The Use of Exercise Echocardiography in the Evaluation of Mitral Regurgitation

Kibar Yared, Kaitlyn My-Tu Lam and Judy Hung*

Abstract: Mitral regurgitation (MR) is the second most common valvular disease in western countries after aortic stenosis. Optimal management of patients with MR depends on the etiology of the regurgitation and is based predominantly on left ventricular function and functional status. Recent outcome studies report high risk subsets of asymptomatic patients with MR, and practice guidelines underscore the importance of a well-established estimation of exercise tolerance and recommend exercise testing to objectively assess functional status and hemodynamic factors.

Keywords: Stress echocardiography, mitral valve, mitral regurgitation, cardiac resynchronization therapy.

INTRODUCTION

Mitral regurgitation (MR) is the second most common valve disease in western countries, after aortic stenosis, representing 32% of single native left-sided valve disease in a recent European survey [1]. MR results from several heterogeneous conditions and its many causes include disorders of the valve leaflets, mitral annulus, chordae tendinae, papillary muscles and the left ventricle. Primary MR is defined as MR resulting from organic valvular pathology such as prolapse, rheumatic change or that due to endocarditis. Secondary MR results from ischemic or myopathic changes to the left ventricle leading to incomplete closure of the mitral leaflets. In the latter conditions, leaflet morphology is relatively normal.

Exercise echocardiography plays an important role in the evaluation and management of chronic mitral regurgitation. It can assist in the evaluation of symptoms, more fully assess the mechanism and severity of regurgitation, determine functional capacity, and assess contractile reserve to help optimize the timing of surgical intervention. In addition, exercise echocardiography has been beneficial in assessing the response of MR to cardiac resynchronization therapy.

This review will summarize the clinical utility of exercise echocardiography in chronic MR, examining both primary and secondary MR.

PATHOPHYSIOLOGY

The regurgitant orifice in MR serves as an “escape valve”, decreasing the impedance to and enhancing left ventricular emptying. The volume of MR flow depends on both the size of the regurgitant orifice and the (reverse) pressure gradient between the left ventricle (LV) and the left atrium (LA) [2]. Both the orifice size and the pressure gradient are dynamic [3-5]. Increases in both preload and afterload and depression of contractility increase left ventricular size, enlarge the mitral annulus and displace the papillary muscles apically thereby increasing the regurgitant orifice. The pressure gradient between the LV and LA can increase with increases in LV afterload, preload as well as contractility.

In chronic MR, volume overload of the left ventricle results in an increase in LV end-diastolic volume (LVEDV). The increase in LVEDV allows augmentation of total stroke volume, while maintaining forward stroke volume near normal. Ejection indices such as ejection fraction and fractional shortening are initially supra-normal due to the low impedance of the outflow circuit; these indices can appear “normal” even after contractile function has been impaired [6].

Although the compensatory mechanisms are effective, the prolonged volume overload ultimately leads to myocardial dysfunction. Consequently, end-systolic volume rises, and ejection fraction and stroke volume decline. Therefore, surgical intervention is usually recommended prior to the onset of LV dysfunction and is important in preventing further deterioration of systolic function and improve survival [7].

The hemodynamic response to exercise in MR depends on the change in the severity of the regurgitant lesion and the ability of the left ventricle to meet increases in demands on workload. These two factors interact in complex ways. The effective regurgitant orifice flow (ERO) can be relatively fixed throughout systole such as in rheumatic mitral valve disease. On the other hand, in ischemic MR, and occasionally in cases with flail mitral leaflets [4], the ERO can be dynamic and may vary with the response of the ventricle to exercise. The response of the ventricle to exercise, another determinant of the response of MR to exercise, depends on its contractile state at rest, as well as its contractile response to exercise.

Risk stratification using exercise echocardiography, especially in asymptomatic patients, becomes important not only in accurate quantification and characterization of the etiology of MR, but also in guiding therapy.

*Address for correspondence to this author at the Cardiac Ultrasound Laboratory, Division of Cardiology, Massachusetts General Hospital, 55 Fruit Street, Blake 256, Boston, Massachusetts, 02114, USA; Tel: 617-726-0995; Fax: 617-726-8383; E-mail: jhung@partners.org
PRIMARY MITRAL REGURGITATION

Symptomatic Patients

The most recent ACC/AHA guidelines for the management of valvular disease [8] include, as a class I indication, surgical intervention once patients develop symptoms associated with severe MR in the setting of normal LV function. Among symptomatic patients with flail leaflets, Ling and Enriquez-Sarano [9] reported an annual mortality rate of 6.3%; at 10 years 90% had died or had undergone surgical correction (Fig. 1). This latter series included many patients who had left ventricular dysfunction or atrial fibrillation and thus might have been considered to be at a higher risk.

With the current guidelines, reasonable surgical candidates who develop symptoms related to MR should undergo surgical correction. However, symptom status can be subjective and variable and it is sometimes difficult to relate those symptoms to severe mitral regurgitation. Patients also often have other co-morbidities that may be contributing to their symptoms. Due to the morbidity and mortality associated with severe MR and the potential benefit of surgical intervention, it is important to differentiate symptoms caused by mitral regurgitation from those of other causes. Differentiating the symptoms of chronic obstructive pulmonary disease (COPD), for example, from those of MR can be extremely challenging. Approaches involving combined cardio-pulmonary function testing during exercise may help distinguish between pulmonary and cardiovascular etiologies of dyspnea [10]. Exercise echocardiography may also unmask and clarify subclinical symptoms. The observation of limiting symptoms with worsening MR during exercise echocardiography suggests that the patient’s symptoms are due to exercise-induced MR.

In symptomatic patients with a clinical picture suspicious for severe MR, but not evident on the resting echocardiogram, exercise echocardiography demonstrating worsening MR helps correlate the pathology with the patient’s symptoms [11]. Similarly, in a study of patients with poor exercise tolerance and rheumatic mitral valve disease with only a mild degree of MR, exercise echocardiography has been helpful in elucidating the origin of the symptoms by provoking severe MR in some patients and significant mitral stenosis in others, with associated pulmonary hypertension.

Fig. (1). Four series examining the natural history of patients with severe MR including a series of patients with flail mitral leaflets reported by Ling and associates (green triangles), many of whom were symptomatic, had atrial fibrillation, or had evidence of left ventricular (LV) dysfunction, and three series reported by Rosen et al. (blue squares), Sarano et al. (black star) and Rosenhek et al. (red circles) in patients who initially were asymptomatic with normal LV function. Although the patients with flail leaflets had a steeper initial attrition rate, all series demonstrated that patients with severe MR have a high likelihood of developing symptoms or other indications for surgery over the course of 6 to 10 years. Modified from Otto CM, Bonow RO. Valvular Heart Disease. In: Libby P, Bonow RO, Mann DL, et al., Eds. Braunwald's Heart Disease. A Textbook of Cardiovascular Medicine. 8th ed. Philadelphia: Saunders Elsevier 2007: 1664.
These findings have been applied to patients without rheumatic heart disease.

**Asymptomatic Patients**

Among asymptomatic patients with initially normal left and right ventricular ejection fractions, severe MR is associated with a high rate of symptoms or left ventricular dysfunction requiring surgery. Mitral valve surgery (repair or replacement) during a 5-year follow-up was independently associated with a reduced risk of death [13]. In 102 asymptomatic patients with normal LV function, the 5-year combined incidence of atrial fibrillation, heart failure, or cardiovascular death was 42 ± 8%. In these patients, surgery also reduced rates of cardiovascular death and heart failure together [13]. In fact, mitral valve surgery was nearly unavoidable over the course of 10 years [14]. Recent studies have also shown that the clinical course of initially asymptomatic primary MR is not necessarily benign [15, 16]. These studies have shown that patients with medically managed asymptomatic MR and an effective regurgitant orifice of > 40 mm² had an excess risk of death and cardiac events (Fig. 2). In addition, cardiac surgery markedly reduced the risk of heart failure and death. Conversely, watchful waiting of asymptomatic patients with severe MR until development of symptoms, LV dysfunction or dilatation, or pulmonary hypertension has recently been advocated [17]. 132 consecutive patients with severe degenerative MR, due to flail leaflet or prolapse, were followed up for 62 ± 26 months. During the follow-up period, 38 patients developed an indication for surgery based on ACC/AHA guidelines. Survival free of any indication for surgery was 92% at 2 years, 78% at 4 years, 65% at 6 years, and 55% at 8 years. Patients with a flail leaflet tended to develop criteria for surgery slightly but, not significantly, earlier than those with mitral valve prolapse. Overall survival was not statistically different from expected survival either in the total group or in the subgroup of patients with flail leaflet.

With exercise, mitral regurgitation that is non-holosystolic can appear de novo or even increase in duration and severity. Stoddard et al. [18] studied 94 patients with mitral valve prolapse and no MR. After symptom-limited exercise using supine bicycle ergometry, 30 patients (32%) developed transient MR. At peak stress, there was no significant difference in ejection fraction between those who developed MR and those who did not. The only hemodynamic variable that differed between the two groups was peak systolic blood pressure, with a greater increase in those who developed MR. During the follow-up period of 38 months, the patients with exercise-induced MR had a six-fold greater incidence of cardiovascular morbid events, particularly syncope and congestive heart failure. Exercise-induced MR and a prior history of syncope were the only independent predictors of a

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**Fig. (2).** Kaplan–Meier estimates of the mean (± standard error) rates of overall survival among patients with asymptomatic mitral regurgitation undergoing medical management, according to the effective regurgitant orifice (ERO). Values in parentheses are survival rates at five years. From Enriquez-Sarano M, Avierinos J-F, Messika-Zeitoun D, et al. Quantitative Determinants of the Outcome of Asymptomatic Mitral Regurgitation. N Engl J Med 2005; 352(9): 875-883.
subsequent cardiovascular event or syncope and exercise-induced MR was the only independent predictor of congestive heart failure. Patients with mitral valve prolapse without MR at rest and no leaflet thickening are usually considered at low risk for morbid events. The study by Stoddard et al. showed that more than 30% of these “low risk” patients have exercise-induced MR and are at a higher risk for morbid events than usually expected [18]. Exercise echocardiography therefore can have important prognostic value in patients with mitral valve prolapse.

Stress echocardiography has been evaluated in the setting of mitral regurgitation secondary to rheumatic heart disease. Symptoms can often appear to be out of proportion to the degree of valvular pathology. Tischler et al. [12] performed echocardiography prior to and after exercise in 14 patients with symptomatic, mild, mixed rheumatic mitral valve disease to ascertain the actual cause of symptoms. These patients had a normal ejection fraction and no more than mild mitral regurgitation or mild mitral stenosis. Diastolic mitral gradients increased with exercise, but an unexpected finding was the development of severe mitral regurgitation in five patients (36%). Patients who developed mitral regurgitation trended toward a diminished exercise capacity. Although decreased exercise capacity was not clearly correlated with the patients’ symptoms, it was felt likely that the acute onset of severe mitral regurgitation was a factor in the limitation of exercise.

Left ventricular contractile function can be impaired even in the presence of a normal ejection fraction in patients with chronic MR because of altered loading conditions [6, 19, 20]. Exercise echocardiography can unmask latent or subclinical LV dysfunction in patients in whom the LV is compensated at rest. An inability to increase the ejection fraction or reduce the end-systolic volume with stress reflects the presence of an impaired contractile reserve, and have both been shown to be reliable early markers for progressive deterioration in myocardial contractility [21].

Lee et al. evaluated functional and prognostic implications of LV contractile reserve in patients with isolated severe MR pre- and post-mitral valve replacement as well as in those being treated medically [22]. Contractile reserve was defined as the difference between the resting and post-exercise EF. An impaired contractile reserve (EF increment post-exercise ≤ 4%) predicted not only the development of late post-operative LV dysfunction (EF < 50%) and morbidity in surgically treated patients but also the occurrence of cardiac events (congestive heart failure and new onset atrial fibrillation) and progressive deterioration of LV function in the medically treated patients. Conversely, an intact contractile reserve (EF increment post-exercise > 4%) predicts preservation of LV function and a favorable clinical outcome irrespective of whether patients were treated medically or surgically. Additionally, evaluation of contractile reserve had an incremental value over rest LV end-systolic volumes in predicting late post-operative LV dysfunction. An important limiting factor in this study is the inevitable variability encountered when measuring post-exercise end-systolic and end-diastolic volumes – the manner in which EF was derived. Accurate tracing of endocardial borders is very challenging in patients with poor acoustic windows and technically difficult studies, and introduces important interobserver variability that limits the general applicability of such a technique.

A similar study used exercise echocardiography prior to mitral valve surgery to identify those patients with asymptomatic, chronic severe MR who were at risk of developing postoperative LV dysfunction [23]. A postoperative ejection fraction of < 50% was best predicted by a pre-operative exercise end-systolic volume index > 25 ml/m^2, an exercise ejection fraction < 68% and an increase in ejection fraction with exercise of < 4% (Table 1) [23].

Evaluation of right ventricular function and pulmonary artery pressure, especially with exercise, can aid in deciding to intervene on patients with severe MR (ACC/AHA Class IIa indication). In patients with mitral valve prolapse, the change in right ventricular ejection fraction with exercise was the only predictor of the need for surgical intervention over 4.7 years of follow-up [9]. Hochreiter et al. studied asymptomatic and symptomatic patients with significant mitral regurgitation due to diverse etiologies (most with LV ejection fraction < 50%). Right ventricular ejection fraction both at rest and during exercise was slightly more predictive of long term mortality than were left ventricular ejection fraction during rest and exercise, symptoms and treadmill exercise time during follow-up [24]. Although assessment of left ventricular performance at rest and post-exercise provides a certain amount of prognostic information, the

### Table 1. Sensitivity and Specificity of Diagnostic Cutoff Values of Preoperative Rest and Exercise Indexes of Left Ventricular Function in Predicting Early Postoperative Left Ventricular Dysfunction

| Variable | Optimal Diagnostic Cut-Off | Specificity (%) | Sensitivity (%) |
|----------|-----------------------------|----------------|----------------|
| ESVI_{pre} | 25 cm^3/m^2                | 83             | 83             |
| EF_{pre}  | 68%                         | 80             | 81             |
| ΔEF_{pre} | 4%                          | 75             | 79             |
| LV {dp/dt} | 1000 mmHg/s                | 73             | 65             |
| ESWS_{rest} | 52.4 x 10^4 dynes/cm^2   | 65             | 64             |
| ESVI_{rest} | 29 cm^3/m^2              | 63             | 66             |
| EF_{rest}  | 66%                         | 51             | 67             |

ESVI_{pre}, end systolic volume index immediately after exercise; EF_{pre}, ejection fraction immediately after exercise; ΔEF_{pre}, change in ejection fraction with exercise; LV {dp/dt}, peak rate of change in left ventricular pressure; ESWS_{rest}, end systolic wall stress at rest; ESVI_{rest}, end systolic volume index at rest; EF_{rest}, ejection fraction at rest. From Leung et al. [23].
assessment of right ventricular function post-exercise has shown utility in prognostication in patients with chronic MR, and suggests a potential role for such an assessment in the selection of patients for operation, irrespective of symptom status. This type of recommendation, however, will require further testing.

The onset of resting pulmonary hypertension (> 50 mm Hg) secondary to severe mitral regurgitation is considered an indication for surgery, for, if left untreated, it is associated with a greater severity of mitral regurgitation and higher operative morbidity and mortality [25]. Furthermore, pulmonary hypertension increases the likelihood of significant tricuspid regurgitation and right ventricular dysfunction. Increased systolic pulmonary artery pressure (estimated from the tricuspid regurgitant jet velocity) during exercise has been used in an uncontrolled setting to identify occult left ventricular dysfunction and need for mitral surgery [26]. The degree of mitral regurgitation is one of the major factors contributing to pulmonary hypertension, and is associated with higher morbidity and mortality in patients with LV dysfunction [27, 28]. However, even in the presence of normal resting pulmonary pressures, measured systolic pulmonary artery pressures of > 60 mmHg post-exercise is an indication for mitral valve intervention [8]. Exercise echocardiography, therefore, can play an important role even in the presence of normal resting pulmonary pressures.

Although exercise capacity is an important parameter of quality of life and provides prognostic information, cardiac determinants affecting it have not been clearly defined in patients with chronic MR. It is well known that LV diastolic function is an important determinant of exercise capacity in normal individuals and in patients with various cardiac disease [29, 30]. To address the contribution of LV diastolic function to exercise capacity, the group of Kim et al. studied 32 patients with severe MR and normal LV ejection fraction. They observed that the early diastolic mitral annulus velocity (E') and pulmonary vein A-wave peak velocity (PVa), both accepted surrogate estimates of LV diastolic function, showed a significant correlation with maximal exercise time [31]. This study also corroborated earlier findings that LV ejection fraction and fractional shortening were poor predictors of exercise capacity [32, 33]. From these results, the authors concluded that LV systolic parameters were not significant determinants of exercise capacity in patients with chronic MR and a preserved EF. Rather, the measurement of E' and PVa was more useful in identifying patients with chronic MR and poor exercise capacity.

In chronic, severe mitral regurgitation, once patients develop symptoms or LV dysfunction, the decision to intervene becomes straightforward. However, decision-making is more challenging in patients with vague, atypical symptoms. It is important to accurately, and in a timely fashion, identify symptoms related to chronic MR as well as occult LV dysfunction. The combination of stress testing with echocardiography can detect and quantify occult symptoms as well as worsening mitral regurgitation. Stress echocardiography, therefore, provides a comprehensive and cost-effective evaluation of patients with primary mitral regurgitation that combines functional, diagnostic, and prognostic information.

**ISCHEMIC MITRAL REGURGITATION**

Ischemic mitral regurgitation (IMR) results from restricted leaflet closure secondary to tethering of the mitral leaflets as a consequence of an infarcted, thinned ventricle. IMR is characteristically dynamic and sensitive to changes in ventricular size, shape, and loading that restrict closure of the mitral leaflet [34, 35]. In ischemic left ventricular dysfunction, the mitral annulus may dilate and the inferoposterior wall bulges outward, displacing the attached papillary muscles apically and outward [36]. The leaflets, tethered at
both ends, cannot close effectively and are restrained within the left ventricle with resultant regurgitation (Fig. 3). Further studies have corroborated that the degree of ischemic MR at rest in patients with systolic dysfunction is determined by local (apical and posterior displacement of papillary muscles) and not global LV remodeling [37, 38].

IMR is a dynamic phenomenon, its severity varying depending on loading conditions [36, 39]. Often patients might complain of dyspnea on exertion, out of proportion to the amount LV dysfunction or MR at rest. Patients with exercise-induced increases in IMR severity incur limited stroke volume adaptation during exercise and this contributes, in part, to the limitation in exercise capacity [40]. Exercise-induced changes in regurgitant volume and in systolic pulmonary pressure are larger in patients who stop their exercise because of dyspnea as compared with those who stop for fatigue [41]. Exercise echocardiography can be extremely useful in qualifying and quantifying a change in the amount of mitral regurgitation seen during exercise; information that cannot be obtained by resting echocardiography.

Pierard and Lancellotti showed that patients with known ischemic LV dysfunction who present with acute pulmonary edema not due to myocardial ischemia demonstrate large exercise-induced increases in mitral regurgitation and related pulmonary pressures [42]. Exercise testing coupled with quantitative Doppler echocardiography could be useful for patients with left ventricular systolic dysfunction in whom acute pulmonary edema develops without an obvious cause. A mild degree of mitral regurgitation at baseline can be associated with large dynamic changes, explaining the clinical spectrum from exertional dyspnea to the occurrence of acute pulmonary edema.

IMR has also been shown to worsen with worsening LV function during exercise [43]. Annular enlargement [44], persistent leaflet tethering [38], LV dilation, sphericization [45], and dysfunction have all been proposed as determinants of ischemic MR. However, in a study of 70 patients in the chronic post-MI phase, with LV ejection fraction < 45% and at least mild MR undergoing semi-supine exercise Doppler echocardiography, ERO at rest did not predict changes in the ERO during exercise [46]. As well, the degree of exercise-induced increase or decrease in MR appeared to relate to local LV remodeling and mitral valvular deformation but not to changes in global LV function, as mentioned previously. Similarly, in a more recent study, changes in ERO were unrelated to the severity of ischemic MR at rest, as well as to the severity of LV dysfunction [47]. Exercise-induced changes in MR were related to changes in wall motion score index, as well as to changes in end-systolic sphericity index. The strongest predictors of exercise-induced changes in ischemic MR in patients with LV dysfunction due to prior MI were exercise-induced changes in mitral deformation (Table 2).

During exercise, the magnitude of changes in IMR is widely different from one patient to another and does not correlate with the degree of MR at rest. Most patients exhibit small increases in the amount of IMR, whereas others have either a large rise or a significant decrease in ERO [46]. The demonstration of an exercise-induced reduction in IMR as a result of recruitable function in the basal part of the inferior wall can be used to predict the reduction in IMR post-revascularization of the coronary artery serving that specific territory [47]. Otherwise, in the case of increased IMR with exercise, perhaps a combination of revascularization and mitral valvular surgery may be necessary.

Ischemic mitral regurgitation may exhibit a broad range of severity and conveys a dismal prognosis [48-50]. The increased mortality risk relates not only to the presence, but also more importantly to the quantified degree of IMR [41, 51]. In patients with ischemic MR and left ventricular dysfunction, quantitative assessment of exercise-induced changes in the degree of MR provides independent prognostic information. Significant exercise-induced increases in MR unmask patients at high risk for morbidity and mortality [51-53]. Predictors of cardiac death included an increase in ERO by ≥ 13 mm² during exercise, an ERO > 20mm² at rest [51], greater LV volumes at rest and lack of contractile reserve during exercise [52].

The use of exercise echocardiography is becoming a more valuable tool in the evaluation of ischemic MR. It can be used to quantify, and determine the reason for limitations in, exercise capacity. As well, it’s utility in testing the dynamic component of IMR in patients with chronic ischemic LV dysfunction presenting with unexplained dyspnea or acute pulmonary edema cannot be ignored. Exercise echocardiography has been shown to be useful in the evaluation and risk stratification of patients with IMR.

**MITRAL REGURGITATION AND CARDIAC DYSSYNCHRONY**

Mitral regurgitation is seen in over half of all patients with symptomatic heart failure and is an independent predictor of mortality [54]. Non-ischemic functional mitral regurgitation (FMR) in dilated cardiomyopathy occurs in the setting of incomplete closure of a structurally normal mitral valve and progressive ventricular remodeling associated with left ventricular dysfunction and dilation. Many patients with chronic LV dysfunction develop limiting symptoms only with activity. However, unfortunately many of our objective assessments of their pathology occur at rest. Exercise capacity in heart failure patients depends on the efficiency of

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**Table 2. Predictors of Exercise-Induced Changes in Mitral Regurgitation**

|                        | Rest     | Exercise | p-value | Δ Value    | p-value |
|------------------------|----------|----------|---------|------------|---------|
| Mitral annular dimension (cm) | 3.7 ± 0.2 | 3.8 ± 0.3 | 0.014   | 0.13 ± 0.32 | 0.0001  |
| Coaptation distance (cm)       | 1.5 ± 0.1 | 1.9 ± 0.6 | 0.0001  | 0.41 ± 0.55 | 0.0001  |
| Tenting area (cm²)             | 3.5 ± 0.3 | 4.4 ± 0.9 | 0.0001  | 0.87 ± 1.34 | 0.0001  |

Adapted from Giga et al. [47].
delivery of oxygen to the exercising muscles. Thus in addition to cardiac output, peripheral factors such as skeletal muscle function, endothelial cell function and autonomic nervous system function play an essential role in exercise tolerance. Multiple studies have demonstrated an increase in functional MR with exercise in patients throughout the range of heart failure severity associated with a decrease in stroke volume [40, 55]. However, the worsening of FMR did not induce a deterioration of the anaerobic thresholds which is determined by peripheral factors [55].

Cardiac resynchronization therapy (CRT) improves exercise tolerance in addition to providing symptomatic and mortality benefits in patients with severe heart failure refractory to medical therapy [56-58]. The potential mechanisms for CRT success are related mainly to optimized LV filling [59], synchronized LV electromechanical coupling resulting in an improvement in LV myocardial performance [59], and a reduction of mitral regurgitation [60, 61] (Fig. 4). The cardiac structural changes associated with CRT include not only volumetric improvement but also true reverse LV structural remodeling, evidenced by progressive reduction in LV mass and restoration of regional wall symmetry [62], improved left ventricular function [59] and improved cardiac synchrony. Multiple studies have shown CRT improves resting MR in the acute and chronic settings with a corresponding worsening in the degree of MR upon interruption of therapy [63-67].

There are varying results describing the effect of CRT on exercise-induced MR prior to the occurrence of LV remodeling. Ennezat et al. showed that CRT attenuated the increase in mitral ERO and regurgitant volume during exercise among 21 patients undergoing symptom-limited exercise stress testing; a phenomenon attributed to an increase in LV contractility (Fig. 5) [64]. Conversely, Madaric et al. did not show an improvement in exercise-induced MR within the 1st week of implantation. However, the attenuation of exercise-induced MR did occur in parallel with LV remodeling at 3 months post-implantation [66]. The varying results may be explained by the response to resynchronization of the two left ventricular papillary muscles [67, 68].

LV asynchronism, as measured by Doppler tissue imaging at rest, substantially contributes to worsening of MR during dynamic exercise in patients with CHF due to LV systolic dysfunction (Fig. 6) [69] Ypenburg et al. studied 25 patients who showed an immediate improvement in MR after CRT was accompanied by an improvement in mitral deformation indices (tenting area, coaptation height and annular contraction) and synchrony between the two LV papillary muscles. Acute loss of resynchronization after interruption of CRT lead to acute recurrence of MR and worsening in mitral deformation indices [67].

D’Andrea et al. described a series of 60 patients with idiopathic dilated cardiomyopathy and QRS interval < 120 ms who were submitted to supine bicycle exercise Doppler echocardiography and cardiopulmonary exercise testing [70]. Dynamic LV dyssynchrony unmasked by exercise was found in more than 50% of the patients. Increased LV dyssynchrony during exercise was independently associated with increased functional MR, reduced exercise capacity, and
lower LV stroke volume at peak exercise. This study illustrates the concept of dynamic dyssynchrony, a notion that needs further investigation to clarify its mechanisms and clinical implications.

There is a close correlation between exercise-induced changes in LV dyssynchrony and functional MR. Acute changes in MR have been observed with the induction and interruption of CRT. Initiation of CRT acutely reduces MR severity at rest and its dynamic component during exercise well before the occurrence of significant LV inverse remodeling [65, 71]. In addition, the interruption of biventricular pacing is associated with an acute increase in MR [63]. Certain clinical implications of dynamic MR have already been reported [42]. The demonstration of worsening dyssynchrony, and consequent increased MR, with exercise deserves further study and may change the criteria for selecting patients for CRT [72].

**SUMMARY**

In summary, exercise echocardiography provides useful data in patients with mitral regurgitation. Information that can be acquired with this modality include:

- An assessment of functional capacity;
- A quantification of change in MR severity during exercise;
- An assessment of contractile reserve of the left ventricle;

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**Fig. (5).** Colour flow (top) and continuous wave (bottom) Doppler echocardiographic recordings in a representative patient at maximal exercise with (Panel A) and without (Panel B) cardiac resynchronisation therapy (CRT). Left ventricular (LV) dP/dt and maximum mitral regurgitation velocity (MR Vmax) were reduced without CRT. ERO, effective regurgitant orifice area; RV, regurgitant flow volume. From Ennezat PV, Gal B, Kouakam C, *et al.* Cardiac resynchronisation therapy reduces functional mitral regurgitation during dynamic exercise in patients with chronic heart failure: an acute echocardiographic study. Heart (British Cardiac Society) 2006; 92(8): 1091-1095.

B. Without CRT.  
ERO 35 mm²; RV 34 ml;  
LV +dP/dt 356 mmHg/s; MR Vmax 470 cm/s

B. Without CRT.  
ERO 35 mm²; RV 34 ml;  
LV +dP/dt 356 mmHg/s; MR Vmax 470 cm/s
Fig. (6). Relationships between intra-LV asynchrony and exercise-induced changes in mitral ERO (left panel) and regurgitant volume (RV) (right panel). From Ennezat PV, Marechaux S, Le Tourneau T, et al. Myocardial asynchronism is a determinant of changes in functional mitral regurgitation severity during dynamic exercise in patients with chronic heart failure due to severe left ventricular systolic dysfunction. Eur Heart J 2006; 27(6): 679-683.

- An evaluation of the response of the right ventricle, especially with worsening MR during exercise;
- Obtaining prognostic information.

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