L’Échocardiographie de stress dans l’Insuffisance Mitrale

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CHU de Limoges, France
Conflict of Interest Disclosure

None
Which parameters?

Exercise Stress echo in MR

- LV/RV geometry and function
- Valvular severity
- Systolic Pulmonary Arterial Pressure

SYMPTOMS?

Outcome and Risk Stratification + Timing of Surgery?
Exercise-Induced Mitral Regurgitation Is a Predictor of Morbid Events in Subjects With Mitral Valve Prolapse

MARCUS F. STODDARD, MD, FACC, CHARLES R. PRINCE, MD, FACC, SUSAN DILLON, RDCS, RITA A. LONGAKER, RCT, GLENN T. MORRIS, MD, NORMAN E. LIDDELL, MD, PhD

Louisville, Kentucky

Objectives. This study attempted to determine whether a subset of patients with mitral valve prolapse and no mitral regurgitation at rest will develop mitral regurgitation during exercise and have a higher than anticipated risk of morbid cardiovascular events.

Background. Mitral regurgitation in patients with mitral valve prolapse identifies a subset of patients at higher risk for morbid events. However, mitral regurgitation in patients with mitral valve prolapse may be intermittent and could go unrecognized. A provocative test to unmask mitral regurgitation in these patients would be useful.

Methods. Ninety-four adult patients with mitral valve prolapse and no mitral regurgitation at rest were studied during supine bicycle ergometry using color flow Doppler echocardiography in the apical four-chamber and long-axis views. Patients were prospectively followed up for morbid events.

Results. Thirty (32%) of 94 patients had exercise-induced mitral regurgitation. Prospective follow-up (mean 38 months) showed more morbid events in the group with than without mitral regurgitation and included, respectively, syncope (43% vs. 5%, p < 0.0001), congestive heart failure (17% vs. 0%, p < 0.005) and progressive mitral regurgitation requiring mitral valve replacement surgery (10% vs. 0%, p < 0.05). Cerebral embolic events, endocarditis or sudden death were rare and not different between groups.

Conclusions. In patients with mitral valve prolapse without mitral regurgitation at rest, exercise provokes mitral regurgitation in 32% of patients and predicts a higher risk for morbid events.

(J Am Coll Cardiol 1995;25:693–9)
Exercise-induced changes in MR

32% of patients increased significantly MR severity

1 third of moderate MR exhibits severe MR

Impact of Exercise-induced increase in MR on Symptom-free Survival

No “real” need for Exercise MR severity “quantification”

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

Exercise-induced changes in MR according to Exercise PHT

Regurgitant Volume

- Changes in RV, ml
  - No Ex-PHT: -5 ± 3.6
  - Ex-PHT: 12.6 ± 4
  - p = 0.004

Effective Regurgitant Orifice

- Changes in ERO, mm²
  - No Ex-PHT: -1 ± 2
  - Ex-PHT: 9 ± 2.5
  - p = 0.006

Impact on Symptom-free Survival and Post-op Outcome

**Exercise PHT (SPAP > 60mmHg)**

- Symptom-free survival, %
  - No exercise PHT: 75±7%
  - Exercise PHT: 35±8%

- Follow-up, months: 6 12 18 24 30 36 42 48

- Adjusted HR=2.8, p=0.01

**Post-operative Events**

<table>
<thead>
<tr>
<th>Event</th>
<th>No Ex. PHT (n=43, 42%)</th>
<th>Ex. PHT (n=59, 58%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All AF, n (%)</td>
<td>4 (9)</td>
<td>15 (25)</td>
<td>0.07</td>
</tr>
<tr>
<td>Early AF, n (%)</td>
<td>1 (2)</td>
<td>4 (7)</td>
<td>0.57</td>
</tr>
<tr>
<td>Hospitalization, n (%)</td>
<td>1 (2)</td>
<td>11 (19)</td>
<td>0.027</td>
</tr>
<tr>
<td>Acute pulmonary edema, n (%)</td>
<td>0 (0)</td>
<td>2 (3)</td>
<td>NA</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>1 (2)</td>
<td>5 (8)</td>
<td>0.38</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>0 (0)</td>
<td>4 (7)</td>
<td>NA</td>
</tr>
<tr>
<td>All events*, n (%)</td>
<td>5 (12)</td>
<td>23 (39)</td>
<td>0.005</td>
</tr>
<tr>
<td>Events without early AF*, n (%)</td>
<td>4 (9)</td>
<td>19 (32)</td>
<td>0.013</td>
</tr>
<tr>
<td>Major CV events*, n (%)</td>
<td>2 (5)</td>
<td>9 (15)</td>
<td>0.16</td>
</tr>
</tbody>
</table>


Magne J, Donal D et al. Heart, 2014
Impact on Symptom-free Survival

n=65 asymptomatic ≥moderate MR, no LV dysfunction/dilatation

Suzuki et al., J Cardiol, 2014
Impact on Symptom-free Survival

n=65 asymptomatic ≥moderate MR, no LV dysfunction/dilatation

n=196 asymptomatic moderate to severe MR, no LV dysfunction/dilatation

Suzuki et al., J Cardiol, 2014

Kusunose et al., Circ CV Imaging, 2013
Ex-induced Changes in sPAP in Healthy

<table>
<thead>
<tr>
<th></th>
<th>All (n = 70)</th>
<th>Age 20-30 (n = 13)</th>
<th>Age 30-40 (n = 10)</th>
<th>Age 40-50 (n = 14)</th>
<th>Age 50-60 (n = 12)</th>
<th>Age 60-70 (n = 11)</th>
<th>Age 70-80 (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASP at rest (mmHg)</td>
<td>27 ± 4</td>
<td>27 ± 4</td>
<td>29 ± 3</td>
<td>28 ± 3</td>
<td>26 ± 4</td>
<td>27 ± 4</td>
<td>28 ± 6</td>
</tr>
<tr>
<td>PASP at first workload step (mmHg)</td>
<td>34 ± 6</td>
<td>31 ± 4</td>
<td>33 ± 5</td>
<td>34 ± 4</td>
<td>31 ± 6</td>
<td>37 ± 9</td>
<td>37 ± 5</td>
</tr>
<tr>
<td>PASP at peak exercise (mmHg)</td>
<td>51 ± 9</td>
<td>45 ± 7</td>
<td>51 ± 6</td>
<td>52 ± 9</td>
<td>53 ± 4</td>
<td>54 ± 12*</td>
<td>58 ± 7*</td>
</tr>
<tr>
<td>Increase in PASP (mmHg)</td>
<td>27 ± 8</td>
<td>22 ± 8</td>
<td>24 ± 7</td>
<td>27 ± 10</td>
<td>29 ± 5</td>
<td>29 ± 9</td>
<td>30 ± 8</td>
</tr>
</tbody>
</table>

- Maximal workload: 152±47W (range: 75-250)
- Ex PHT: 36% of 60-70yo
  50% of >70yo
- Maximal workload in Ex PHT: 142±51W

*Mahjoub et al. EJE, 2009*
Ex-induced Changes in sPAP in Healthy

- Different maximal reached workload;
- Different changes in sPAP slope;
- Different kinetics;
- Different physiological mechanisms
Ex-induced Changes in sPAP in Healthy

Assessed for eligibility (n= 1413)

Excluded (n=902)
- Myocardial Ischemia: 689
- Left Ventricular dysfunction: 104
- Resting PASP > 35mmHg: 70
- Others: 39

Current Analysis (n=511)

Echocardiographic assessment of pulmonary artery systolic pressure following treadmill stress testing

Arshad A. Khan1, Mohammad Al-Omary1, Ian Renner2, Ehtesham Ul Haque3, Avedis Ekmejian1, Mumtaz Hussain2, Laurent Quiqueree1, Nicholas J. Collins1, and Stuart Turner1

1Cardiovascular Department, John Hunter Hospital, Locked Bag 1, HRMC, Newcastle, NSW 2300, Australia; 2University of Newcastle, Newcastle, NSW, Australia; and 3Middleboro ARH Hospital, Middleboro, KY, USA

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>&lt;30 years</th>
<th>31–50 years</th>
<th>51–70 years</th>
<th>&gt;70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
<td>511 (100)</td>
<td>38 (7)</td>
<td>156 (31)</td>
<td>280 (55)</td>
<td>37 (7)</td>
</tr>
<tr>
<td>Age, years</td>
<td>53 ± 14</td>
<td>22 ± 3</td>
<td>43 ± 5</td>
<td>56 ± 5</td>
<td>75 ± 4</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>350 (68)</td>
<td>26 (68)</td>
<td>106 (68)</td>
<td>193 (69)</td>
<td>25 (68)</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>52 (10)</td>
<td>5 (13)</td>
<td>18 (12)</td>
<td>23 (8)</td>
<td>6 (16)</td>
</tr>
<tr>
<td>HTN, n (%)</td>
<td>61 (12)</td>
<td>3 (8)</td>
<td>22 (14)</td>
<td>24 (9)</td>
<td>12 (32)</td>
</tr>
<tr>
<td>Hypercholesterolaemia, n (%)</td>
<td>163 (32)</td>
<td>2 (5)</td>
<td>55 (35)</td>
<td>80 (29)</td>
<td>26 (70)</td>
</tr>
<tr>
<td>Smoking/ex-smoker, n (%)</td>
<td>204 (40)</td>
<td>8 (21)</td>
<td>77 (49)</td>
<td>102 (36)</td>
<td>17 (46)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28 ± 6</td>
<td>25 ± 5</td>
<td>27 ± 6</td>
<td>29 ± 5</td>
<td>30 ± 5</td>
</tr>
</tbody>
</table>

Khan et al. EHJ CVI, 2016
Ex-induced Changes in sPAP in Healthy

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Resting PASP</th>
<th>pePASP</th>
</tr>
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<tr>
<td>&lt; 30 years</td>
<td>27</td>
<td>34</td>
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<td>26</td>
<td>36</td>
</tr>
<tr>
<td>51–70 years</td>
<td>28</td>
<td>40</td>
</tr>
<tr>
<td>&gt; 70 year</td>
<td>30</td>
<td>41</td>
</tr>
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*Khan et al. EHJ CVI, 2016*
Exercise-induced Early Abrupt increase in SPAP

n=111 asymptomatic patients with ≥ moderate MR and preserved LVEF

Event-free Survival, %

- Log rank: p=0.035
- HR=1.99, 95%CI: 1.00-3.77
- p=0.038

Follow-up time (years)

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
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<tbody>
<tr>
<td>87</td>
<td>71</td>
<td>60</td>
<td>42</td>
<td>23</td>
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<tr>
<td>24</td>
<td>20</td>
<td>13</td>
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Multivariate Analysis

- Models X^2
- Baseline data
- + Peak BNP
- + Early Δ SPAP≥15mmHg

Toubal et al, AHA 2016
LV Contractile Reserve

LV contractile reserve is associated with better LV function and outcomes after mitral valve surgery.

63% of CR+ in patients with asymptomatic severe MR

Lee et al. Heart, 2005, 91: 1407-12
Impact of LVCR on Outcome

LV contractile reserve using GLS

Cardiac Event-free Survival, %

Follow-up, months

CR+

74±8%

68±7%

45±8%

42±8%

p=0.003

CR-

Adjusted HR=2 (1.0-4.1) p=0.04

LV contractile reserve using LVEF

Cardiac Event-free Survival, %

Follow-up, months

CR+

63±8%

63±8%

CR-

61±7%

50±8%

p=0.20

Adjusted HR=1.22 (0.9-1.7) p=0.23

Magne et al., Eur Heart Journal, 2013
Take Home Messages!

✓ Exercise stress echocardiography: in which patient?
  o Asymptomatic severe MR with preserved LV function
  o Asymptomatic moderate MR

✓ Exercise stress echocardiography: which parameter?
  o Systolic PAP
    • Early abrupt changes and PHT occurrence
  o MR severity
  o LV contractile reserve (2D speckle tracking?)
MAIN THEMES
Imaging in heart failure
Interventional imaging

Call for abstracts
1 April – 31 May
Correlations between Exercise-Induced Changes in MR and in SPAP

- Changes in RV, ml
  - $r=0.64$, $p<0.0001$

- Changes in SPAP, mmHg
  - Changes in ERO, mm
    - $r=0.63$, $p<0.0001$

Stop for dyspnea
Impact on Symptom-free Survival

**Resting PHT (SPAP >50mmHg)**

- Symptom-free survival, %
- Follow-up, months

- Adjusted HR=2.1, p=NS

**Exercise PHT (SPAP >60mmHg)**

- Symptom-free survival, %
- Follow-up, months

- Adjusted HR=2.8, p=0.01

## Impact of preop Ex. PHT on Postop Outcome

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LV Geometry and Function during Exercise

- 74 chronic primary MR in NYHA class I or II undergoing MV repair
- Exercise-induced changes in LV: ↓ postop LVEF
- Exercise parameters are the best predictors of postoperative LV dysfunction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Optimal Diagnostic Cutoff Value</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESVI_\text{EXE}</td>
<td>25 cm$^3$/m$^2$</td>
<td>83%</td>
<td>83%</td>
</tr>
<tr>
<td>EF_\text{EXE}</td>
<td>68%</td>
<td>80%</td>
<td>81%</td>
</tr>
<tr>
<td>ΔEF_\text{EXE}</td>
<td>4%</td>
<td>75%</td>
<td>79%</td>
</tr>
<tr>
<td>LV dP/dt</td>
<td>1,000 mm Hg/s</td>
<td>73%</td>
<td>65%</td>
</tr>
<tr>
<td>ESWS_\text{REST}</td>
<td>52.4 × 10^3 dynes/cm$^2$</td>
<td>65%</td>
<td>64%</td>
</tr>
<tr>
<td>ESVI_\text{REST}</td>
<td>29 cm$^3$/m$^2$</td>
<td>63%</td>
<td>66%</td>
</tr>
<tr>
<td>EF_\text{REST}</td>
<td>66%</td>
<td>51%</td>
<td>67%</td>
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</table>

Leung et al. JACC, 1996
LV Contractile Reserve

Rest

GLS = -24.3%

Exercise

EDV = 140ml, ESV = 51ml LVEF = 64%

GLS = -18%

EDV = 153ml, ESV = 36ml LVEF = 76%
Exercise-induced Changes in LVEF and GLS

From 2 centers: asymptomatic primary MR (n=112, 60% of severe), preserved LV function

1/3 of discrepancy between the 2 methods

Magne et al., Eur Heart Journal, 2013
Relationship between LVCR and BNP Level

LV contractile reserve using GLS

LV contractile reserve using LVEF

Ex-induced changes in GLS

Ex-induced changes in LVEF

r = -0.48, p < 0.0001

r = -0.17, p = 0.11

Magne et al., Eur Heart Journal, 2013
Exercise BNP and Impact on Outcome

BNP level significantly increase during exercise

Exercise BNP is determined by ex. LV longitudinal function

Magne, Mahjoub, Pibarot, Pirlet, Pierard, Lancellotti. Eur J Heart Fail. 2012
Exercise BNP and Impact on Outcome

Exercise BNP level and outcome

Incremental prognostic value of exercise BNP

- Adjusted incidence of cardiac events, %
  - Tertile 1 (Ex. BNP: 5-29 pg/mL)
  - Tertile 2 (Ex. BNP: 30-62 pg/mL)
  - Tertile 3 (Ex. BNP: 63-412 pg/mL)

- Prediction of cardiac events, $\chi^2$:
  - Demographic and echo. data: 24.3
  - + Resting BNP: 35.8
  - + Exercise BNP: 45.6

- p = 0.02

The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography

Patrizio Lancellotti\textsuperscript{1,2}, Patricia A. Pellokka\textsuperscript{3}, Werner Budts\textsuperscript{4}, Farooq A. Chaudhry\textsuperscript{5}, Erwan Donal\textsuperscript{6}, Raluca Dulgheru\textsuperscript{1}, Thor Edvardsen\textsuperscript{7}, Madalina Garbi\textsuperscript{8}, Jong-Won Ha\textsuperscript{9}, Garvan C. Kane\textsuperscript{3}, Joe Kreeger\textsuperscript{10}, Luc Mertens\textsuperscript{11}, Philippe Pibarot\textsuperscript{12}, Eugenio Picano\textsuperscript{13}, Thomas Ryan\textsuperscript{14}, Jeane M. Tsutsui\textsuperscript{15}, and Albert Varga\textsuperscript{16}
Ex. PHT, RV function and Outcome

n=196 asymptomatic moderate to severe MR, no LV dysfunction/dilatation

Cardiac event-free survival

Multivariate Analysis: prediction of event

Kusunose et al., Circ CV Imaging, 2013