My Approach to the Echocardiographic Evaluation of Mitral Valve Regurgitation

Como Eu Faço Avaliação Ecocardiográfica na Regurgitação Valvar Mitral

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Diagnosis; Echocardiography; Mitral Valve Insufficiency.

Introduction

Chronic mitral valve regurgitation is a very common disease that must be differentiated into primary (structural mitral valve disease) and secondary (left ventricular [LV] disease) types to ensure appropriate management and treatment. Echocardiography is an essential exam in the etiological diagnosis to quantify a valve lesion and its repercussion as well as being decisive for defining the best surgical timing. Intraoperative echocardiography, such as MitraClip® placement, is a Class I indication in mitral valve repair and interventional treatment.

Untreated mitral regurgitation (MR) is associated with worse outcomes due to the adverse consequences of volume overload on the cardiac chambers, whereas early intervention has shown excellent results for primary MR. However, what is the mechanism of MR?

This answer and its quantification decisively influence the choice of mitral valve intervention.

My approach to mitral valve evaluation

The first step of mitral valve evaluations is to determine the presence of any structural mitral valve changes. In Brazil, the most common cause of primary MR cases is rheumatic disease, followed by mitral valve prolapse. Mitral annulus calcification is a common cause in older patients, while radiation can occasionally affect the mitral valve in patients undergoing radiotherapy.

When rheumatic involvement of the mitral valve is identified (the so-called dome opening), it is important to determine the presence or absence of associated mitral stenosis or other valve lesions. In cases of mitral valve prolapse, fibroelastic disease (with thin cusps and generally localized prolapse) must be differentiated from Barlow’s disease, in which the cusps are redundant and well thickened and the prolapse is diffuse. Prolapse syndrome is present in the latter case, and some studies have shown a correlation with sudden death from cardiac arrhythmia.

The association between mitral valve prolapse, aortic ectasia and Marfan syndrome should be investigated. Senile calcification presents a clear scenario, with mitral annulus calcification and the possibility of associated mitral stenosis. In such cases, lesions are rarely severe. Mitral valve thickening induced by radiation is associated with a history of neoplasia and chest radiotherapy.

These pathologies define most primary MR cases. Cases without structural mitral annular changes but with LV dilatation and dysfunction, as occurs in dilated cardiomyopathy with annular dilatation and secondary mitral reflux, or contractile changes in the inferior or inferolateral wall due to myocardial infarction with impaired posterior mitral cusp coaptation, are defined as secondary MR, with the valve problem being a consequence rather than the cause.

After discerning of the valve lesion mechanism, it is important to quantify the mitral damage and its hemodynamic repercussions. MR can be quantified by qualitative (Color Doppler evaluation of the regurgitant jet), semi-quantitative (vena contracta [VC] evaluation), and quantitative (evaluation of the effective regurgitant orifice [ERO], regurgitant volume [RV], and regurgitant fraction [RF]) analyses. These parameters can be analyzed using the proximal isovelocity surface area method or flow analysis.

Quantitative parameters currently have the greatest diagnostic value, in the mitral valve regurgitation important (Table 1).
Two-dimensional echocardiography and Doppler are able to quantify the MR degree and evaluate these parameters, but three-dimensional echocardiography more accurately evaluates ERO and VC. Yosefy et al. used real-time three-dimensional echocardiography to show that, in most cases, the region of proximal convergence of the regurgitant flow (proximal isovelocity surface area method) is hemielliptic, not hemispheric, and more accurate for this quantification.6

Two-dimensional transesophageal echocardiography, and particularly three-dimensional echocardiography, provides more accurate anatomical detailing of the mitral valve and an etiological definition when necessary, but the quantification of the degree of valve regurgitation using this information remains inaccurate.

Once mitral valve regurgitation is defined as important, the results depend on the presence of symptoms and the presence or absence of LV dysfunction, with the need for surgery being well defined. Non-surgical patients in New York Heart Association functional classes I and II present a mortality rate of about 4.1% per year compared to those in functional classes III and IV, whose mortality rate is 34% per year. However, the results are not so promising if the ejection fraction (EF) is lower than 60% or the LV systolic diameter (LVSD) is greater than 40 mm, as these parameters are predictors of LV dysfunction in the postoperative period and worse prognosis.7 Ideally, patients should undergo surgery before the onset of such a condition, and the use of echocardiography is fundamental for their monitoring.

The next step after defining MR as primary or secondary and quantifying it is to consider the disease stages.8

### Stages of primary MR

**MR risk**

Primary MR involves discreet mitral prolapse with normal coaptation, the absence of MR or mild central MR, and a VC < 0.3 cm.

**Progressive MR with evident prolapse but normal cusp coaptation**

This stage involves a central MR jet occupying 20–40% of the left atrium in which the VC is < 0.7 cm, RV is < 60 mL, RF is < 50%, and ERO is < 0.40 cm². No increased LV or pulmonary arterial hypertension are noted.

**Asymptomatic with severe MR**

This stage involves prolapse with a loss of cusp coaptation or flail; MR with a central jet occupying > 40% of the left atrium or eccentric holosystolic jet; and a VC ≥ 0.7 cm, RV ≥ 60 mL, RF ≥ 50%, and ERO ≥ 0.40 cm². It also features enlarged left chambers and pulmonary arterial hypertension at rest or on exertion. Stage C1 is defined as LVEF > 60% and LVSD < 40 mm, while stage C2 is defined as LVEF ≤ 60% and LVSD ≥ 40 mm.

**Symptomatic severe MR**

Secondary MR involves normal cords, cusps, and mitral annulus in a patient with coronary artery disease or dilated cardiomyopathy. No mitral or mild central MR is seen, while the VC is < 0.3 cm. The LV is normal or with infarction or dilatation due to primary myocardial disease. Symptoms of ischemia or heart failure may be present.

**Progressive MR with parietal abnormality and LV dysfunction**

This stage involves possible annular dilatation and loss of coaptation. The RV is < 60 mL, while the RF is < 50%. No increased LV or pulmonary arterial hypertension is noted. Symptoms of ischemia or heart failure may be present.

**Asymptomatic severe MR**

This stage involves a parietal abnormality and/or LV dilatation as well as annular dilatation and cusp coaptation failure. The RV is ≥ 60 mL, RF ≥ 50%, and ERO ≥ 0.40 cm², with an ERO ≥ 0.2 cm² being more sensitive. Contractile changes with LV dysfunction or cardiomyopathy-induced dysfunction are evident, and symptoms of ischemia or heart failure may be present.

**Symptomatic severe MR**

This stage involves a parietal abnormality and/or LV dilatation. It also features annular dilatation with an RV ≥ 60 mL, RF ≥ 50%, and ERO ≥ 0.40 cm² as well as contractile changes in LV dysfunction or cardiomyopathy-induced dysfunction. Symptoms of ischemia or heart failure may be present in addition to dyspnea on exertion with reduced exercise tolerance.

In cases of significant MR, it is important to mention the basic Carpentier’s classification used to choose the surgical mitral approach (Table 2 and Figure 1).

### Stages of secondary MR

**MR risk**

Secondary MR involves normal cords, cusps, and mitral annulus in a patient with coronary artery disease or dilated cardiomyopathy. No mitral or mild central MR is seen, while the VC is < 0.3 cm. The LV is normal or with infarction or dilatation due to primary myocardial disease. Symptoms of ischemia or heart failure may be present.

**Progressive MR with parietal abnormality and LV dysfunction**

This stage involves possible annular dilatation and loss of coaptation. The RV is < 60 mL, while the RF is < 50%. No increased LV or pulmonary arterial hypertension is noted. Symptoms of ischemia or heart failure may be present.

**Asymptomatic severe MR**

This stage involves a parietal abnormality and/or LV dilatation as well as annular dilatation and cusp coaptation failure. The RV is ≥ 60 mL, RF ≥ 50%, and ERO ≥ 0.40 cm², with an ERO ≥ 0.2 cm² being more sensitive. Contractile changes with LV dysfunction or cardiomyopathy-induced dysfunction are evident, and symptoms of ischemia or heart failure may be present.
structural changes but with annular dilatation that causes cusp coaptation failure with consequent valve reflux. This is caused by involvement of the LV due to chamber dilatation and/or dysfunction induced by dilated cardiomyopathy (secondary MR).

Type II classification refers to cord prolapse, elongation, or rupture with annular prolapse as the main finding. In this situation, fibroelastic disease must be differentiated from Barlow’s disease, for which echocardiography is very useful. In the first entity, the degree of degeneration is mild and the prolapse is generally more localized (in the P2 and/or A2 segments) without calcification points and with mild to moderate annular dilatation. In this situation, surgical intervention is highly successful. In Barlow’s disease, the annular degeneration is more severe and affects more segments. (When the prolapse involves more than three segments with extension to the posterior commissure, annulus calcification and moderate annular dilatation, valve repair is possible but not simple; when the prolapse involves more than three valve segments and extends to the anterior commissure with significant calcification (annulus and cusps) and large annular dilatation, valve repair is unlikely due to technical difficulty).\textsuperscript{10}

The use of intraoperative transesophageal echocardiography is essential during mitral valve repair surgery, and some criteria must be observed to evaluate its success. The distance from the P2 stump must be up to 20 mm, the coaptation A2–P2 zone must be smaller than 10 mm, the postero-lateral angle must be lower than 45°, and the LA/LV gradient must not indicate LV inflow tract stenosis. The LV outflow tract gradient should be analyzed since it should present a small cavity, septal hypertrophy (>15 mm), smaller mitral-aortic angulation (<120°), narrow mitral annulus, shorter distance from the septum to the anterior mitral cusp (<25 mm), and a distance from the P2 stump > 20 mm, as these factors increase the propensity of mitral valve anterior systolic motion (Figure 2).\textsuperscript{11}

The diameter of the tricuspid annulus should be analyzed before mitral repair since a tricuspid annulus ≥ 40 mm or ≥ 21 mm/m² is an indication for tricuspid surgery regardless of the degree of regurgitation through this valve.\textsuperscript{5,12}

Carpentier’s type III classification refers to restricted cusp motion, which can be seen in rheumatic (primary) and ischemic (secondary) disease cases. In these cases, restricted cusp motion is recognized either by commissure fusing, as in rheumatic disease, or by the lack of ventricular wall support, as in ischemic disease, leading to valve coaptation failure.\textsuperscript{9} In both situations, surgical repair is unfavorable, even when performed by an experienced surgeon.\textsuperscript{13}

There have been great advances in mitral valve repair in cases of primary valve regurgitation since valve repair is associated with low operative mortality, good survival, increased quality of life, and low bleeding rates compared to valve replacement. Surgical repair has excellent success rates in patients with preserved ventricular function. These findings have encouraged early surgery in asymptomatic patients with severe MR, even those with an EF > 60% or LVSD < 40 mm, as long as the valve repair probability is >95% with low operative risk (<1%) as defined in the 2017 update on valve disease of the American Heart Association/American College of Cardiology (AHA/ACC).\textsuperscript{12}

Tables 3 and 4 show the AHA/ACC recommendations,\textsuperscript{12} highlighting any differences versus the 2014 guideline,\textsuperscript{5} and Figure 3 shows a conduct guideline for chronic mitral valve regurgitation.

Complementary evaluation of chronic MR

Stress echocardiography

Stress echocardiography findings predict latent ventricular dysfunction before surgical intervention in patients with mitral valve prolapse using the mean global longitudinal strain (GLS). Patients with a mild GLS change (<2%) have no contractile reserve.\textsuperscript{15}
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Figure 2 – Schematic model of the mid-esophageal five-chamber cross-section considering the points that should be analyzed for predisposing dynamic LVOT gradient.

Table 3 – Recommendations for chronic primary mitral regurgitation intervention.

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recomendações</th>
<th>Comentários</th>
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<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve surgery is recommended for asymptomatic patients with chronic severe MR (stage D) and an LVEF &gt; 30%</td>
<td>The 2014 recommendation currently remains</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and left ventricular dysfunction (LVEF ≤ 60% and/or LVSD ≥ 40 mm, stage C2)</td>
<td>The 2014 recommendation currently remains</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve repair is more commonly recommended than valve replacement when the surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior cusp</td>
<td>The 2014 recommendation currently remains</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve repair is more commonly recommended than valve replacement when the surgical treatment is indicated for patients with chronic severe primary MR involving the anterior cusp when a successful and durable repair can be performed</td>
<td>The 2014 recommendation currently remains</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Concomitant mitral valve repair (or replacement) is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other reasons</td>
<td>A recomendação de 2014 permanece atualmente</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
<td>Mitral valve surgery is acceptable for asymptomatic patients with chronic severe primary mitral regurgitation (stage C1) and preserved left ventricular function (LVEF &gt; 60% and LVSD &lt; 40 mm) when the likelihood of repair success and durability without residual MR exceeds 95% with an expected mortality rate of less than 1% when performed in a referral hospital (center)</td>
<td>The 2014 recommendation currently remains</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
<td>Mitral valve surgery is acceptable for asymptomatic patients with chronic severe primary mitral regurgitation (stage C1) and preserved left ventricular function (LVEF &gt; 60% and LVSD &lt; 40 mm) with progressively increased left ventricular size or consistent EF decreases in imaging studies</td>
<td>New: Severe MR patients with an EF ≤ 60% or LVSD ≥ 40 mm have already developed left ventricular systolic dysfunction; thus, operating them before reaching these parameters was considered rational in several studies, particularly when the left ventricular size is progressively increasing or EF is decreasing</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve repair is acceptable for asymptomatic patients with chronic non-rheumatic severe primary MR (stage C1) and preserved LV function (LVEF &gt; 60% and LVSD &lt; 40 mm) with a high probability of successful and durable repair, especially in cases of new-onset atrial fibrillation or pulmonary hypertension at rest (systolic pulmonary artery pressure &gt; 50 mmHg)</td>
<td>The 2014 recommendation currently remains</td>
</tr>
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MR progressively leads to severe MR (“mitral regurgitation generates mitral regurgitation”). The concept is that the initial MR level causes LV dilatation, which increases stress in the mitral tract, causing additional valve damage, more severe MR, and additional LV dilatation, thus starting a perpetual cycle of LV volume increases and MR progression. This volume causes LV overfill and leads to irreversible LV dysfunction, worsening the prognosis. Patients with severe MR and an EF ≤ 60% or LVSD ≥ 40 mm already present with LV systolic dysfunction. A study suggested that to normalize LV function and size after mitral repair, LVEF should be >64% and LVSD < 37 mm. It is reasonable to consider intervention when longitudinal follow-up shows a progressively decreased EF near 60% or a progressive LVSD increase near 40 mm. Nevertheless, asymptomatic patients with stable dimensions and excellent exercise capacity can be safely observed.

Mitral valve surgery is reasonable for patients with severe secondary MR. The MitraClip® device is placed using the tip-to-tip technique in the presence of a catheter. This new method has been studied and approved for clinical use. It simulates the surgical repair technique by Alfieri. The MitraClip® strategy can significantly improve symptoms in patients with severe symptomatic primary MR and a higher surgical risk. This strategy must be safe and present no difference in long-term mortality.

The MitraClip® intervention depends on prolapse type, with the prolapse involving the P2–A2 segments being the most appropriate for this intervention. This device can be used to treat severe symptoms caused by primary MR, although it does not promote better results than surgery. The MitraClip® is approved for patients with primary MR, severe symptoms, and a high surgical risk. Other catheter-based methods used to treat MR include percutaneous valve replacement and ring placement.

Referral for surgical intervention

MitraClip® The MitraClip® device is placed using the tip-to-tip technique in the presence of a catheter. This new method has been studied and approved for clinical use. It simulates the surgical repair technique by Alfieri. The EVEREST study reported that the original MitraClip® strategy can significantly improve symptoms in patients with severe symptomatic primary MR and a higher surgical risk. This strategy must be safe and present no difference in long-term mortality.

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Figure 3 – Practical conduct guide for chronic mitral valve regurgitation.

<table>
<thead>
<tr>
<th>Severe MR</th>
<th>Secondary MR</th>
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<tbody>
<tr>
<td>Vena contracta ≥ 0.7 cm</td>
<td>CAD</td>
</tr>
<tr>
<td>R vol. &gt; 60 Ml</td>
<td>HF</td>
</tr>
<tr>
<td>RF ≥ 50%</td>
<td>Consider CRT</td>
</tr>
<tr>
<td>ERO ≥ 0.4 cm²</td>
<td></td>
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<table>
<thead>
<tr>
<th>Primary MR</th>
<th>Secondary MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive MR</td>
<td>CAD</td>
</tr>
<tr>
<td>(stage B)</td>
<td>HF</td>
</tr>
<tr>
<td>Vena contracta &lt; 0.7 cm</td>
<td>Consider CRT</td>
</tr>
<tr>
<td>R vol. &lt; 60 Ml</td>
<td></td>
</tr>
<tr>
<td>RF &lt; 50%</td>
<td></td>
</tr>
<tr>
<td>ERO &lt; 0.4 cm²</td>
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<table>
<thead>
<tr>
<th>Symptomatic (stage D)</th>
<th>Asymptomatic (stage C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF &gt; 30%</td>
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<table>
<thead>
<tr>
<th>LVEF 30% to ≤ 60%</th>
<th>AF or PSAP &gt; 50mm Hg</th>
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</thead>
<tbody>
<tr>
<td>LVSD ≥ 40 mm (stage C2)</td>
<td>(stage C1)</td>
</tr>
<tr>
<td>LVEF &gt; 60%</td>
<td>Persistent NYHA class III-IV symptoms</td>
</tr>
<tr>
<td>LVSD &lt; 40 mm (stage C1)</td>
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<table>
<thead>
<tr>
<th>AF or PSAP &gt; 50mm Hg (stage C1)</th>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>Progressive LVSD increase or decreased EF</th>
<th>Likelihood of a successful repair &gt;95% and mortality &lt;1%</th>
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<tbody>
<tr>
<td>Yes</td>
<td></td>
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<tr>
<td>No</td>
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<table>
<thead>
<tr>
<th>Severe asymptomatic MR (stage C)</th>
<th>Progressive MR (stage B)</th>
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<tr>
<td>Persistent NYHA class III-IV symptoms</td>
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<table>
<thead>
<tr>
<th>MV surgery (IIb)</th>
<th>MV surgery (I)</th>
<th>MV surgery (IIa)</th>
<th>MV repair (IIa)</th>
<th>Periodic follow-up</th>
<th>MV surgery (IIb)</th>
<th>Periodic follow-up</th>
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<tr>
<td>No</td>
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**R vol.**: regurgitant volume; **RF**: regurgitant fraction; **EF**: ejection fraction; **AF**: atrial fibrillation; **ERO**: effective regurgitant orifice; **LV**: left ventricle; **LVEF**: left ventricular ejection fraction; **MV**: mitral valve; **CRT**: cardiac resynchronization therapy; **LVSD**: left ventricular systolic diameter; **PSAP**: pulmonary artery systolic pressure; **CAD**: coronary artery disease; **HF**: heart failure.

Percutaneous annuloplasty

The percutaneous annuloplasty aims to correct functional MR (secondary to LV dilatation) through catheterization. Percutaneous mitral valve repair is most commonly used for posterior cusp prolapse. Annuloplasty is performed indirectly or directly. In the indirect technique, the internal jugular vein is pulsed and the catheter is inserted into the coronary sinus. This involves approximately two-thirds of the mitral valve annulus' circumference. The prosthetic ring tightens the mitral valve annulus in the coronary sinus, reducing its diameter and consequently reducing the degree of mitral valve regurgitation. The problem with this method is that it can compress the circumflex artery. Therefore, it is important to perform left catheterization alter device placement to evaluate arterial patency.

An arterial puncture is performed in direct annuloplasty, and the catheter is retrogradely inserted into the LV with a series of anchors placed around the mitral valve annulus. These anchors are fixed and place tension on the mitral valve annulus, reducing its diameter. The advantage of this method is that it does not compress the coronary artery.

Transcatheter mitral valve procedure

The transcatheter mitral valve procedure is still in its initial phase. Although the MitraClip® is already a transcatheter surgery option approved by the United States Food and Drug Administration, catheter implantation is used to place surgical bioprostheses. The purpose of this approach is to place the heart valve in the mitral valve position using a catheter. It is already a transcatheter replacement in patients with severe ischemic MR. According to the authors, mitral valve repair was associated with an unacceptable recurrence rate, with moderate or severe MR within 2 years (58.8% vs 3.8%), a decreased quality of life, and heart failure–related hospitalizations.

Another randomized study supported the use of mitral valve replacement in patients with severe ischemic MR. According to the authors, mitral valve repair was associated with an unacceptable recurrence rate, with moderate or severe MR within 2 years (58.8% vs 3.8%), a decreased quality of life, and heart failure–related hospitalizations.

Secondary MR considerations

Both forms of secondary MR result from enlarged ventricles and lateral displacement of the papillary muscles or a parietal abnormality that impairs posterior mitral cusp coaptation.

If the myocardium is viable, myocardial revascularization or percutaneous coronary intervention should be considered for patients with severe secondary MR and secondary LV systolic dysfunction induced by ischemia. Although the effect on ischemic MR varies, revascularization in patients with a low EF can improve their long-term prognosis. Mitral valve repair in ischemic MR during myocardial revascularization is controversial, with possible beneficial results but a higher rate of complications. One study showed that, in a period of 2 years, 68% of patients undergoing mitral valve repair experienced reduced MR severity only if treated with myocardial revascularization.

Another randomized study supported the use of mitral valve replacement in patients with severe ischemic MR. According to the authors, mitral valve repair was associated with an unacceptable recurrence rate, with moderate or severe MR within 2 years (58.8% vs 3.8%), a decreased quality of life, and heart failure–related hospitalizations.

It remains unclear whether the treatment of secondary MR will benefit these patients, but the COAPT study demonstrated that the use of a MitraClip® associated with drug therapy was superior at a 2-year interval with significantly reduced hospitalization and mortality rates compared to drug therapy alone.

Conclusion

Primary and secondary MR are two completely different diseases whose natural history, lesion mechanism, treatment strategy, and response to treatment differ. The origin of secondary MR should also be divided into ischemic or non-ischemic, as there are important approach differences between them. These MR phenotypes can be defined using echocardiography, which, in addition to guiding patient selection and conduct, is essential for the diagnosis and choice of therapeutic approaches.

Authors’ contributions

Research conception and design: Camarozano AC; data collection: Camarozano AC; data analysis and interpretation: Camarozano AC; manuscript writing: Camarozano AC, Camarozano LM; critical review of the manuscript for important intellectual content: Camarozano AC; table preparation: Camarozano LM.

Conflict of interest

The authors have declared that they have no conflict of interest.

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