Exercise-induced functional mitral regurgitation in heart failure and preserved ejection fraction: a new entity

Sylvestre Maréchaux1,2,3, Julia Terrade1, Frédéric Biausque4, Yann Lefetz4, Régis Deturck4, Philippe Asseman5, Thierry H. Le Jemtel6, and Pierre V. Ennezat2,5*

1Centre Hospitalier Régional et Universitaire de Lille, Service d’explorations fonctionnelles cardiovasculaires, Lille, France; 2EA 2693, Université de Lille 2, Faculté de Médecine, Lille, France; 3Département de physiologie, Faculté de Médecine de Lille, 59000 Lille, France; 4Centre Hospitalier de Lens, département de cardiologie, France; 5Centre Hospitalier Régional et Universitaire de Lille, Soins intensifs cardiologicals, Lille, France; and 6Division of Cardiology, Tulane University School of Medicine, New Orleans, LA, USA

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We report here the worsening of functional mitral regurgitation (MR) during dynamic exercise Doppler echocardiography in four female patients with heart failure and preserved ejection fraction. MR worsened concomitantly to an increase in systolic mitral tenting area and in \(E/E_a\) ratio, whereas local left ventricular (LV) remodelling was not substantially aggravated by exercise. We accordingly suggest that exercise-induced increase in LV filling or left atrial pressure that in turn leads to increase in mitral tenting area worsens functional MR during exercise.

Keywords
- Functional mitral regurgitation
- Left ventricular filling pressure
- Exercise Doppler echocardiography
- Heart failure with preserved ejection fraction

Case report

We here report four patients (40- to 84-year-old) with severe exertional dyspnoea who were referred for exercise echocardiography. A history of long-standing hypertension and heart failure with preserved left ventricular (LV) ejection fraction (HFpEF) (requiring mechanical ventilation in Case 3) in the past 6 months was found in all patients. Two patients (Cases 2 and 3) had diabetes mellitus. Coronary angiography was normal and renal artery stenosis was ruled out in all by Doppler ultrasound examination of the renal arteries and renal angiography in three patients. QRS width was normal. Symptom-limited exercise Doppler echocardiography was performed on a semi-recumbent bicycle ergometer starting at a 25 W workload with 20 W increments every 3 min. Beta-blockers were withdrawn 48 h before stress testing. Mitral valve apparatus and subapparatus were normal in all but in Case 4 who showed slightly calcified mitral annulus but without any valvular abnormality. Neither EKG nor wall motion abnormalities developed during exercise. Functional mitral regurgitation (MR) worsened during exercise in these patients (Case 2, loop 1; Case 3, loop 2; and Case 4, loop 3) (Table 1). The increase in MR during exercise was paralleled by an increase in mitral tenting area (Figure 1), in \(E/E_a\) ratio at low workload (Figure 2) and in left atrial (LA) size (Table 1). The rise in systolic pulmonary pressure was obvious in all patients (Figure 3). Importantly, the posterior papillary muscle (PPM)–fibrosa length, an important index of local LV remodelling, did not increase (Cases 1 and 4) during exercise. LV outflow tract velocity–time integral decreased or failed to increase in these four patients, thereby indicating that exercise-induced worsening of MR blunted the increase in forward stroke volume in these patients with pronounced exercise intolerance (Figure 3). In one patient (Case 2), non-invasive data were in agreement with those of right heart catheterization which showed a dramatic increase in mean pulmonary artery pressure (30–50 mmHg) and in mean pulmonary capillary wedge pressure (23–35 mmHg) during a minimal isometric exercise (Figure 4).

* Corresponding author: Intensive Care Unit, Cardiology hospital, Bd Pr J Leclercq, 59037 Lille Cedex, France. Tel: +33 3 20 44 53 30, Fax: +33 3 20 44 56 04, Email: ennezat@yahoo.com

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Table 1  Doppler echocardiographic data at rest and during exercise of five patients with heart failure and preserved ejection fraction and trivial mitral regurgitation at rest

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Workload (W)</th>
<th>Heart rate (bpm)</th>
<th>SBP (mmHg)</th>
<th>LVEF (%)</th>
<th>LVEDV index (mL/m²)</th>
<th>LVOT VTI (cm)</th>
<th>E/A</th>
<th>E/a</th>
<th>Left atrial area (cm²)</th>
<th>Tenting area (cm²)</th>
<th>PPM fibrosa (mm)</th>
<th>ERO (mm²)</th>
<th>RV (mL)</th>
<th>TTG (mmHg)</th>
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<tr>
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<td>Ex</td>
<td>Rest</td>
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<td>Ex</td>
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<td>10</td>
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</tbody>
</table>

SBP, systolic blood pressure; LVEF, left ventricle ejection fraction; EDV, end-diastolic volume; ERO, effective regurgitant orifice; RV, regurgitant volume; TTG, tricuspid gradient; Ex, exercise.

Discussion

In spite of the absence of significant structural abnormalities of the mitral valve, QRS widening, and local LV remodeling, exercise-induced functional MR in HFpEF may increase during exercise. The contribution of exercise to functional MR in HFpEF may be related to an increase in LA pressure and LA volume, which can be induced by the increase in cardiac output during exercise. The LA atrial pressure at rest is a key determinant of LV filling pressure..

Supplementary data

Supplementary data are available at European Journal of Echocardiography online.

References

**Figure 1** Exercise-induced increase in mitral regurgitation that is trivial at rest in a patient with heart failure and preserved left ventricular ejection fraction. The increase in mitral effective regurgitant orifice area is paralleled by an increase in mitral tenting area (Case 2).

**Figure 2** Exercise-induced increase in $E/E_a$ ratio in a patient with heart failure and preserved left ventricular ejection fraction and exercise-induced increase in severity of a trivial functional mitral regurgitation at rest (Case 2).
Figure 3 Failure to increase left ventricular forward stroke volume and rise in systolic transtricuspid pressure gradient are illustrated in this patient with heart failure and preserved left ventricular ejection fraction and exercise-induced worsening of mitral regurgitation (Case 2).

Figure 4 Right heart catheterism data showing an increase in pulmonary capillary wedge pressure (PCWP) and in pulmonary artery pressure (PAP) in Patient 2 during an isometric exercise.