Stress Echocardiography in Valvular Heart Disease
Moving Beyond CAD

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Stress Echo in Valve Disease

Who needs testing?

What test to do?

What parameters to measure and focus on?

How to use the information in patient management?
Superiority of Stress Echocardiography over ANY OTHER MODALITY

Diagnostic Evaluation and Planning strategies for Management in
1. Co-existing Valvular Heart Disease
2. Dynamic obstructive disease,
3. Unexplained dyspnea, correlating
4. Exercise hemodynamics to function, pressures and diastology
# Exercise Vs Bicycle Echo

## Cardiopulmonary Pathologies Which Can Be Evaluated by Exercise Echocardiography

<table>
<thead>
<tr>
<th>Pathology</th>
<th>TSE</th>
<th>BSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial ischemia</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Contractile reserve</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Exercise-induced PHTN</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Exercise-induced LVDD</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Exercise-induced IAS</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Exercise-induced AVF</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Valvular function</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Dynamic LV obstruction</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Perioperative risk</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
Management strategy for patients with severe aortic stenosis

Severe Aortic Stenosis

- Vmax greater than 4 m/s
- AVA less than 1.0 cm²
- Mean gradient > 40 mm Hg

Undergoing CABG or other heart surgery?

- Yes
  - Symptoms?
    - Yes
      - Equivocal
        - Exercise test
          - Normal
            - LV ejection fraction
              - Less than 0.50
                - Yes
                  - Severe valve calcification, rapid progression, and/or expected delays in surgery
                    - No
                      - Clinical follow-up, patient education, risk factor modification, annual echo
                - Normal
                  - Yes
                    - Aortic Valve Replacement
                      - Preoperative coronary angiography
            - Less than 0.50
              - No
                - Clinical follow-up, patient education, risk factor modification, annual echo
          - Normal
            - Yes
              - Aortic Valve Replacement
                - Preoperative coronary angiography
      - No
        - Aortic Valve Replacement
          - Preoperative coronary angiography
    - No
      - Symptom:
        - ↓BP
          - Class I
            - Aortic Valve Replacement
              - Preoperative coronary angiography
          - Class IIb
            - Aortic Valve Replacement
              - Preoperative coronary angiography
          - Class I
            - Aortic Valve Replacement
              - Preoperative coronary angiography
          - Class IIb
            - Aortic Valve Replacement
              - Preoperative coronary angiography
          - Class I
            - Aortic Valve Replacement
              - Preoperative coronary angiography
          - Class IIb
            - Aortic Valve Replacement
              - Preoperative coronary angiography
      - Normal
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            - Yes
              - Aortic Valve Replacement
                - Preoperative coronary angiography
      - No
        - Aortic Valve Replacement
          - Preoperative coronary angiography

Re-evaluation
Exercise Test in AS: Clinical and EKG

Amato et al, Heart 2001
ST depression and outcomes

Das et al, Eur Heart J 2005
Symptoms and outcomes
Exercise Echo and Outcomes in AS
Role of Gradient and EF Reserve

Lancellotti et al Circulation 2005
Marechaux et al Echocardiography 2007
Usefulness of exercise-stress echocardiography for risk stratification of true asymptomatic patients with aortic valve stenosis

Sylvestre Maréchaux, Zeineb Hachicha, Annaïk Bellouin, Jean G. Dumesnil, Patrick Meimoun, Agnès Pasquet, Sébastien Bergeron, Marie Arsenault, Thierry Le Tourneau, Pierre Vladimir Ennezat, and Philippe Pibarot


Table 4  Univariate and multivariate analysis of association between baseline variables and event risk in the whole cohort (n = 135) with variables entered in dichotomous format

<table>
<thead>
<tr>
<th>Variables</th>
<th>(%) of patients with variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Age ≥ 65 years</td>
<td>58</td>
<td>2.16 (1.30–3.72)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
<td>2.10 (0.90–4.10)</td>
<td>0.08</td>
</tr>
<tr>
<td>Rest systolic blood pressure &gt;135 mmHg</td>
<td>55</td>
<td>1.71 (0.78–2.85)</td>
<td>0.03</td>
</tr>
<tr>
<td>LV hypertrophy</td>
<td>41</td>
<td>1.90 (1.17–3.08)</td>
<td>0.009</td>
</tr>
<tr>
<td>Rest mean gradient &gt;35 mmHg</td>
<td>50</td>
<td>3.70 (2.21–6.41)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Exercise Δ mean gradient &gt;20 mmHg</td>
<td>21</td>
<td>2.10 (1.22–2.52)</td>
<td>0.008</td>
</tr>
<tr>
<td>Exercise LV ejection fraction &lt;70%</td>
<td>38</td>
<td>1.61 (1.00–2.62)</td>
<td>0.05</td>
</tr>
</tbody>
</table>
Exercise Echo in AS

Rest

1.6 MHz

GEL 2D

+18 mm Hg

Peak exercise

1.6 MHz

GEL 2D

FIND E11.7 cm
LONG. 38 cm
FIND E12.7 cm
LONG. 38 cm
FIND E12.9 cm
LONG. 38 cm

1.6 MHz

GEL 2D

FIND E12.7 cm
LONG. 38 cm
FIND E12.9 cm
LONG. 38 cm
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Impact on Outcome</th>
<th>Impact on AVR ESC versus ACC guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>Onset of symptoms</td>
<td>ESC 1 ACC 2b</td>
</tr>
<tr>
<td>BP response</td>
<td>in daily life, cardia</td>
<td>ESC 2A ACC 2b</td>
</tr>
<tr>
<td>EKG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vent Arrhythmias</td>
<td>Onset of symptoms</td>
<td>ESC 2B</td>
</tr>
<tr>
<td>ST depression</td>
<td>in daily life, cardiac</td>
<td></td>
</tr>
<tr>
<td>Echo</td>
<td>Increase in mean gradient &gt; 18 ; &gt; 20 mm hg</td>
<td>Spontaneous symptoms, cardiac death, AVR</td>
</tr>
<tr>
<td></td>
<td>Decrease or minimal increase in EF</td>
<td>Spontaneous symptoms, cardiac death, AVR</td>
</tr>
</tbody>
</table>
Caveats

Increase in transvalvular gradient may not always correlate with presence or onset of symptoms during stress echo in AS.

Transvalvular gradient depends on:
1. severity of AS at rest
2. aortic valve compliance
3. concomitant CAD
4. LV contractile reserve
5. duration of exercise
6. maximal heart rate
7. workload achieved
Newer Stress Parameters in AS

Tissue Doppler and Stress Echocardiography
Van Pelt et al Heart 2007

Lack of substantial increase in S’ between rest and exercise as a sign of LV contractile abnormality in AS

Correlates with BNP, exercise duration and increase in systolic pressure
Background—We sought to investigate the use of a new parameter, the projected effective orifice area (EOA\textsubscript{proj}) at normal transvalvular flow rate (250 mL/s), to better differentiate between truly severe (TS) and pseudo-severe (PS) aortic stenosis (AS) during dobutamine stress echocardiography (DSE). Changes in various parameters of stenosis severity have been used to differentiate between TS and PS AS during DSE. However, the magnitude of these changes lacks standardization because they are dependent on the variable magnitude of the transvalvular flow change occurring during DSE.
Some Formulas

EOA ( proj) = EOA res + Valve compliance x (250 - Q rest)

Valve compliance = slope of the regression equation of the EOA to flow rate (mil/sec)

or absolute increase in AVA with dobutamine infusion / increase in flow rate

Valve resistance = 1333 x mean gradient / flow rate = SV/ejection time

Stroke work loss = 100 x (mean gradient / mean gradient + systolic pressure)
Low Flow/Low-Gradient AS

Class IIa

1 Dobutamine stress echocardiography is reasonable to evaluate patients with low-flow/low-gradient AS and LV dysfunction. *(Level of Evidence: B)*

2 Cardiac catheterization for hemodynamic measurements with infusion of dobutamine can be useful for evaluation of patients with low-flow/low-gradient AS and LV dysfunction. *(Level of Evidence: C)*
Low Flow Low Gradient AS
Role of Pharmacologic Stress Echo

AVA < 1 sq cm
MG : <30-<40 mm hg
EF < 40%

AVR ± CABG
Medical treatment
AVR? Medical?
DSE in Low Flow Low Gradient AS and Normal Ejection Fraction

1. Increasingly recognized and challenging entity

2. EF $\geq 50\%$, low mean gradients $< 30$ mm hg, AVA $< 1$ sq cm

3. Low indexed stroke volume, $< 35$ml/sqm, small concentric remodelled ventricles

4. Important to rule out technical errors prior to making the diagnosis. Consider EOA projected, Zva, Energy Loss index

5. ? Role of Dobutamine challenge to increase CO to differentiate
<table>
<thead>
<tr>
<th>Indications</th>
<th>Stress Data</th>
<th>Parameters</th>
<th>Impact on Outcome</th>
<th>Impact of decision making ESC and ACC Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MITRAL STENOSIS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic MS (MVA &lt; 1.5 sq cm)</td>
<td>Clinical</td>
<td>Symptoms or PASP &gt; 60 mm hg exercise testing</td>
<td>ESC 2A ACC1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Echo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic MS (MVA &lt; 1.5 sq cm)</td>
<td>Echo</td>
<td>PASP &gt; 60 or mean mitral gradient &gt; 15 mm hg with exercise</td>
<td>ACC 2b</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean mitral gradient &gt; 20 mm hg with DSE</td>
<td>Clinical deterioration and need for surgery</td>
<td>ACC 2b</td>
</tr>
</tbody>
</table>
Mitral stenosis

- MVA ≥1.5 cm²
  - Yes: Favorable morphology for PMBV?
  - No: MVA <1.5 cm²

- MVA <1.5 cm²
  - Yes: Favorable morphology for PMBV?
  - No: Resting PAP >50 mm Hg or Exercise PAP >60 mm Hg or new-onset AF

  - No: New-onset AF?
    - Yes: Class IIa
    - No: Class IIb

  - Yes: Class I
  - No: Class I

- Yes: PMBV (no LA clot, MR ≤2+)
  - No: Surgical MV repair or replacement

- Yes: Clinical follow-up
  - No: Annual echocardiography
At rest there is significant overlap of gradients in patients with varying severity of MS

Exercise echo helps to further stratify patients based on their severity

Cheriex et al
In Jnl of Cardiol 1994
Stress Echo in MS
CAVEATS

1. Atrial fibrillation: importance of averaging
2. Avoidance of use of pressure half time which can be shortened with tachycardia
3. Presence of cocomitant mitral regurgitation which may increase gradient and PA pressure
Exercise Echo in MS

Rest

MVA 1.21 cm²

MPG 13.8 mm Hg

TTPG 37 mm Hg

Exercise

MPG 28.4 mm Hg

TTPG 89.6 mm Hg
Semi supine Bike

Mitral flow velocity

Tricuspid regurg. velocity

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>30-Watts</th>
<th>Peak Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (b/min):</td>
<td>55</td>
<td>116</td>
<td>159</td>
</tr>
<tr>
<td>DFT (ms):</td>
<td>607</td>
<td>228</td>
<td>200</td>
</tr>
<tr>
<td>SV (ml):</td>
<td>66</td>
<td>59</td>
<td>57</td>
</tr>
<tr>
<td>$Q_{mean}$ (ml/s):</td>
<td>109</td>
<td>259</td>
<td>284</td>
</tr>
<tr>
<td>$\Delta P_{mean}$ (mmHg):</td>
<td>5</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>TTPG (mmHg):</td>
<td>42</td>
<td>69</td>
<td>74</td>
</tr>
</tbody>
</table>
Stress Echo and Mitral Regurgitation

**Known Severe MR**

1. Look for Exercise capacity
2. Pulmonary HTN new / worse
3. LV response

**Mild or No MR and Unexplained Dyspnea, Pulmonary HTN**

1. Exercise capacity
2. New or worsening MR
3. Worsening Pul HTN
4. LV response
Chronic Severe Mitral Regurgitation

Reevaluation

Clinical evaluation + Echo

Symptoms?

No

LV function?

Normal LV function
EF > 0.60
ESD < 40 mm

New onset AF? Pulmonary HT?

Yes

Class I

MV repair
If not possible, MVR

No

Class Ila

MV repair likely?*

Yes*

Class Ila

MV repair

No

Class Ila

MV repair

Yes

Class Ila

MV repair

No

Clinical eval every 6 mos
Echo every 6 mo

Class Ila

MV repair

Chordal preservation likely?

Yes

Medical therapy

No
Class I (evidence and/or general agreement that surgery is useful and effective)

- Symptoms caused by mitral regurgitation (acute or chronic)

- Asymptomatic patients with severe MR and mild-moderate LV dysfunction defined as an:
  - ejection fraction 30–60% and
  - end systolic dimension 45–55 mm

Class IIa (conflicting evidence and/or divergence of opinion but the weight of evidence/opinion favours surgical intervention)

- Asymptomatic patients with normal LV function and
  - atrial fibrillation or
  - pulmonary hypertension (>50 mm Hg at rest or >60 mm Hg with exercise)

- Asymptomatic patients with
  - ejection fraction 50–60% or
  - end systolic dimension 45–55 mm

- Severe left ventricular systolic dysfunction (ejection fraction <30% and/or end systolic dimension >55 mm) if chordal preservation is highly likely
<table>
<thead>
<tr>
<th>Indications</th>
<th>Stress Data</th>
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<th>Impact of decision making ESC and ACC Guidelines</th>
</tr>
</thead>
</table>
| MITRAL REGURGITATION |             | **Exercise capacity**  
|                      |             | **Symptoms**  
| Asymptomatic MR      | Clinical    | PASP > 60 mm hg with exercise testing  
|                      |             | Increase in ERO >/=10 sq mm  
|                      | Echo        | Increase in EF < 4 %  
|                      |             | Increase in LVESV index > 25ml/sq m  
|                      |             | Increase in GLS < 1.9%  
|                      |             | Development of symptoms  
|                      |             | reduced symptom free survival  
|                      |             | post-op LV dysfunction  
|                      |             | cardiac morbidity  
|                      |             | deterioration of LV function  
| Symptomatic MR       | Echo        | PASP > 60mm hg  
|                      |             | Severe MR during exercise  
|                      |             | ACC 2b  

**ESC and ACC Guidelines**

- **ACC 2A**
Functional and prognostic implications of left ventricular contractile reserve in patients with asymptomatic severe mitral regurgitation

R Lee, B Haluska, D Y Leung, C Case, J Mundy, T H Marwick


---

**Cumulative event-free survival (%)**

- CR+: 1.00
- CR−: 1.00 censored
- CR−: 0.00
- CR−: 0.00 censored

Log rank = 4.73, p = 0.03

**Number at risk:**

- CR+: 19, 14, 10, 6, 3
- CR−: 22, 16, 11, 6, 3

**EF (%)**

- CR+: 90, 80, 70, 60, 50, 40, 30, 20
- CR−: 90, 80, 70, 60, 50, 40, 30, 20

**Time from surgery (months):**

- Before
- 6
- 12
- 24–36

**Time after surgery (months):**

- Before
- 6
- 12
- 24–36

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No hallucinations present.
Exercise echo can unmask severe MR and marked increase in PASP in patients with dyspnea and mild MR. ERO at rest does not correlate with dynamic changes in ERO with exercise.

Lebrun F et al JACC 2001
Determinants of MV Dynamics

Characteristics of Exercise Induced Functional MR (FMR)

1. Greatly varies among patients
2. Does not correlated with FMR at rest
3. Does not correlate with LV dysfunction
4. Mainly correlates with changes in mitral valve deformation
5. Affected by local rather than global LV function and remodelling
6. Favorably affected by recruitable contractile reserve
Functional Mitral Regurgitation: Interplay of Dynamics
Exercise echo in Functional MR
Stress Echo

PE=pulmonary edema
FMR=functional MR

Bigi et al Cardiovascular Ultrasound 2009
Exercise echocardiography predicts development of left ventricular dysfunction in medically and surgically treated patients with asymptomatic severe aortic regurgitation

S Wahi, B Haluska, A Pasquet, C Case, C M Rimmerman, T H Marwick
Conclusions—Contractile reserve on exercise echocardiography is a better predictor of left ventricular decompensation than resting indices in asymptomatic patients with aortic regurgitation. In patients undergoing aortic valve replacement, contractile reserve had a better correlation with resting ejection fraction on postoperative follow up. Measurement of contractile reserve may be useful to monitor the early development of myocardial dysfunction in asymptomatic patients with aortic regurgitation, and may help to optimise the timing of surgery.

*(Heart 2000;84:606–614)*
## Predictors of LV Decompensation by Stress Echocardiography in Patients With Asymptomatic Severe AI and Normal LV Function

<table>
<thead>
<tr>
<th>Measurements</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction post exercise</td>
<td>0.001</td>
</tr>
<tr>
<td>Decrease &gt; 2%</td>
<td></td>
</tr>
<tr>
<td>FS post exercise</td>
<td>0.02</td>
</tr>
<tr>
<td>&lt;48%</td>
<td></td>
</tr>
<tr>
<td>LV WS rest</td>
<td>0.02</td>
</tr>
<tr>
<td>&gt;103 g/cm²</td>
<td></td>
</tr>
<tr>
<td>LV WS post exercise</td>
<td>0.02</td>
</tr>
<tr>
<td>&gt;88 g/cm²</td>
<td></td>
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</tbody>
</table>
Stress Echo And Prosthetic Valves

Normal prosthetic valves inherently stenotic due to small EOA

Type of prosthesis: mechanical versus bioprosthetic/stentless location and annulus size (aortic) determine gradients

Resting gradients tend to overlap for normal and abnormal functioning prosthesis many times

In general, gradients across prosthetic valves will increase depending on transvalvular flow rate

The exaggerated/absolute percentage of increase maybe the most important factor provided by stress echo
Evaluation of St Jude and Medtronic Hall Prosthesis By Stress Echo

Small size of aortic prosthesis

technical factors contributing to increased gradients across aortic prosthesis

Note that normal functioning aortic prosthesis can have substantial increases in gradient with exercise

Circulation 1989; 80;116-23
Normal increase of TMG is mild with no or mild increase in EOA by P1/2 time. A 100% or greater increase is likely pathological.

van de Brink et al. Am J Cardiol 1992
Stress Echo in HOCM

REST

STRESS
Kay Role of Stress Echo in HCM: provocation, hemodynamics, arrhythmias, worsening MR
Exercise Echo and Dyspnea Evaluation
In Chronic Lung Disease

- Normal patients
- Chronic lung disease and normal resting PA pressures
- Chronic lung disease and abnormal resting PA pressures

Imp: regardless of PASP pts with chronic lung disease have exercise induced increase in PASP reflecting abnormal PVR
Exercise Echo in Dyspnea Evaluation

**Peak TR**
- Rest: TRV = 2.5 m/sec, PAP = 30 mmHg
- Peak - 60W: TRV = 3.2 m/sec, PAP = 46 mmHg

**Mitral valve Inflow velocity**
- Rest: E = 80 cm/sec
- Intermediate - 45W: E = 110 cm/sec

**Mitral annular tissue velocity**
- Rest: E = 9 cm/sec, E/E' = 9
- Intermediate - 45W: E = 7 cm/sec, E/E' = 16
Conclusion Pulmonary artery systolic pressure at peak exercise can reach values $\geq 60$ mmHg in many healthy individuals older than 60 with good exercise capacity. However, high levels of PASP $> 60$ mmHg for low level of exercise should be considered abnormal.
Dynamic Diastology

with Exercise

E  E'  E/E'

Normal

↑  ↑  ↔

DFP

↑  ↑  □□

DFP  diastolic filling pressure