The Role of Echo in Asymptomatic Severe VHD

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Disclosure
Philippe Pibarot

Financial relationship with industry:

- Edwards Lifesciences: Echo CoreLab - SAPIEN 3
- V-Wave: Echo CoreLab
- Cardiac Phoenix: Research Grant for Echo CoreLab
- Ionis Pharmaceuticals

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- Research and Heart & Stroke Foundation of Quebec
2014 AHA/ACC Valvular Heart Disease (VHD) Guidelines

Concept of Valve Disease Stages

- **At risk for disease**
  - Stage A
    - Follow

- **Progressive disease**
  - Stage B
    - Echo
    - Stress Echo

- **Severe disease (asymptomatic)**
  - Stage C1
  - Stage C2
    - Intervene

- **Severe disease (symptomatic)**
  - Stage D
Case #1 Asymptomatic Patient with Severe AS (C1 Stage)

- 65 y.o. woman with calcific AS
- Asymptomatic
- LVEF: 60%
- AS severity on echo:
  - Severely calcified valve
  - Peak jet velocity: 5.1 m/s (1 Yr ago: 4.8 m/s)
  - Peak/mean gradient: 104/64 mmHg
  - AVA: 0.65 cm² Indexed AVA: 0.35 cm²/m²
Exercise testing can provide valuable information in patients with VHD, especially in those whose symptoms are difficult to assess.

- It can be combined with echocardiography.
- It has a proven track record of safety, even among asymptomatic patients with severe AS.
- Exercise testing has generally been underutilized in patients with VHD and should constitute an important component of the evaluation process.
Exercise Testing to Unmask Symptoms in AS

Case
Normal test:
9 METS
No fall in BP

Das et al Eur Heart J 2005; 26:1309-13
Clinical Dilemma in Asymptomatic Severe AS (C1 Stage)

Early « Prophylactic » AVR? OR Watchful waiting?
Asymptomatic Aortic Stenosis: It Is Not Simple Anymore

Robert O. Bonow

J Am Coll Cardiol 2015;66:2839-41
Early Surgical versus Conservative Strategies in Patients with Asymptomatic Severe AS

291 Patients treated with early AVR (Initial AVR)
1515 Patients treated with watchful waiting (Conservative)

Aortic valve-related death

Log-rank P=0.003

All-cause death

Log-rank P<0.001

Taniguchi et al. JACC 2015
### Guidelines on Management of VHD: Indications for AVR in Asymptomatic Severe AS

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Recommendation for AVR</th>
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| ESC-EACTS 2012   | Asymptomatic patients if low surgical risk and one or more of the following findings is present:  
• Very severe AS (peak aortic velocity >5.5 m/s)  
• Severe valve calcification and a rate of peak aortic velocity progression ≥0.3 m/s/year | IIa   |
| ACC-AHA 2014     | Asymptomatic patients low surgical risk and:  
• Very severe AS (peak aortic velocity ≥5.0 m/s)  
• Aortic velocity progression ≥0.3 m/s/year  
• Severe AoV Calcification            | IIa   IIb|

**Case:**
- Peak aortic velocity: 5.1 m/s
- Progression 0.3 m/s/yr
- Severe AoV Calcification

*Vahanian et al. EHJ 2012*  
*Nishimura, Otto et al. JACC 2014*
Case #4: Look At the Valve!
Severe Aortic Valve Calcification

Valve Calcification
(≥3/4)

Case #4: Severe AoV Calcification

Rosenhek et al N Engl J Med
2000; 343:611-7
Aortic Valve Calcification by Echo
Quantification of Valvular Calcification by CT

None  Mild  Moderate  Severe

Messika-Zeitoun, JACC, 2004;110:356-362
AoV Calcium Score Predicts Mortality

Clavel et al. JACC 2014
Exercise-stress echocardiography for risk stratification in “true asymptomatic” AS

Maréchaux et al, Eur Heart J 2010
Cardiac Event-free Survival according to Ex-PHT

PHT: 55% at exercise (SPAP>60) vs. 6% at rest
Exercise PHT: 2-fold increase in cardiac events

## Guidelines on Management of VHD: Indications for AVR in Asymptomatic Severe AS

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  • Increase of mean gradient with exercise by >20 mmHg  
  • Markedly elevated BNP levels confirmed by repeated measurements and without other explanations  
  • Excessive LV hypertrophy in the absence of hypertension                                      | IIb    |

**Case:**

- Ex. increase in gradient: +39 mmHg

**Exercise Gradients**

151/103 mmHg
Look at the arteries:
Patients with calcific AS often have concomitant hypertension.

30-80% of patients with calcific AS have hypertension.
Valvulo-Arterial Impedance: A New Parameter to Estimate Total (Valvular + Arterial) LV Hemodynamic Load

\[ Z_{va} = \frac{LVSP}{SVi} = \frac{SAP + \Delta P_{Mean}}{SVi} \]

Case #1: \( Z_{va} = 5.1 \)

>3.5: Moderate
>4.5: Severe
Impact of Valvulo-Arterial Impedance on Overall Survival

Follow-up (years)

Survival (%)

544 Pts.
≥ moderate AS
Asymptomatic

Hachicha et al.
JACC 54;
1003-1011; 2009

Adjusted Hazard Ratios:

3.5≤Z_{va}<4.5: 1.7 (95% CI: 1.4-5.6); p=0.01
Z_{va}≥4.5: 2.0 (95% CI: 1.4-6.6); p=0.006
Look at the Left Ventricle:

Beyond the LV ejection fraction
What Our Eyes See Is Not Necessarily What Our Heart Feels

Philippe Pibarot  Éric Larose

Laval Hospital Research Center/Quebec Heart Institute, Laval University, Quebec, Que., Canada
Severe Aortic Stenosis

**Diastole**

**Systole**

Wall Thickening: 30%
LVEF: 60%

Longitudinal Shortening: 12%

Pibarot & Dumesnil et al., JACC, 2012
One third of asymptomatic patients with severe AS and normal LVEF have reduced longitudinal function: sub-clinical LV dysfunction

GLS measured by speckle tracking

Case: GLS=13%
LV Longitudinal Shortening: A Surrogate Marker of Myocardial Fibrosis

Weidemann et al. Circulation. 120:577-584, 2009
Prognostic Significance of Myocardial Fibrosis Measured by CMR in Patients with Severe AS

Azevedo et al., JACC 2010;56:278-87
### Guidelines on Management of VHD: Indications for AVR in Asymptomatic Severe AS

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• Markedly elevated BNP levels confirmed by repeated measurements and without other explanations  
• Excessive LV hypertrophy in the absence of hypertension | IIb   |

**Case:** BNP: 190 pg/ml
Risk of Mortality according to BNP “Activation”: Ratio of Measured BNP / normal value of BNP in Asymptomatic AS

Clavel et al. JACC; 63, 2014
Clinical Dilemna in Asymptomatic Severe AS:

Early « Prophylactic » AVR?
OR
Watchful waiting?
Clinical Dilemma in Asymptomatic Severe AS:

Early « Prophylactic » AVR?

OR

Active Surveillance!

With Multi-Modality Approach:

Anatomic / hemodynamic severity of AS:

- Very severe AS ($V_{\text{max}} > 5$ m/s)
- Ex. Δ gradient $\geq 20$ mmHg
- Severe AoV Ca (MDCT)

Total (valvulo+arterial) load

- $Z_{va} > 4.5$

LV structure and function:

- GLS $\leq 16$
- Myocardial fibrosis (CMR)
- BNP Ratio $> 1$
# Guidelines on Management of VHD: Indications for Surgery in Asymptomatic Severe MR

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Recommendation for Mitral Valve Repair</th>
<th>Class</th>
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<tbody>
<tr>
<td>ACC-AHA 2014</td>
<td>Asymptomatic chronic primary severe MR with preserved LV function (LVEF &gt; 60% and LVESD &lt; 40 mm) with:</td>
<td>IIa</td>
</tr>
<tr>
<td></td>
<td>• ≥ 95% likelihood of durable repair without MR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Expected operative mortality &lt; 1%</td>
<td></td>
</tr>
<tr>
<td>ACC-AHA 2014</td>
<td>Asymptomatic chronic primary severe MR with preserved LV function with high likelihood of durable repair with:</td>
<td>IIa</td>
</tr>
<tr>
<td></td>
<td>• New Onset of AF or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Resting PHT (SPAP &gt; 50 mmHg)</td>
<td></td>
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</tbody>
</table>

*Nishimura, Otto et al. JACC 2014*
Prognostic Value of LV Longitudinal Strain and LA Volume in Asymptomatic MR

**Global Longitudinal Strain**

- GLS < 20%
- GLS ≥ 20%

**LA Volume**

- iLA volume < 40 ml/m²
- iLA volume ≥ 40 ml/m²

Magne et al. Heart 2012
Case #1 Asymptomatic Patient with Moderate MR
42 y.o. man, Barlow disease, no risk factor

r = 0.91 cm
ERO = 24 mm²
RV = 43 ml
Exercise Stress Echo

125 watts   9 Mets   Exercise: 8 min 49 s   Stop for dyspnea

HR= 155, SBP= 175, DBP=125
Exercise

<table>
<thead>
<tr>
<th>State</th>
<th>ERO (mm²)</th>
<th>RV (ml)</th>
<th>SPAP (mmHg)</th>
<th>HR (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>24</td>
<td>43</td>
<td>35</td>
<td>88</td>
</tr>
<tr>
<td>Low-Exer</td>
<td>30</td>
<td>55</td>
<td>55</td>
<td>115</td>
</tr>
<tr>
<td>Peak-Exer</td>
<td>49</td>
<td>74</td>
<td>76</td>
<td>153</td>
</tr>
</tbody>
</table>
Exercise-induced Changes in MR Severity

32% of patients increased significantly MR severity ($\Delta RV > 15\text{ml}$, $\Delta ERO > 10\text{mm}^2$) during exercise.

Magne J et al. JACC, 20;56:300-9;2010
Impact of Exercise-induced Increase in MR on Symptom-free Survival

Follow-up, months

Symptom-free survival, %

Changes in RV<15ml
81±6%
53±12%
p=0.0015

Changes in RV≥15ml
67±8%
26±11%

Unadjusted HR=1.8, 95%CI: 1.2-2.4

Magne J et al. JACC, 20;56:300-9;2010
Correlations between Exercise-Induced Changes in MR and in SPAP

\[ r = 0.64, \quad p < 0.0001 \]

Changes in RV, ml

Changes in SPAP, mmHg

\[ r = 0.63, \quad p < 0.0001 \]

Changes in ERO, mm²

Changes in SPAP, mmHg

Stop for dyspnea

Impact of PHT on Symptom-Free Survival

Resting PHT (SPAP ≥ 50mmHg)

- 16% of patients
- 59±7% symptom-free survival

Adjusted HR=2.1, p=NS

Exercise PHT (SPAP ≥ 60mmHg)

- 57% of patients
- 75±7% symptom-free survival

Adjusted HR=3.4, p=0.002

Severe organic MR

EXERCISE ECHO

SUBCLINICAL LV DYSFUNCTION
2D Speckle Tracking at Rest

GLS = -24.3%
2D Speckle Tracking at Exercise

BNP:
17 pg.ml⁻¹
67 pg.ml⁻¹

GLS_{exercise} = -18\%
LV Contractile Reserve in Asymptomatic MR: Liège-Québec Study

LVCR+: ΔLVEF>4%

Absence of LVCR (GLS) associated with 2-fold increase in cardiac events after adjusting for other resting and exercise echo parameters

Magne et al. Eur Heart J 2013
## Pre-op predictors of post-op EF<50%

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cut-off</th>
<th>AUC</th>
<th>Sens</th>
<th>Spec</th>
</tr>
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<tbody>
<tr>
<td><strong>Rest</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA volume</td>
<td>78 ml</td>
<td>0.79</td>
<td>64%</td>
<td>87%</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>67%</td>
<td>0.48</td>
<td>92%</td>
<td>29%</td>
</tr>
<tr>
<td>GLS</td>
<td>18.1%</td>
<td>0.69</td>
<td>77%</td>
<td>76%</td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>70%</td>
<td>0.72</td>
<td>69%</td>
<td>70%</td>
</tr>
<tr>
<td>GLS</td>
<td>18.5%</td>
<td>0.82</td>
<td>85%</td>
<td>76%</td>
</tr>
<tr>
<td><strong>Ex-induced changes</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>6.6%</td>
<td>0.74</td>
<td>92%</td>
<td>53%</td>
</tr>
<tr>
<td>GLS</td>
<td>1.9%</td>
<td>0.80</td>
<td>92%</td>
<td>74%</td>
</tr>
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Lancellotti, Piérard JASE, 2008
## Summary – Role of Echo in Asymptomatic Severe MR (C1)

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<td>Asymptomatic severe MR and symptoms on exercise</td>
<td>I</td>
</tr>
<tr>
<td>ESC-EACTS</td>
<td>Pulmonary hypertension on exercise (systolic PA pressure &gt;60 mmHg)</td>
<td>IIb</td>
</tr>
<tr>
<td>Future Perspective</td>
<td>LA Dilation&lt;br&gt;Impaired resting GLS&lt;br&gt;Impaired contractile reserve (ΔGLS on exercise)</td>
<td>?</td>
</tr>
</tbody>
</table>
Severe Valve Disease

Asymptomatic (Stage C1) with no IIa indication of intervention

Positive Stress Test

Rest LV GLS <16% <18% (MR)

Exercise PHT Ex. SPAP ≥ 60 mmHg

Valve Replacement / Repair?

*ACC/AHA NOT ESC guidelines

Aortic Regurgitation
Aortic Stenosis
Mitral Regurgitation
Mitral Stenosis

AR
LVEF ≥ 50%
LVESD ≤ 50mm
LVEDD ≤ 65mm

AS
LVEF ≥ 50%
Vmax <5m/s
Mean Gradient <60mmHg
ΔVmax <0.3m/s/yr

MR
LVEF >60%
LVESD <40mm
Sinus Rhythm
SPAP <50mmHg
Successful Repair <95%
Or Mortality ≥1%

MS
Very Severe MVA <1cm² T₁/₂ ≥ 220
Unfavorable morphology,
LA clot, > mild MR
Severe MVA <1.5cm² T₁/₂ ≥ 150
- Sinus rhythm
- AF with unfavorable morphology,
LA clot, > mild MR

Very Severe MV A <1cm² T₁/₂ ≥ 220
Unfavorable morphology,
LA clot, > mild MR
Severe MVA <1.5cm² T₁/₂ ≥ 150
- Sinus rhythm
- AF with unfavorable morphology,
LA clot, > mild MR

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