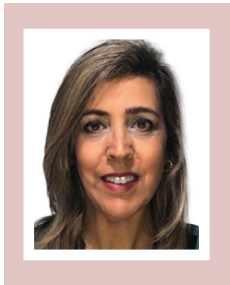


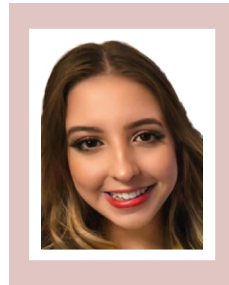
My Approach to the Echocardiographic Evaluation of Mitral Valve Regurgitation

Como Eu Faço Avaliação Ecocardiográfica na Regurgitação Valvar Mitral

¹Federal University of Paraná, Curitiba, PR, Brazil. Pontifícia University Católica (PUC),² Curitiba, PR, Brazil.



Ana Cristina Camarozano¹



Luisa Maria Camarozano²

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.¹

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.

Keywords

Diagnosis; Echocardiography; Mitral Valve Insufficiency.

Mailing Address: Ana Cristina Camarozano •

E-mail: a.camarozano@yahoo.com.br

Manuscript received 4/6/2020; revised 5/10/2020; accepted 1/27/2021

DOI: 10.47593/2675-312X/20213402ecom12

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.²

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.³

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.⁵ 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).

Table 1 – Reference values for important mitral valve regurgitation⁵

Parameter	Value
Central regurgitant jet or eccentric jet	Occupies > 40% of the LA Holosystolic
Vena contracta	≥ 0,7 cm
Regurgitant volume	> 60 mL
Regurgitant fraction	> 50%
ERO	≥ 0.40cm ²

AE: átrio esquerdo; ERO: orifício regurgitante.

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

This stage involves important prolapse and cusp coaptation failure or flail; a central jet > 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, pulmonary arterial hypertension, dyspnea on exertion, and reduced exercise tolerance.

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.

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).

Type I classification refers to a mitral annulus without

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).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 posterolateral 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).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.^{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.⁹ In both situations, surgical repair is unfavorable, even when performed by an experienced surgeon.

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).¹²

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

Tabela 2 – Classificação de Carpentier sobre o movimento das cúspides mitrais para planejamento e abordagem cirúrgica.⁹

Type	Motion
I	Normal cusp motion (e.g., mitral annular dilatation)
II	Excessive cusp motion (e.g., mitral cord prolapse and rupture or elongation)
III	Restricted cusp motion (e.g., commissural fusion and myocardial infarction)

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.¹³

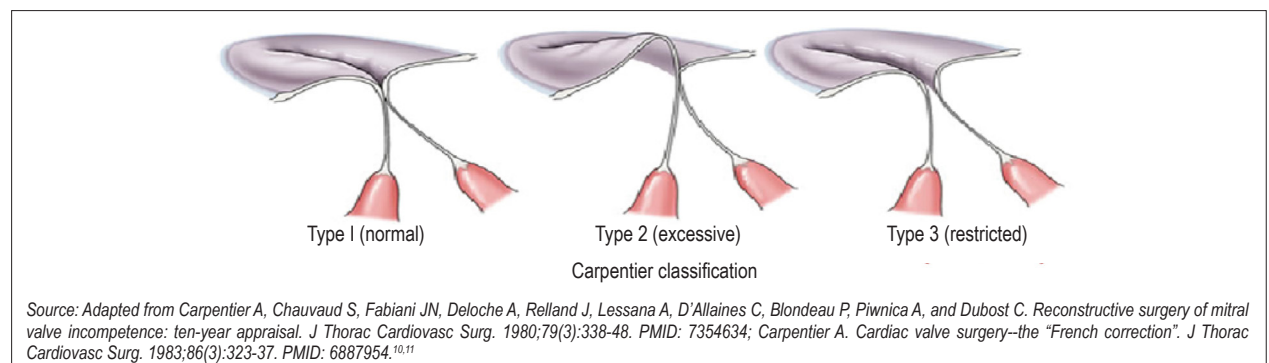
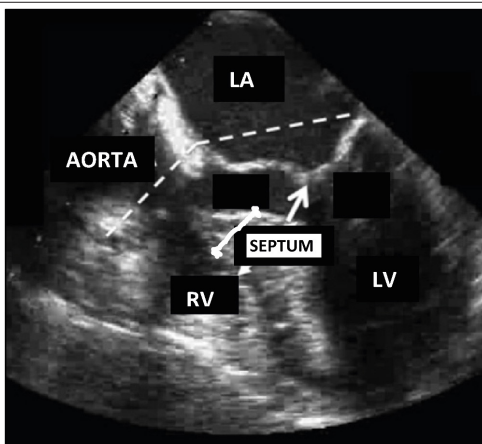


Figure 1 – Classificação de Carpentier.



Source: Adapted from Varghese R, Itagaki S, Anyanwu AC, Trigo P, Fischer G, Adams DH. Predicting systolic anterior motion after mitral valve reconstruction: using intraoperative transesophageal echocardiography to identify those at greatest risk. *Eur J Cardiothorac Surg.* 2014;45(1):132-7; discussion 137-8. doi: 10.1093/ejcts/ezt234.¹³ LA, left atrium; LV, left ventricle; RV, right ventricle.

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.

COR	LOE	Recomendações	Comentários
I	B	Mitral valve surgery is recommended for asymptomatic patients with chronic severe MR (stage D) and an LVEF > 30%	The 2014 recommendation currently remains
I	B	Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and left ventricular dysfunction (LVEF = 30–60% and/or LVSD ≥ 40 mm, stage C2)	The 2014 recommendation currently remains
I	B	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	The 2014 recommendation currently remains
I	B	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	The 2014 recommendation currently remains
I	B	Concomitant mitral valve repair (or replacement) is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other reasons	A recomendação de 2014 permanece atualmente
IIa	B	Mitral valve surgery is acceptable for asymptomatic patients with chronic severe primary mitral regurgitation (stage C1) and preserved left ventricular function (LVEF > 60% and LVSD < 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)	The 2014 recommendation currently remains
IIa	C	Mitral valve surgery is acceptable for asymptomatic patients with chronic severe primary mitral regurgitation (stage C1) and preserved left ventricular function (LVEF > 60% and LVSD < 40 mm) with progressively increased left ventricular size or consistent EF decreases in imaging studies	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
IIa	B	Mitral valve repair is acceptable for asymptomatic patients with chronic non-rheumatic severe primary MR (stage C1) and preserved LV function (LVEF > 60% and LVSD < 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 > 50 mmHg)	The 2014 recommendation currently remains

Source: Adapted from Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2017;135(25):e1159-e1195. doi: 10.1161/CIR.0000000000000503.¹⁴ COLOR, recommendation; EF, ejection fraction; LOE, level of evidence; LVEF, left ventricle ejection fraction; LVSD, left ventricle systolic diameter.

Table 4 – Recommendations for secondary mitral regurgitation intervention.

Class	Recommendations for secondary MR intervention	Comments
Ila	Mitral valve surgery is reasonable for patients with severe secondary MR (stages C and D) undergoing cardiac surgery	The 2014 recommendation currently remains
Ila	It is reasonable to preserve the mitral valve cords and annuloplasty in a symptomatic severe patient (NYHA III-IV) with ischemic MR (stage D) and persistent symptoms	New: Valve repair has been associated with a greater chance of moderate and severe MR than mitral valve replacement in patients with severe ischemic and symptomatic MR and no mortality difference in a 2-year follow-up.
IIb	Mitral valve repair or replacement can be considered for stage D symptomatic severe patients (NYHA III-IV) with chronic severe MR and persistent symptoms despite optimized therapy	The 2014 recommendation currently remains
IIb	The mitral repair indication is uncertain for a patient with moderate chronic ischemic MR (stage B) who underwent myocardial revascularization surgery	No clinical benefit was demonstrated for mitral valve repair in this population, with an increased risk of postoperative complications (neurological events and supraventricular arrhythmia)

Source: Adapted from Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159-e1195. doi: 10.1161/CIR.0000000000000503.¹² MR, mitral regurgitation; NYHA, New York Heart Association.

The presence of stress-induced MR or stress MR worsening increases the morbidity rate and pulmonary artery systolic pressure > 60 mmHg of patients, decreasing their functional capacity, which allows the identification of patients at higher risk. Although patients with severely increased MR and pulmonary arterial hypertension on exertion benefit from early elective mitral valve surgery, the presence of pulmonary hypertension is considered a IIb class indication for mitral valve repair in asymptomatic patients without LV dysfunction or dilation in the European Society of Cardiology and ACC guidelines.^{14,15}

Intervention criteria based on symptoms and the LV

Referral for surgical intervention

Unless surgery is contraindicated, all patients with severe and symptomatic MR should be considered for surgery. Whether the valve is repaired or replaced, surgery usually improves patients' symptoms. However, while awaiting the onset of symptoms, these patients present worse long-term outcomes since many develop incipient or latent LV dysfunction.

The AHA/ACC guidelines recommend surgery for asymptomatic patients with evidenced LV dysfunction⁵ due to adequate conditions for cardiac performance (increased preload and decreased afterload). The normal EF in severe primary MR must be greater than the truly normal EF. Therefore, when the EF decreases to <60% (or 64%), LV systolic dysfunction is possible. If the EF decreases to < 60%, valve repair should be performed in asymptomatic patients; in this context, a gradually decreased EF should also be considered. An LVSD > 40 mm is another sign of systolic dysfunction; however, if repair success is very probable, surgery should be considered. Surgery is associated with high risk and myocardial recovery uncertainty in patients with advanced systolic dysfunction (EF < 30%) and chronic primary MR; thus, each case must be evaluated individually.

In the past, due to high surgical mortality and adverse consequences of mitral valve replacement, these patients were followed up until the onset of LV symptoms or

dysfunction. With advanced technology and valve repair techniques, consideration of the earliest approach is currently recommended. However, in cases of a low possibility of repair, close follow-up should be the chosen strategy, as the premature placement of valve prostheses essentially substitutes one disease for another, with risks of thromboembolism, bleeding, and need for future interventions.

Reference center studies have shown a postoperative success rate greater than 98% and low surgical mortality in posterior cusp prolapse repair. The success rate of anterior cusp prolapse repair is 90–95% and surgical mortality is lower than 1%, with excellent 20-year durability.^{16,17}

There are several types of repair, the most commonly used being posterior prolapse with triangular or quadrangular resection, anterior prolapse with artificial cords, and commissure prolapse with commissuroplasty. Almost all techniques include annuloplasty rings for greater support and durability. The mitral valve can be replaced using a mechanical or biological prosthesis with effort made to preserve the mitral cords.

Referral for percutaneous 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.²⁰ 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.¹⁹

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.¹⁹

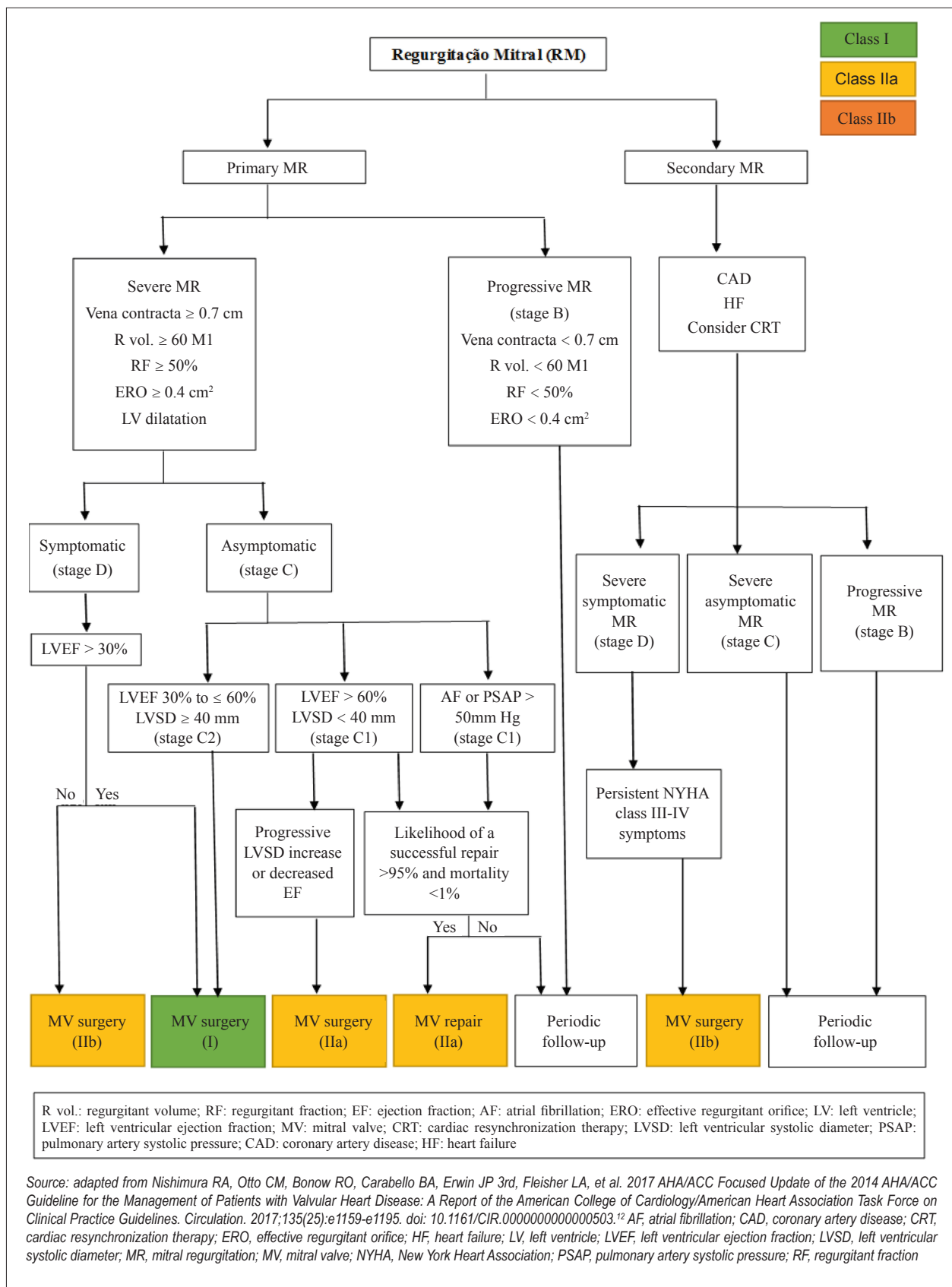


Figure 3 – Practical conduct guide for chronic mitral valve regurgitation.

Percutaneous annuloplasty

The percutaneous procedure 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.²⁰ 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 after 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.²¹

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.²² 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.²³

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.²⁴

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.²⁵

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.

References

1. Hahn RT, Abraham T, Adams MS, Bruce CJ, Glas KE, Lang RM, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr.* 2013;26(9):921-64. doi: 10.1016/j.echo.2013.07.009
2. Han HC, Ha FJ, Teh AW, Calafiore P, Jones EF, Johns J, et al. Mitral valve prolapse and sudden cardiac death: a systematic review. *J Am Heart Assoc.* 2018;7(23):e010584. doi: 10.1161/JAHA.118.010584
3. Cozzarín A, Cianciulli TF, Saccheri MC, Lax JA, Simonetti ME, Zappi A, et al. Severe mitral regurgitation after radiotherapy. *Echocardiography.* 2014;31(2):E37-40. doi: 10.1111/echo.12409
4. Chehab O, Roberts-Thomson R, Ng Yin Ling C, Marber M, Prendergast BD, Rajani R, et al. Secondary mitral regurgitation: pathophysiology, proportionality and prognosis. *Heart.* 2020;106(10):716-23. doi: 10.1136/heartjnl-2019-316238
5. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;129(23):2440-92. doi: 10.1161/CIR.0000000000000029
6. Yosefy C, Levine RA, Solis J, Vaturi M, Handschumacher MD, Hung J. Proximal flow convergence region as assessed by real-time 3-dimensional echocardiography: challenging the hemispheric assumption. *J Am Soc Echocardiogr.* 2007;20(4):389-96. doi: 10.1016/j.echo.2006.09.006
7. Grigioni F, Enriquez-Sarano M, Ling LH, Bailey KR, Seward JB, Tajik AJ, et al. Sudden death in mitral regurgitation due to flail leaflet. *J Am Coll Cardiol.* 1999;34(7):2078-85. doi: 10.1016/s0735-1097(99)00474-x
8. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton

- RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(23):e521-643. doi: 10.1161/CIR.0000000000000031. Erratum in: *Circulation*. 2014;129(23):e651. Erratum in: *Circulation*. 2014;130(13):e120. Dosage error in article text.
9. Carpentier A, Chauvaud S, Fabiani JN, Deloche A, Relland J, Lessana A, et al. Reconstructive surgery of mitral valve incompetence: ten-year appraisal. *J Thorac Cardiovasc Surg*. 1980;79(3):338-48. PMID: 7354634. AND Carpentier A: Cardiac Valve Surgery—the “French Correction”. *J Thorac Cardiovasc Surg*. 1983; 86:323-337
 10. Lancellotti P, Moura L, Pierard LA, Agricola E, Popescu BA, Tribouilloy C, Hagendorff A, Monin JL, Badano L, Zamorano JL; European Association of Echocardiography. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr*. 2010;11(4):307-32. doi: 10.1093/ejechocard/jeq031
 11. Varghese R, Itagaki S, Anyanwu AC, Trigo P, Fischer G, Adams DH. Predicting systolic anterior motion after mitral valve reconstruction: using intraoperative transoesophageal echocardiography to identify those at greatest risk. *Eur J Cardiothorac Surg*. 2014;45(1):132-7; discussion 137-8. doi: 10.1093/ejcts/ezt234
 12. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159-e1195. doi: 10.1161/CIR.0000000000000503
 13. Magne J, O'Connor K, Mahjoub H. Evaluation and impact on outcome of left ventricular contractile reserve in asymptomatic degenerative mitral regurgitation. *Eur Heart J*. 2011;32:(Suppl):170.
 14. Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC); European Association for Cardio-Thoracic Surgery (EACTS); Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J*. 2012;33(19):2451-96. doi: 10.1093/eurheartj/ehs109
 15. American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons, Bonow RO, Carabello BA, Kanu C, de Leon AC Jr, Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists; endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation*. 2006;114(5):e84-231. doi: 10.1161/CIRCULATIONAHA.106.176857. Erratum in: *Circulation*. 2007;115(15):e409. Erratum in: *Circulation*. 2010;121(23):e443.
 16. Castillo JG, Anyanwu AC, El-Eshmawi A, Adams DH. All anterior and bileaflet mitral valve prolapses are repairable in the modern era of reconstructive surgery. *Eur J Cardiothorac Surg*. 2014;45(1):139-45; discussion 145. doi: 10.1093/ejcts/ezt196
 17. Suri RM, Schaff HV, Dearani JA, Sundt TM 3rd, Daly RC, Mullany CJ, et al. Survival advantage and improved durability of mitral repair for leaflet prolapse subsets in the current era. *Ann Thorac Surg*. 2006;82(3):819-26. doi: 10.1016/j.athoracsur.2006.03.091
 18. Alfieri O, Maisano F, De Bonis M, Stefano PL, Torracca L, Oppizzi M, et al. The double-orifice technique in mitral valve repair: a simple solution for complex problems. *J Thorac Cardiovasc Surg*. 2001;122(4):674-81. doi: 10.1067/mtc.2001.117277
 19. Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, Smalling RW, Siegel R, Rose GA, Engeron E, Lohin C, Trento A, Skipper ER, Fudge T, Letsou GV, Massaro JM, Mauri L; EVEREST II Investigators. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364(15):1395-406. doi: 10.1056/NEJMoa1009355. Erratum in: *N Engl J Med*. 2011;365(2):189. Glower, Donald G [corrected to Glower, Donald D].
 20. Feldman T, Cilingiroglu M. Percutaneous leaflet repair and annuloplasty for mitral regurgitation. *J Am Coll Cardiol*. 2011;57(5):529-37. doi: 10.1016/j.jacc.2010.10.012
 21. Guilherme F, Attizzania B. Tratamento transcaterter da insuficiência mitral grave no Brasil: uma novidade na área. *Rev Bras Cardiol Invasiva*. 2015 [citado 2021 abr 6];23(2):82-83. Disponível em: <https://www.elsevier.es/en-revista-revista-brasileira-cardiologia-invasiva-233-articulo-tratamento-transcaterter-da-insuficiencia-mitral-S0104184315000351>
 22. El Sabbagh A, Reddy YNV, Nishimura RA. Mitral Valve Regurgitation in the Contemporary Era: Insights Into Diagnosis, Management, and Future Directions. *JACC Cardiovasc Imaging*. 2018;11(4):628-43. doi: 10.1016/j.jcmg.2018.01.009
 23. Michler RE, Smith PK, Parides MK, Ailawadi G, Thourani V, Moskowicz AJ, Acker MA, Hung JW, Chang HL, Perrault LP, Gillinov AM, Argenziano M, Bagiella E, Overbey JR, Moquete EG, Gupta LN, Miller MA, Taddei-Peters WC, Jeffries N, Weisel RD, Rose EA, Gammie JS, DeRose JJ Jr, Puskas JD, Dagenais F, Burks SG, El-Hamamsy I, Milano CA, Atluri P, Voisine P, O'Gara PT, Gelijns AC; CTSN. Two-year outcomes of surgical treatment of moderate ischemic mitral regurgitation. *N Engl J Med*. 2016;374(20):1932-41. doi: 10.1056/NEJMoa1602003
 24. Goldstein D, Moskowicz AJ, Gelijns AC, Ailawadi G, Parides MK, Perrault LP, Hung JW, Voisine P, Dagenais F, Gillinov AM, Thourani V, Argenziano M, Gammie JS, Mack M, Demers P, Atluri P, Rose EA, O'Sullivan K, Williams DL, Bagiella E, Michler RE, Weisel RD, Miller MA, Geller NL, Taddei-Peters WC, Smith PK, Moquete E, Overbey JR, Kron IL, O'Gara PT, Acker MA; CTSN. Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation. *N Engl J Med*. 2016;374(4):344-53. doi: 10.1056/NEJMoa1512913
 25. Baron S, Kumbhani DJ. Cardiovascular outcomes assessment of the mitralclip percutaneous therapy for heart failure patients with functional mitral regurgitation – COAPT. *American College of Cardiology*, 2020 [cited 2021 Apr 4]. Available from: <https://www.acc.org/latest-in-cardiology/clinical-trials/2018/09/21/2012/coapt>