	R	R
8.	• Intermediate global CHD risk • ECG interpretable and able to exercise	M	R	R	R	M	R	R
9.	• Intermediate global CHD risk ECG uninterpretable OR unable to exercise		M	M	R	M	R	R
10.	• High global CAD Risk • ECG interpretable and able to exercise	A	M	M	M	M	M	R
11.	• High global CAD Risk • ECG uninterpretable OR unable to exercise		M	M	M	M	M	R

Safety of Stress Echocardiography

- Safety was evaluated using an international registry of over 85,000 examinations from 71 centers in over 17 countries
- From 1998-2004
- Cases included exercise, dobutamine and dipyridamole stressors
- All were shown to be safe, but there were relative differences
- There were 6 deaths: 5 with dobutamine and 1 with dipyridamole

Am J Cardiol 2006; 98:541-43

Complications During Stress Echocardiography

Complication	Dobutamine	Dipyridamole	Exercise
Acute myocardial infarction	11	5	1
Sustained ventricular tachycardia	27	1	2
Ventricular fibrillation	11	2	0
Cardiac rupture	5	0	1
Asystole	2	4	0
Transient ischemic attack/Stroke	3	3	0
Hypotension/shock	2	4	0
Third-degree atrioventricular block	2	0	0

Modified from *Am J Cardiol* 2006; 98:541-43

Abdominal Aortic Aneurysms

- No cited incidence of aortic aneurysm rupture
- Compared to exercise, the blood pressure response tends to be less with dobutamine and therefore, it is likely safer than exercise
- Pellika in 1996 demonstrated no events in 98 pts with AAA ≥ 4 cm

Using Stress Echo to Delineate Myocardium at Risk

- Use to quantify severity and extent of myocardium at risk
- Can use this information to provide prognostic risk
- Total risk can be calculated by summing the abnormal segmental score at peak stress divided by the number of segments (16) according to the ASE guidelines

Mortality of Patients According to Total Extent of WMA

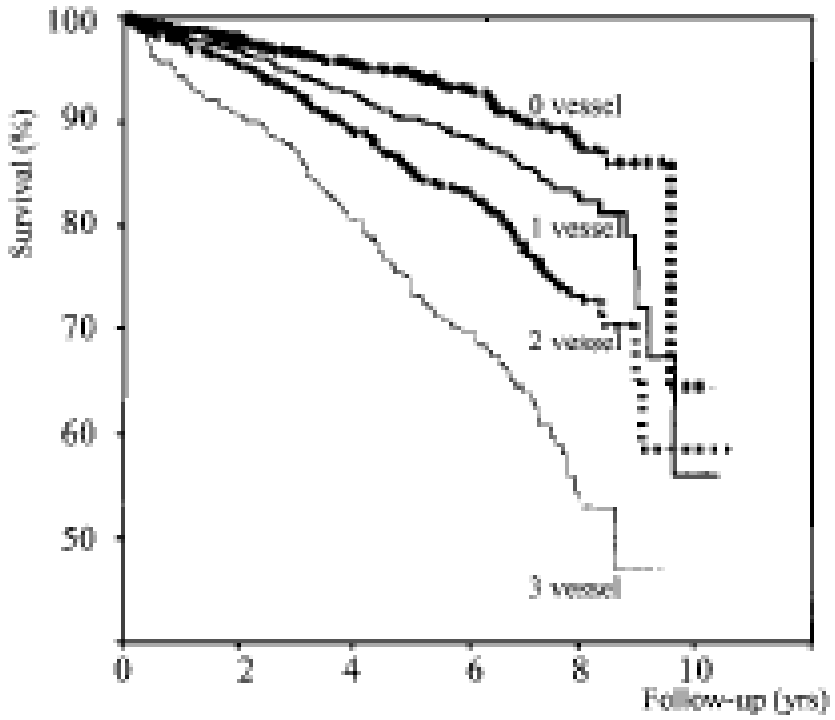


Figure 4. Mortality of patients according to total extent of wall motion abnormalities (summed stress score) at peak stress.

Marwick, et al, *Circulation* 2001

Mortality after Dobutamine Stress Echo

	Normal	Ischaemia	Scar
Ischaemia	$p < 0.0001$		
Scar	$p < 0.0001$	$p < 0.14$	
Mixed	$p < 0.0001$	$p < 0.005$	$p < 0.02$

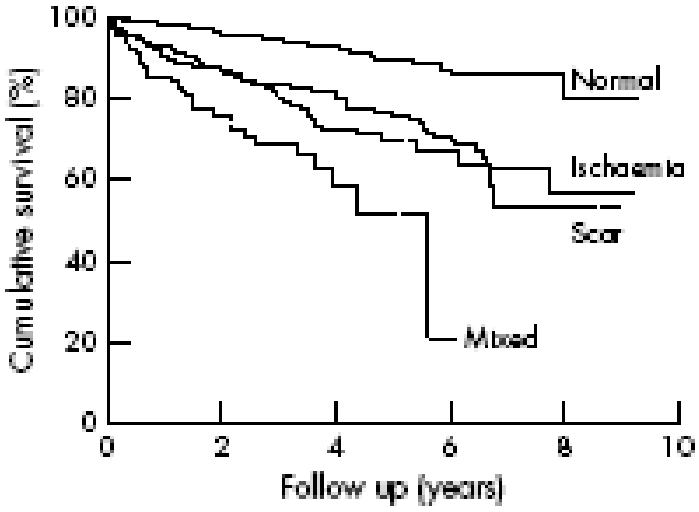


Figure 7 Cardiac mortality after dobutamine stress echocardiography ($n = 3156$ patients).[24]

Marwick, et al, *Circulation* 2001

Stress ECG versus Stress ECHO: Prognosis

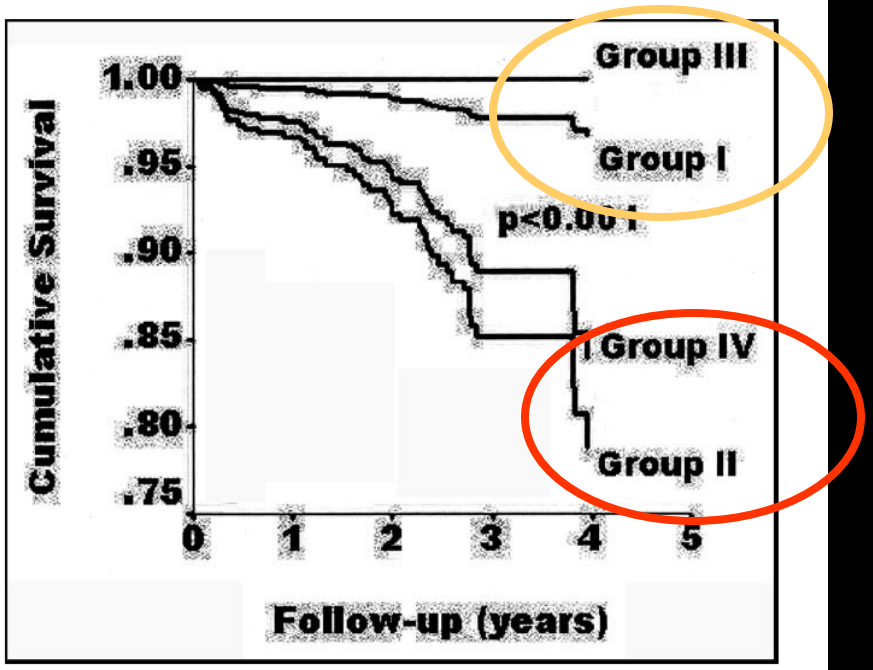


Figure 1. Event-free survival probability function on a 4-group analysis based on proportional hazards model. A significant difference between a normal and an abnormal stress echocardiographic finding (groups I and III vs groups II and IV, $p < 0.001$), independent of stress ECG results is shown. Group I = normal stress echocardiographic and ECG findings; group II = abnormal stress echocardiographic and normal stress ECG findings; group III = normal stress echocardiographic and abnormal stress ECG findings; group IV = abnormal stress ECG and echocardiographic findings.

Group I: Normal stress ECHO, normal stress ECG

Group II: Abnormal stress ECHO, normal stress ECG

Group III: Normal stress ECHO, abnormal stress ECG

Group IV: Abnormal stress ECHO, abnormal stress ECG

Mahenthiran, *Am J Cardiol* 2005

Stress Echo Adds to Duke Treadmill Score

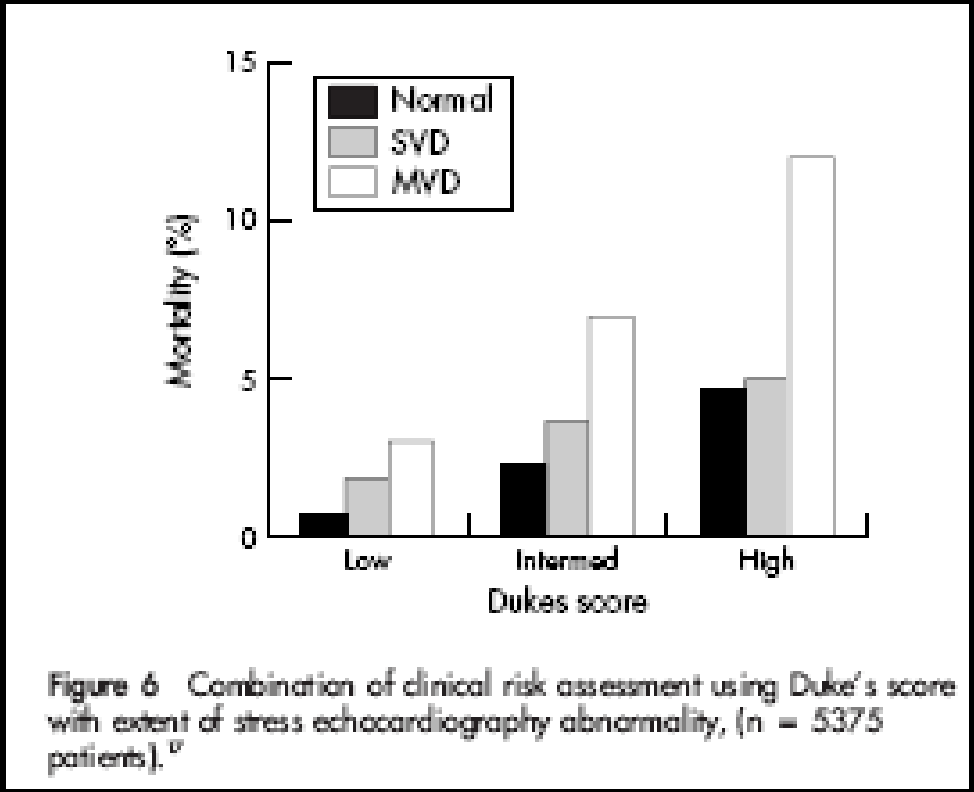
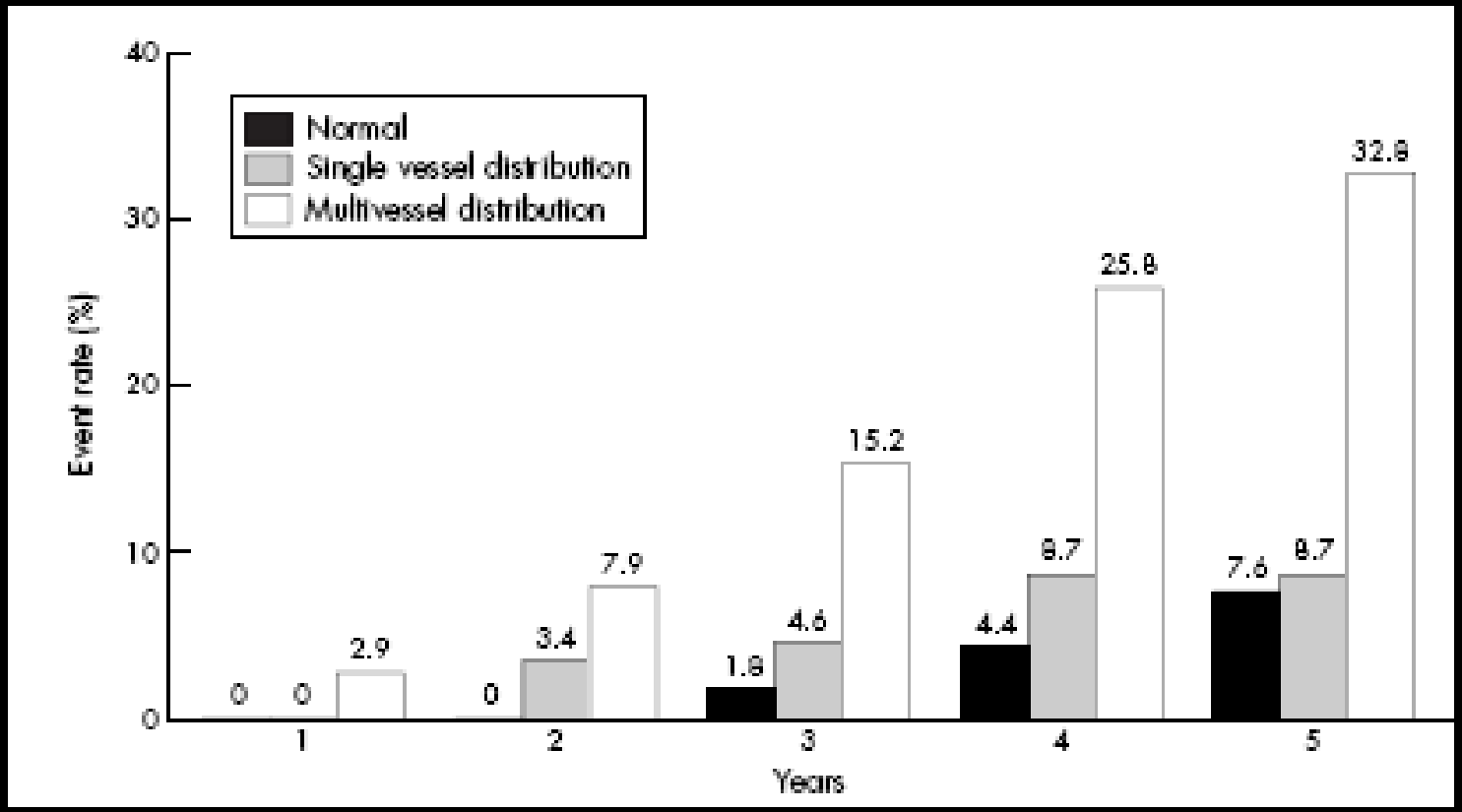


Figure 6 Combination of clinical risk assessment using Duke's score with extent of stress echocardiography abnormality, (n = 5375 patients).[9]

Senior, et al *Heart* 2005

Prognosis Based on Wall Motion Abnormalities



Senior, et al *Heart* 2005

Dobutamine Stress Echo and Viability

- Viability is present if there is improvement in contractility with low dose, i.e. 2.5-10mcg of dobutamine
- If there is return to baseline or further reduction in wall motion with higher dose, ischemia is demonstrated
- A ***biphasic*** response is considered to predict the best outcome with revascularization

J Am Coll Cardiol 1998;32:921-6

Myocardial Contrast Echo

- Helps to discern the endocardium during stress echocardiography
- Allows for visualization in patients who might otherwise not have adequate images
- Several studies have shown significant improvement in the assessment of left ventricular function and volumes with the use of contrast when compared to MR as a gold standard

JASE, Article in press 2008

Contrast Safety

- The Food and Drug Administration (FDA) ***removed*** the black-box warning contraindicating the use of echo contrast agents in patients who are acutely unwell (eg, acute myocardial infarction or worsening congestive cardiac failure)
- Contrast is contraindicated in patients with known right to left shunts and previous hypersensitivity or anaphylactoid response to contrast

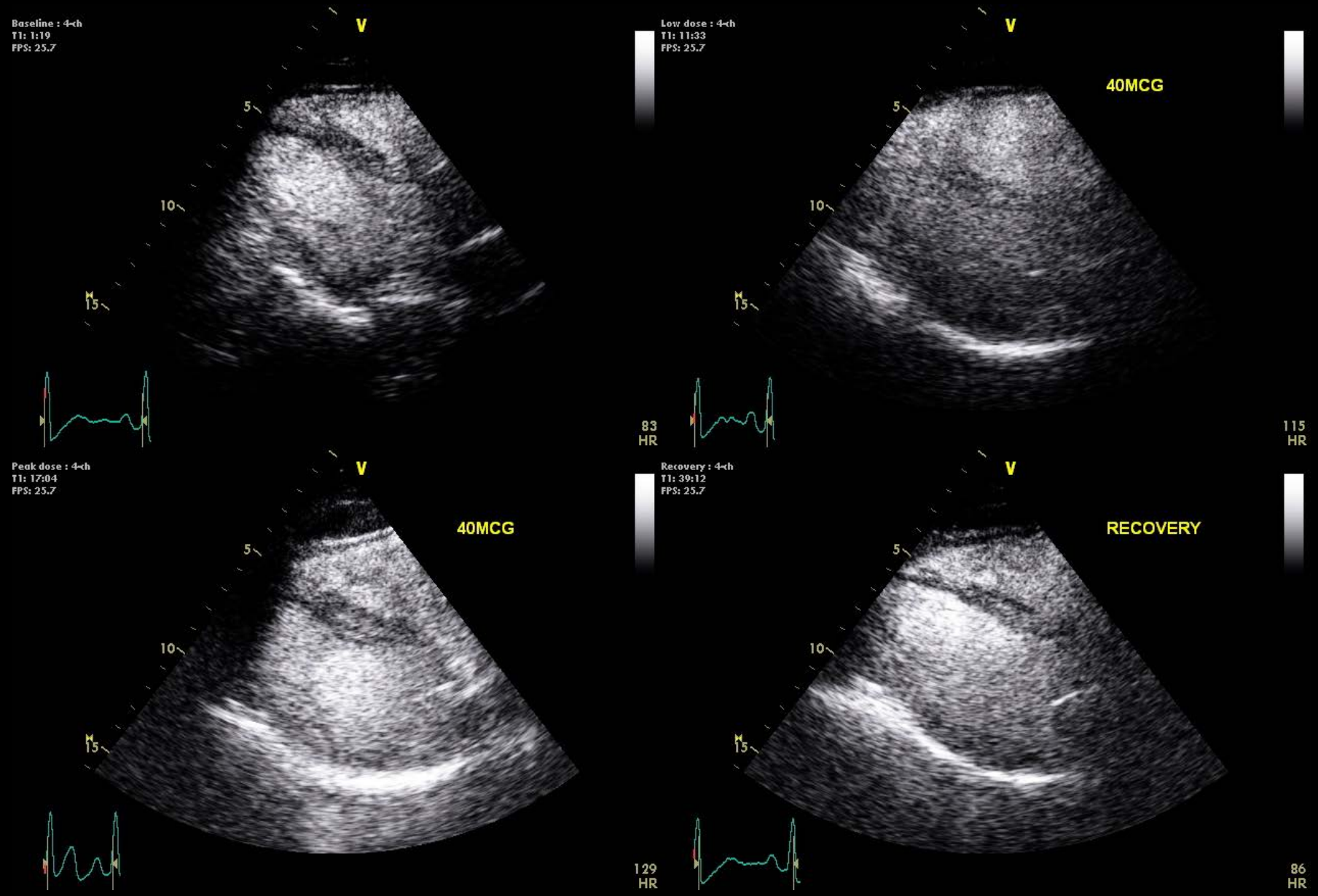
Case Presentations

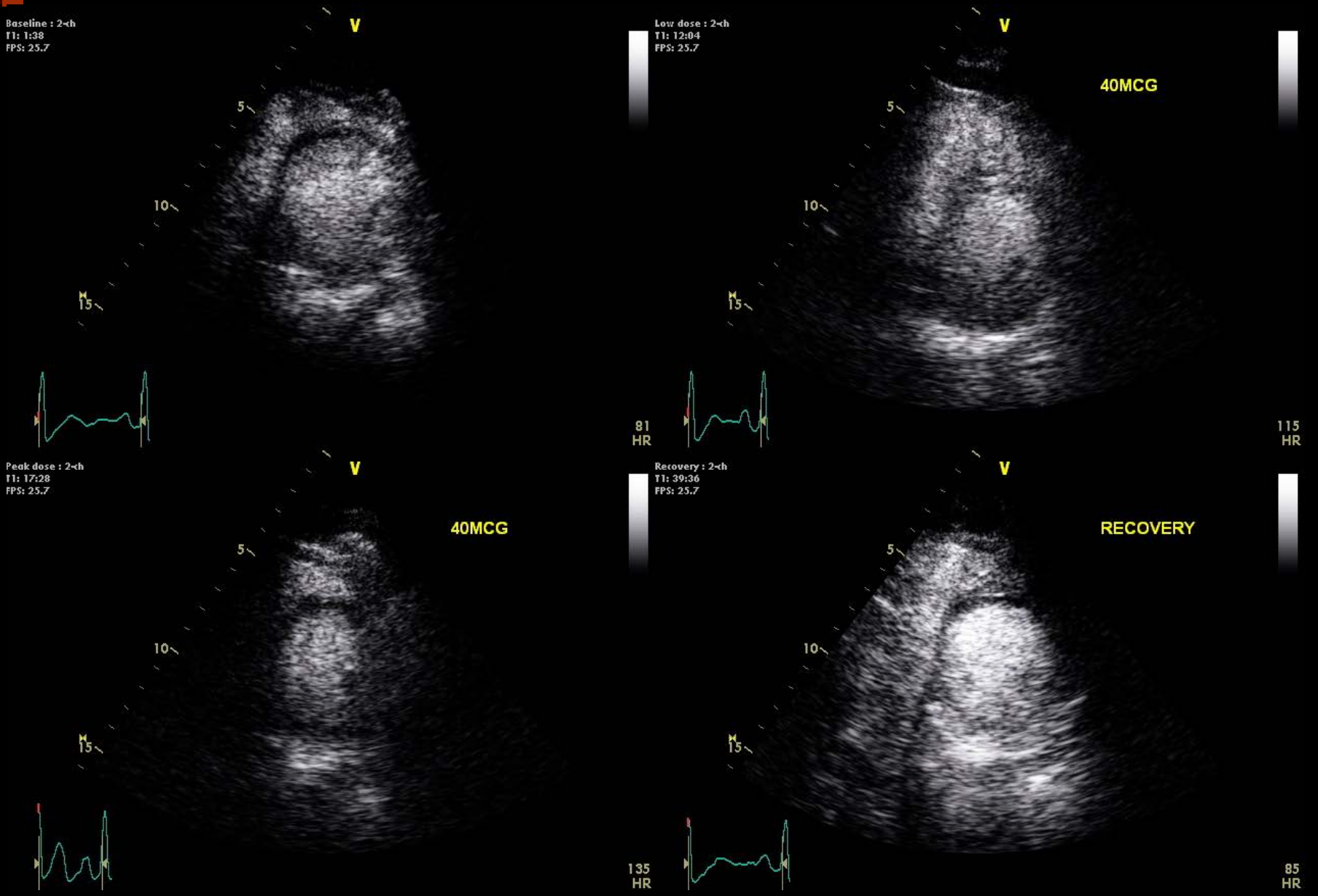
CASE 3

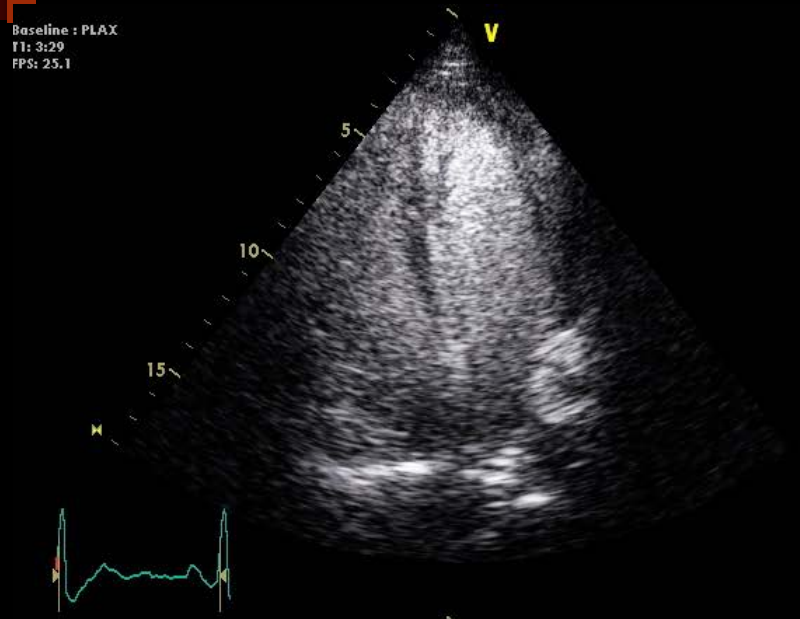
60 yo with HTN, HLD with atypical chest pain until 3 wks ago when started having pain after working or walking fast. Pain radiates to bilateral arms.

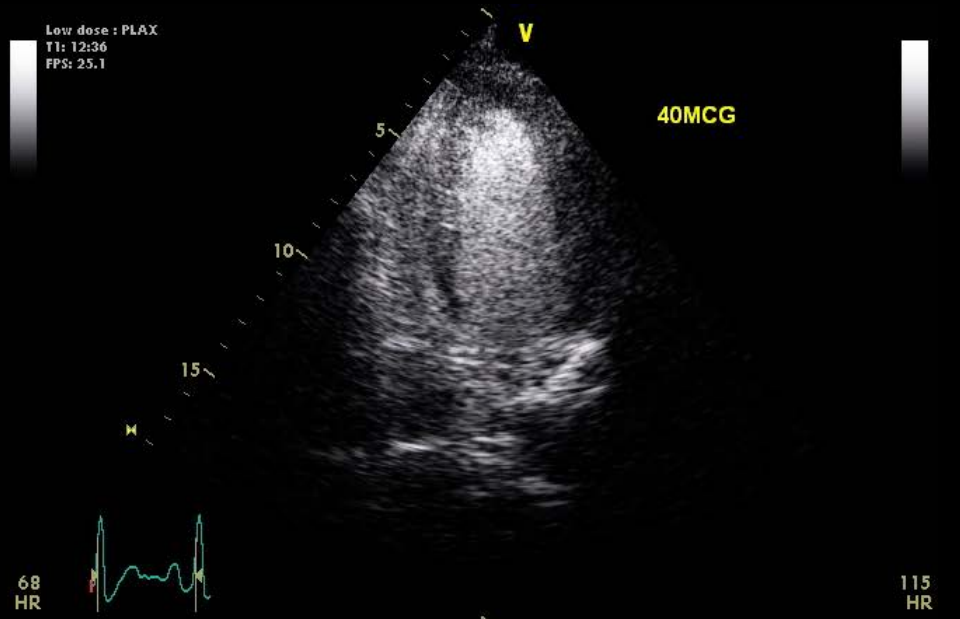
He had a treadmill test in which he had same sx after exercising for only 5.5 min with nondiagnostic ECG changes.

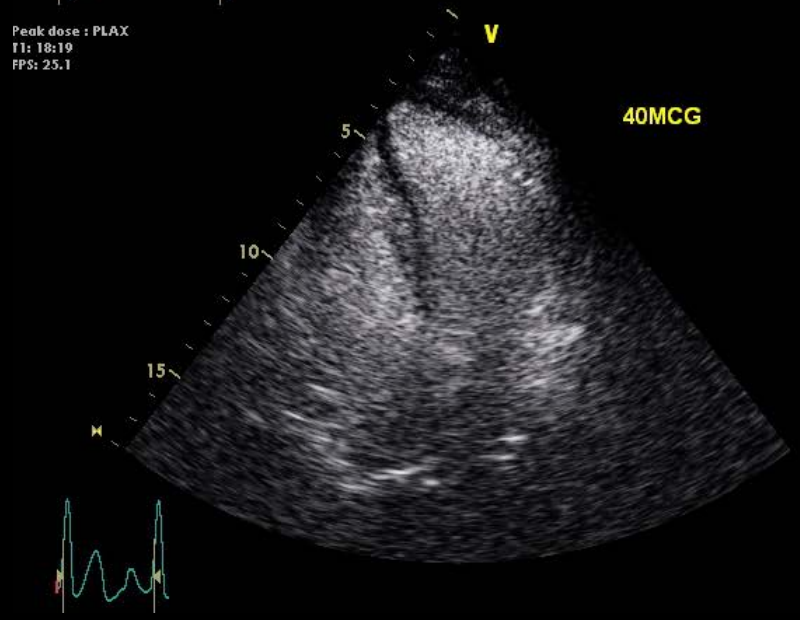
Underwent DSE in which he had same arm pain and had ST elevation in inferior leads but no other changes. He reached target HR.

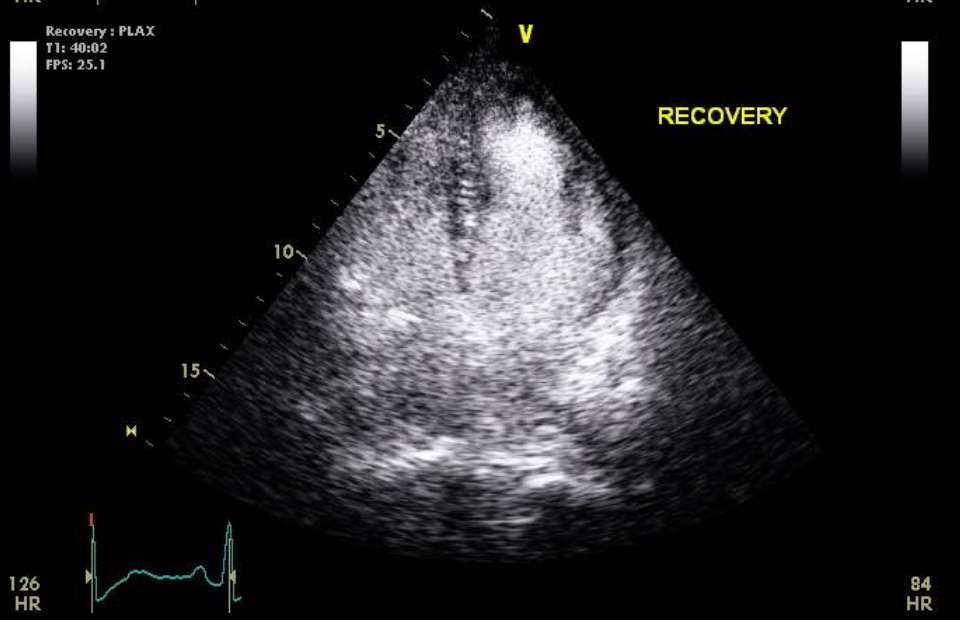

Baseline : 4-ch
T1: 1:19
FPS: 25.7
Low dose : 4-ch
T1: 11:33
FPS: 25.7
40MCG
83
HR
115
HR
Peak dose : 4-ch
T1: 17:04
FPS: 25.7
40MCG
Recovery : 4-ch
T1: 39:12
FPS: 25.7
RECOVERY
129
HR
86
HR

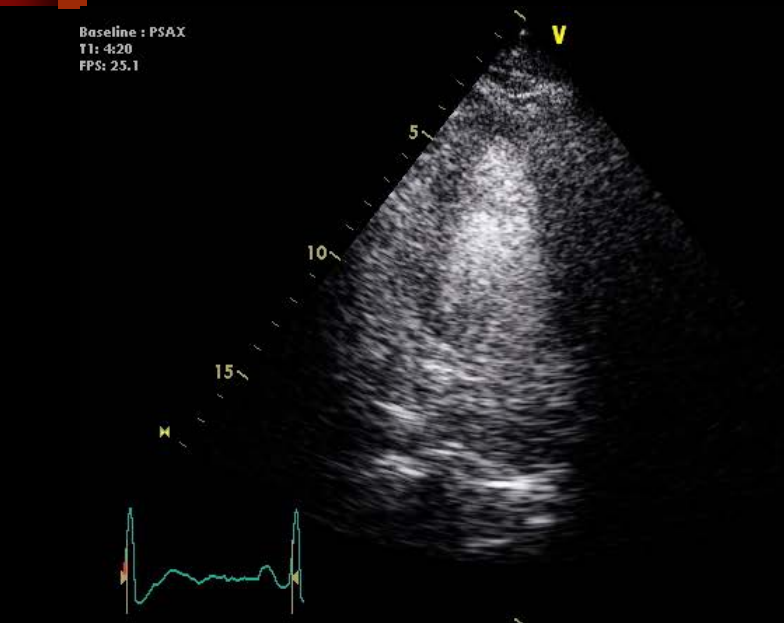

Baseline : 2ch
T1: 1:38
FPS: 25.7
Low dose : 2ch
T1: 12:04
FPS: 25.7
40MCG
81
HR
115
HR
Peak dose : 2ch
T1: 17:28
FPS: 25.7
40MCG
Recovery : 2ch
T1: 39:36
FPS: 25.7
RECOVERY
135
HR
85
HR

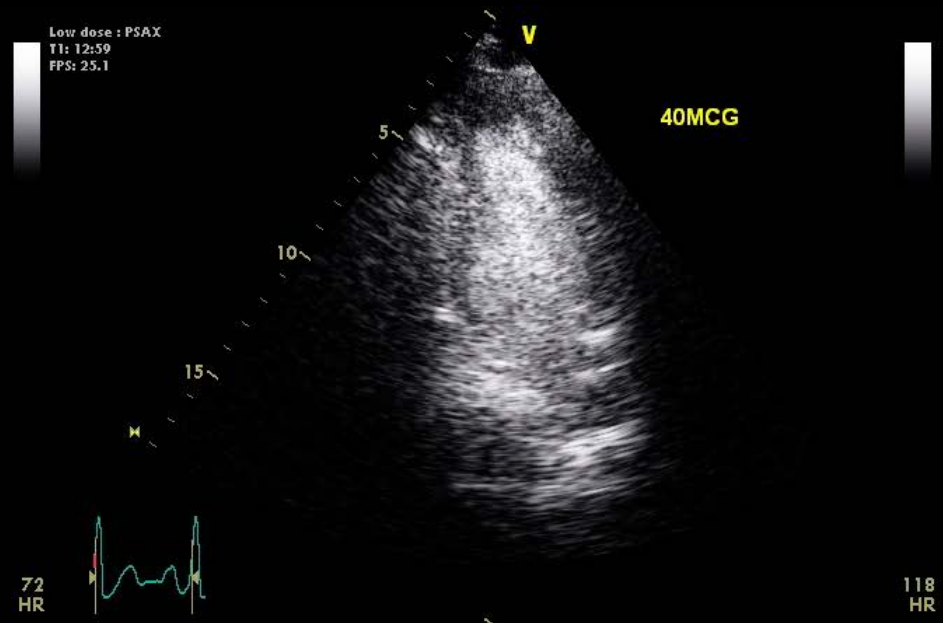

Baseline : PLAX
T1: 3:29
FPS: 25.1
V
5
10
15
68
HR

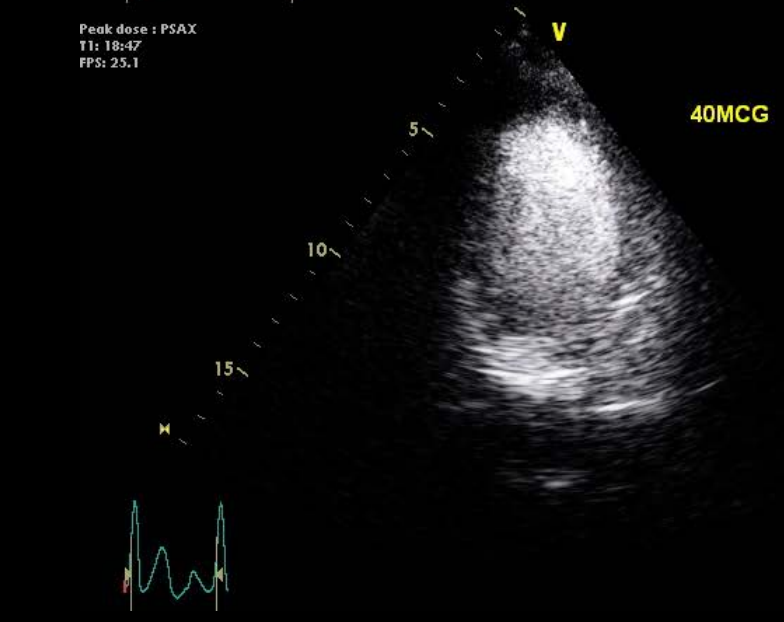

Low dose : PLAX
T1: 12:36
FPS: 25.1
40MCG
V
5
10
15
115
HR

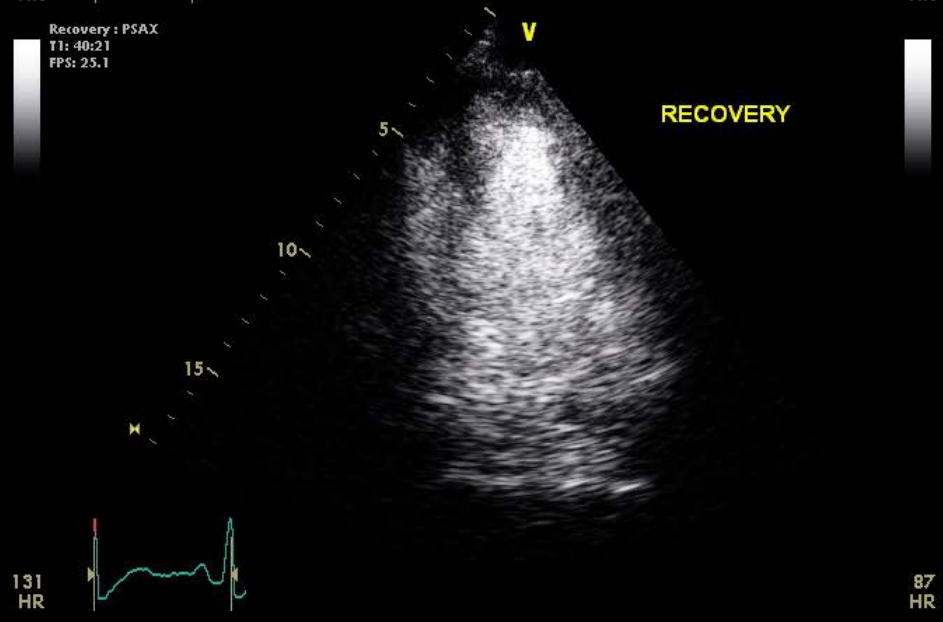

Peak dose : PLAX
T1: 18:19
FPS: 25.1
40MCG
V
5
10
15
126
HR


Recovery : PLAX
T1: 40:02
FPS: 25.1
RECOVERY
V
5
10
15
84
HR

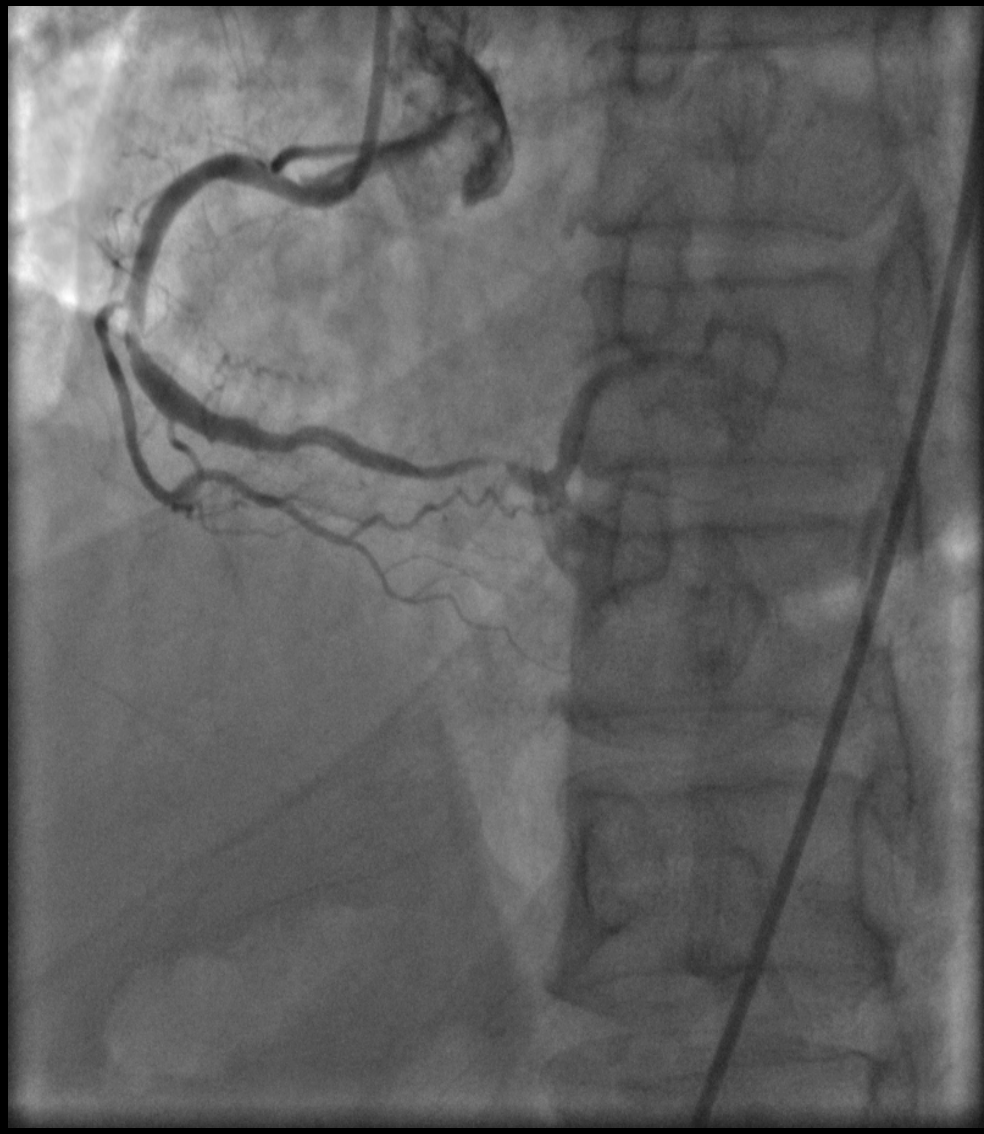

Baseline : PSAX
T1: 4:20
FPS: 25.1
V
5
10
15


Low dose : PSAX
T1: 12:59
FPS: 25.1
V
40MCG
5
10
15
72
HR
118
HR


Peak dose : PSAX
T1: 18:47
FPS: 25.1
V
40MCG
5
10
15


Recovery : PSAX
T1: 40:21
FPS: 25.1
V
RECOVERY
5
10
15
131
HR
87
HR

CATHETERIZATION RESULTS



Possible Board Questions from ASE Echo Review Course

- For comparative studies of MRI, SPECT and echo, how many segments are recommended?
  1. 24
  2. 27
  3. 16
  4. 17
  5. 14

- Which segment cannot be seen in the parasternal long view?

1. Mid inferoseptum
2. Basal inferolateral wall
3. Mid anteroseptum
4. Mid anterior wall
5. 1 and 4
6. 3 and 4

- Regarding methods of quantitation of regional wall motion:

1. Endocardial excursion method is centroid independent
2. Wall thickening method is independent of center of reference
3. Translation and rotation do not affect endocardial excursion method
4. Centroid methods improve sensitivity of stress echo