Non-Ischemic Stress Echocardiography: Patients you may see in your lab
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“I have nothing to disclose.”

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Outline
- Review safety parameters and basic protocols
- Stress echo for assessment of valvular heart disease:
  2014 ACC/AHA Valvular Heart Disease Guidelines
  1. Aortic Stenosis
  2. Aortic Regurgitation (see syllabus)
  3. Mitral Stenosis
  4. Mitral Regurgitation
  5. Tricuspid Regurgitation (see syllabus)
- Patient-Prosthesis M-M (see syllabus)
- 4. Hypertrophic Cardiomyopathy
- 5. Diastolic stress test

Summary

Safety
- Risk is that of physical exercise; ultrasound is safe
- 1/2500 incidence of MI
- 1/10000 death
- Contraindications to Exercise Stress Echo:

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
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<tbody>
<tr>
<td>Acute MI (upto 48 h)</td>
<td>LMCA stenosis</td>
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<tr>
<td>Unstable angina-high risk</td>
<td>Severe HTN (SBP&gt;220, DBP&gt;110 mm Hg)</td>
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<td>Uncontrolled arrhythmia</td>
<td>Lack of diagnostic US windows</td>
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<tr>
<td>Acute PE</td>
<td>Inability to exercise</td>
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<tr>
<td>Symptomatic Severe AS</td>
<td>Tachy/brady arrhythmia</td>
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<tr>
<td>Acute Aortic Dissection</td>
<td>HCM</td>
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<tr>
<td>Acute myocarditis/pericarditis</td>
<td>AV nodal blocking agents not held</td>
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<td>Heart failure-symptomatic</td>
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Adapted from Otto et al 2012
Patient History
- NPO 3-4 hours--clear diet
- Review meds (AV-nodal blocking agents held 1:2 doses, when indicated)

Pre-test assessment

Exercise Stress echo Protocol
- Baseline screening Echo: If a recent assessment has not been performed---baseline assessment of LV function, valve function, cardiac chamber dimensions, LV wall thickness and wall motion, as well as aortic root size.
- Tissue harmonic imaging recommended: better endocardial border visualization, less near-field artifact
- Threshold for use of Contrast (at least 2 segments poorly visualized)---inject contrast at peak exercise, but after color Doppler data acquired.

ECG Exercise parameters to note
- Heart rate each minute
- BP end of each stage
- Time of exercise
- Heart rate recovery
- Exertion level (subjective)
- Angina onset and duration
- Other symptoms
- ECG:
  - ST depression/elevation ,time, leads
  - Arrhythmias
Exercise-Recommended (in general)

- **Treadmill**: usually Bruce Protocol (usually higher workload and HR than bicycle)
- **Imaging** at rest and immediately post-exercise. Additional imaging when near baseline recovery to assess for late-onset ischemia
- **Bicycle**: supine or upright (BP usually higher with bicycle)
- **Imaging** at baseline, 25W, peak stress, recovery
- 25W increase in exercise q 2-3 min (can start at 10W)
- Recommended exercise modality when Doppler information is needed.

When to stop

- Target Heart Rate Achieved (at least 80-85% APMHR)
- New moderate RWMA (or more pronounced from baseline) (1/2000 incidence of MI or VF)
- Hypotension (> 10 mm Hg decrease in SBP)
- Arrhythmias (significant 4%: SVT or VT)
- Hypertension (severe: SBP >220/110 mm Hg)
- **Symptoms**—limiting angina, dizziness, gait imbalance—**Dyspnea**

**Generally non-ischemic indications for stress tests are symptom-limited**

Stress echo in Valvular Heart Disease—exercise recommended in general

- To assess clinical/hemodynamic significance of severe regurgitation/stenosis in asymptomatic patient
- **OR**
- To assess symptomatic patient with moderate regurgitation/stenosis
Exercise testing is reasonable to assess physiological changes with exercise and to confirm the absence of symptoms in asymptomatic patients with a calcified aortic valve and an aortic velocity \( \geq 4.0 \text{ m/s} \) or mean pressure gradient \( \geq 40 \text{ mm Hg} \) (stage C).

(Level of Evidence: B)

2014 AHA/ACC Valvular Heart Disease Guidelines

1. Aortic Stenosis

- Class IIa
  - Exercise testing is reasonable to assess physiological changes with exercise and to confirm the absence of symptoms in asymptomatic patients with a calcified aortic valve and an aortic velocity \( \geq 4.0 \text{ m/s} \) or mean pressure gradient \( \geq 40 \text{ mm Hg} \) (stage C).
  - (Level of Evidence: B)

2. Abnormal findings in severe AS

- Exercise-induced angina, dyspnea early in exercise, dizziness or syncope
- Limited exercise tolerance
- Abnormal blood pressure response (hypotension or lack of increase in BP by at least 20 mm Hg)
- Arrhythmia

- It is unclear if there is prognostic value to measuring hemodynamics and Doppler information in asymptomatic severe AS.

3. Class III: Harm

- Exercise testing should not be performed in symptomatic patients with AS when the aortic velocity is \( \geq 4.0 \text{ m/s} \) or mean gradient \( \geq 40 \text{ mm Hg} \) (stage D).
  - (Level of Evidence: B)

Who does not need a stress test with AS?
Who needs a DSE to assess AS?

What is the protocol?

How do we interpret the results?

Role of DSE in evaluation of Aortic Stenosis

A. Normal LVEF, Normal Flow, High Gradient
B. Normal LVEF, Low Flow, Low Gradient
C. Normal LVEF, Normal Flow, Low Gradient
D. Decreased LVEF, Low Flow, Low Gradient
Dobutamine dose 5, 10, 15, 20 mcg/kg/min
LVOT diameter measured at baseline
LVOT VTI, AV VTI, AV peak vel, AV peak grad, AV mean gradient measured at each stage
Overall assessment of LV function may be performed at each stage with apical 4 and 2 chamber views

General DSE Protocol for LFLGSAS

CT Calcium Score may be of benefit

REST: LVEF 20%, SVI 20 mL/m2; Peak AV vel 350 m/s, Pk Grad 50 mm Hg; mean 31 mm Hg, DI 0.14, AVA 0.4 cm2

PEAK 15 mcg: LVEF 30%, SVI 29 mL/m2; Peak AV vel 452 m/s, Peak Grad 81 mm Hg; mean 48 mm Hg. DI 0.16. AVA 0.5 cm2

Pt referred for and underwent TAVR
2. Mitral Stenosis

Class I:

"Exercise testing with Doppler or invasive hemodynamic assessment is recommended to evaluate the response of the mean mitral gradient and pulmonary artery pressure in patients with MS when there is a discrepancy between resting Doppler echocardiographic findings and clinical symptoms or signs. (Level of Evidence: C)

Nishimura, RA et al. 2014 AHA/AC Valvular Heart Disease Guideline

Mitral stenosis with exercise

Indications for consideration of intervention in pt with equivocal resting echo:

- MVA > 1.5 cm², PHT < 150 ms, and no other cause of dyspnea.
- Or MVA 1.0 - 1.5 cm² with no symptoms

- Pulmonary pressures with exercise >60-70 mm Hg” (need to assess IVC size as well)
- Mean MV gradient > 15 mm Hg
- MVA <1.0 cm² not likely to be able to increase SV and augment PASP

Most centers have treadmills, but supine bicycle allows for more optimal assessment of Doppler information.

- Decrease in functional capacity
- Increase in mean MV gradient
- Concomitant increase in MR
- "Exercise-induced pulmonary hypertension"

"Exercise –induced pulmonary hypertension”

(Continuity equation not pressure-half time method should be used is calculating MVA with exercise)

MS: Exercise preferred over Dobutamine
Mean MV grad 5 mmHg
Increased to 27 mm Hg at peak.

TR grad 42 mm Hg
Increased to 74 mm Hg at peak.

MS-exercise

Picano, E et al. JACC 2009, 54(24):2251-2260

Class II a:
"Exercise hemodynamics with either Doppler echocardiography or cardiac catheterization is reasonable in symptomatic patients with chronic primary MR when there is a discrepancy between symptoms and the severity of MR at rest (stages B and C) (Level of Evidence: B)."

Nishimura, RA et. 2014 AHA/ACC Valvular Heart Disease Guidelines

3. Chronic Mitral Regurgitation

Assess for worsening regurgitation with exercise (vena contracta, RV)
Decreased exercise tolerance
Increase in pulmonary pressures (> 60 mm Hg)
Assess ventricular size and function, Speckle tracking for GLS, E/e'

Mitral regurgitation Protocol—Dobutamine not recommended
Semi-supine exercise protocol


Change in E/e' to estimate LV filling pressures obtained between HR 90-105 bpm (due to e’ and a’ wave fusion at higher HR)

Between 32 and 66% of pts with moderate MR develop severe MR during exercise  (Magne J et al Circ 2010;122:33-41) 

At Rest: MR moderate by RV 54 mL and VC TR gradient 43 mm Hg

At Peak: MR severe with RV 79 mL

TR gradient of 78 mm Hg

Picano E et al. JACC 2009 54(24)2251-2260

Lack of Contractile Reserve (< 2% increase in GLS) in degenerative MR has been shown to be a marker of decreased cardiac event-free survival and predictive of early post-op LV decompensation (Magne J et al Eur Heart J. 2011;32(Suppl):170)

68 yo axx pt with mod-severe MR from Barlow MV disease.

REST: RV 54mL
Normal LVEF 65%, GLS -26%

EXERCISE: severe MR, RV 70 mL
Normal LVEF 72%, decrease in GLS to ~17% (Absence of contractile reserve by 2D speckle tracking)

Cardiac MR showed presence of mid wall myocardial fibrosis—area of late gadolinium hyperenhancement.

1 yr later developed CHF and LV dysfunction (LVEF 43%)
Symptom limited stress on cardiac meds.

Baseline:
- BP 92/60 mm Hg HR 65 bpm
- ECG : NSR with occasional PVC

Exercise:
- Peak HR 108 bpm (70% APIMHR), BP 105/60 mm Hg
- 8.2 METs
- ECG: Occasional PVCs and trigeminy
- No ST changes.

Shortness of breath with exercise

66yo woman, smoker with CAD, h/o VF arrest 6 yrs ago, inferior MI, RCA stent, ICD, 3+ MR on TEE, COPD (my patient)

MR 3+ at rest; 3-4+ post-stress
Mild mitral stenosis at rest (mean gradient of 5 mm Hg, increases to mean of 7 mm Hg)
PA Pressure of 39 mm Hg at rest; 43 mm Hg post-stress
TR 2+ at rest and post-stress
Excellent functional capacity. Normal LV dimensions. EF increases from 50-60%, inferior RWMA

A. Refer for MV replacement (severe MR with exercise with mild mitral stenosis)?

Or

B. Continued close follow-up, Smoking cessation and treatment of COPD?

Patient management?

B. Patient with ongoing medical therapy with repeat stress echo 2 years later with mild-moderate mitral regurgitation with exercise, and no change in pulmonary pressures.
1. Treadmill exercise testing is reasonable to determine functional capacity and response to therapy in patients with HCM (Level of Evidence: C).

2. Treadmill testing with monitoring of an ECG and BP is reasonable for SCD risk stratification in pts with HCM (Level of Evidence: B).

3. In pts with HCM who do not have resting peak gradients ≥ 50 mm Hg, exercise echocardiography is reasonable for the detection and quantification of exercise-induced dynamic LVOT obstruction (Level of Evidence: B).

Exercise testing in HCM without significantly increased LVOT gradients is relatively safe. One study of > 3000 pts over 10 years showed just one adverse outcome (VT which responded to cardioversion).

HCM---safety of ESE

Semi supine bicycle exercise or treadmill Bruce protocol recommended

Standard protocol, symptom limited

Stop if symptoms, or LVOT > 50 mm Hg, hypotension, arrhythmia

Also assess MR severity
Increased LVOT gradients with exercise predict development of heart failure symptoms

Septal reduction surgery may be recommended with severe CHF symptoms or LVOT gradient > 50 mm Hg (rest or with exercise).

LV wall thickness >= 30 mm is marker for SCD.

Increase in SBP < 20-25 mm Hg marker of increased risk of sudden cardiac death shown by multiple studies. Fletcher, GF et al. AHA Exercise standards for testing and training. Circ. 2013;128:873-934. (However unclear if this is only due to treatable exercise induced LVOT obstruction)

Non-sustained VT in exercise is not a clear prognostic indicator unless there is also VF.

HCM (assess LVOT gradient and MR with exercise, only if resting, LVOT gradient < 50 mm Hg)

Case HCM

49 yo man with HCM, ASH, SAM, redundant elongated MV chordae medically managed with vague symptoms of post-prandial dyspnea.

Prior stress echo LVOT at rest 12 mm Hg; Peak 64 mm Hg.


Medications optimized. Follow-up stress echo 6 months later.

HCM-- rest

IVSd 16 mm; PWd 10mm
ASH, SAM mitral valve
Trace MR (Mild AI)
Rest LVOT gradient 4 mm Hg
Trace MR

HCM-peak

LVOT peak gradient 40 mm Hg

HCM-peak

Hyperdynamic LV
No increase in MR
Case HCM exercise response

- Improved functional capacity (7 min 33 sec, compared to 4 min 34 sec previously… still with mildly decreased functional capacity. Test terminated due to fatigue.
- Hyperdynamic LV function with exercise, no arrhythmias.
- Limited increase in BP with exercise 124/82 mm Hg at rest, increased to 133/84 at peak exercise. But prior test with drop in BP with exercise, and pt on all cardiac meds on current study.
- Improved LVOT gradients at rest and peak exercise (4 mm Hg compared to 12 mm Hg at rest; 40 mm Hg compared to 64 mm Hg at peak)

Continued medical therapy was recommended.

May be helpful to assess for diastolic dysfunction as an occult cause of dyspnea.

I.e. Patients with Grade I diastolic dysfunction at rest and normal LV filling pressures are good candidates for this test

5. Diastolic stress test
   2016 ASE Guidelines

Normal cardiac response to exercise:
- Increased stroke volume
- Increased myocardial relaxation
- Increased early diastolic filling (suction)
- No change in LV filling pressures

Abnormal response:
- Reduced ventricular relaxation (htn, ischemia, HCM)
- Unable to increase cardiac output appropriately without an increase in filling pressures

Basis for Diastolic Stress Test

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<th>Normal</th>
<th>Abnormal</th>
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<tr>
<td>Mitral E</td>
<td>Increases</td>
<td>Greatly Increases</td>
</tr>
<tr>
<td>Mitral e'</td>
<td>Increases</td>
<td>No change</td>
</tr>
</tbody>
</table>
| E/e'   | No change or Dec 6-8 | Increases > 13
| PASp   | < 40 mm Hg | > 40 mm Hg |

Diastolic parameters with exercise

Diastolic Stress Test Protocol

Bicycle exercise preferred (increase by 25 W every 3 min), but treadmill is good also (not dobutamine)

Diastolic parameters persist 5-10 min post-exercise, so treadmill exercise may be used.

Assess 2D images, mitral inflows, tissue Doppler mitral annulus, TR gradient at rest and each stage (bike) or rest and early recovery (treadmill) — don't want to use fused E/A beats

Can assess for ischemia first, then diastolic function

If using contrast, tissue Doppler data will not be valid

E/E' (medial) correlates well with filling pressures in rest and exercise

Abnormal test if all 3 criteria are met:

- Avg E/e’ > 14 or septal E/e’ > 15 with exercise
- Peak TR velocity > 2.8 m/s (TR gradient > 31 mm Hg) with exercise
- Septal e’ < 7 cm/s or lateral e’ < 10 cm/s at baseline

Normal Diastolic Stress Test if both criteria met; otherwise, indeterminate

Example of abnormal diastolic findings with exercise

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<td>Myriad indications and usefulness of stress echo beyond just ischemia evaluation. High Level of Experience/Expertise required.</td>
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ACC/AHA 2014 guidelines support the use of dobutamine stress echo for evaluation of patients with low flow, low gradient severe AS with decreased LVEF:

Exercise echo for MS, MR to assess severity and symptoms with exercise in cases where clinical significance of the underlying valvular lesion is unclear:

ACC/AHA 2011 Guidelines support use of exercise stress echo in HCM if clinical significance is unclear and LVOT gradient < 50 (30)mm Hg.

2016 ASE Diastolic Function Guidelines support use of exercise stress echocardiography to assess diastolic dysfunction as a cause of dyspnea in patients with grade 1 diastolic dysfunction and normal LV filling pressures.