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Transcatheter mitral valve repair with clip for treatment of secondary or functional mitral insufficiency. Literature review

Reparo transcater valvar mitral com clipe para o tratamento da insuficiência mitral secundária ou funcional.

Revisão da literatura

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ABSTRACT – Mitral insufficiency is one of the most common acquired heart valve diseases and a common cause of heart failure, often in response to mitral annulus dilation. In such cases, the condition is referred to as functional or secondary and may be associated with ischemic heart disease or other dilated cardiomyopathies of varying etiology. Mitral valve insufficiency is common among older patients or individuals with several comorbidities, who are often not eligible for conventional mitral valve surgery due to high risk of intraoperative death and complications. Surgical outcomes (valve repair or replacement) may also be limited, particularly in patients with functional mitral insufficiency (class IIb indication according to most international guidelines). Several less invasive clip-based transcatheter mitral valve repair techniques have been developed. These have been addressed in several randomized trials in the last few years, such as the EVEREST-II, the MITRA-FR and the COAPT trials. Positive COAPT trial outcomes supported the indication of mitral clip procedures in functional mitral regurgitation patients with favorable anatomy, who remain symptomatic despite optimal medical treatment. Patients with “disproportionate” mitral insufficiency (i.e., large degree of mitral regurgitation relative to ventricular dysfunction) are those who benefit most from the intervention, with lower rates of hospital readmission and death. These outcomes prompted the incorporation of novel technologies (MitraClip® NTR, MitraClip® XTR and Pascal). Major features of these devices, such as longer clip arms, capability of independent grasping of anterior and posterior leaflets, and wider arm width range are reviewed in detail in this article.

Keywords: Mitral valve insufficiency; Transcatheter mitral valve repair; MitraClip®; Pascal

RESUMO – A insuficiência valvar mitral é uma das doenças valvares adquiridas mais comuns, sendo causa frequente de insuficiência cardíaca, em geral decorrente de dilatação do ânulo valvar. Nesse caso, é chamada de funcional ou secundária e pode estar relacionada à doença isquêmica cardíaca ou a outras cardiopatias dilatadas, de diversas etiologias. Essa valvopatia acomete frequentemente pacientes mais idosos ou com muitas comorbidades e que, por vezes, não podem ser tratados de forma convencional pela cirurgia valvar mitral, em função do alto risco operatório de morte e complicações. Além disso, especialmente no contexto da insuficiência mitral funcional, os resultados cirúrgicos podem ser, muitas vezes, limitados (plástica ou troca valvar), sendo indicação IIb pela maioria das diretrizes mundiais. Nesse contexto, desenvolveram-se diversas técnicas menos invasivas para o reparo transcater valvar mitral com clipe. Nesses últimos anos, diversos estudos avaliaram essas técnicas, como os randomizados EVEREST-II, Mitra-FR e COAPT. Em função dos resultados positivos do estudo COAPT, a indicação do clipe mitral para insuficiência mitral funcional foi reforçada nos pacientes com anatomia favorável que permanecem sintomáticos, apesar de medicação otimizada. Os pacientes com menor disfunção ventricular e maior insuficiência mitral, chamada de “desproporcional”, são aqueles que apresentam mais benefícios com a técnica, com redução das taxas de necessidade de re-hospitalização e morte. Diante desses resultados, novas tecnologias vêm sendo incorporadas (MitraClip® NTR, MitraClip® XTR e Pascal), com a utilização de cliques mitrais com braços mais longos, possibilidade de clipagem dos folhetos anterior e posterior de forma independente e alternativa de dispositivos com maior largura do braço. Esses aspectos são revisados detalhadamente no presente artigo.

Descritores: Insuficiência da valva mitral; Reparo transcater mitral; MitraClip®; Pascal

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INTRODUCTION

Mitral valve insufficiency (MI) is one of the most common acquired heart valve diseases and may be caused by abnormalities at different sites of the mitral valve apparatus, such as leaflets, annulus, *chordae tendinae* and papillary muscles.¹⁻⁴ Mitral valve insufficiency may be categorized as primary (degenerative) or secondary (functional). Degenerative MI results from structural valve deformity, whereas secondary MI is associated with annular dilatation, often in response to ischemic heart disease or other dilated cardiomyopathies of varying etiology.³

MI is the leading cause of heart failure (HF) in response to heart valve disease and may progress to advanced disease if not properly treated. An estimated 80% of patients suffering from MI require at least one hospital admission per year, mostly to intensive care units. However, mitral valve disease is more common in older patients and individuals with several comorbidities, who are often not eligible for conventional mitral valve surgery due to high risk of intraoperative death and complications.^{2,4,5} Surgical outcomes (valve repair or replacement) may also be limited, particularly in patients who are refractory to medical treatment (class IIb indication according to most international guidelines).⁵⁻⁸ Wider access to novel therapeutic modalities are therefore needed, particularly for the large group of patients with limited therapeutic options due to high surgical risk or potentially limited surgical outcomes.

TRANSCATHETER MITRAL VALVE REPAIR

Several less invasive heart valve disease treatment techniques have been developed in the last decade (Figure 1)^{2,9},

including transcatheter mitral valve repair (TMVR), which is a percutaneous procedure for endovascular repair of incompetent mitral valves.^{2,9} MitraClip® is currently the only transcatheter system available for clinical use in Brazil. This system is based on the Alfieri procedure (Figure 2), in which two orifices are created by uniting the anterior and posterior leaflets of the mitral valve.¹⁰ In this procedure, the catheter is introduced through the femoral vein and the right atrium into the left atrium using a standard transseptal approach over a guidewire and dilator. The system has a clip attached to its distal end, which is positioned orthogonally to the mitral valve and over the origin of the regurgitant jet (Figure 2). Mitral valve leaflets are then held together and coaptation restored, with significant MI reduction. Primary clinical and anatomical criteria for MitraClip® indication are summarized in table 1.

Data supporting approval of this device for clinical use were derived from several “real world” registry studies – European studies in particular – and the North American randomized trial EVEREST II (Endovascular Valve Edge-to-Edge Repair Study). In the latter study, 279 patients with chronic moderate-severe (3+) or severe (4+) MI secondary to poor anterior and posterior leaflet coaptation were randomized (2:1) to TMVR with MitraClip® or traditional surgical treatment (valve replacement or repair). The primary efficacy endpoint (defined as survival, need for surgical valve replacement or moderate-severe or severe residual mitral regurgitation at 12 months) was reached by 55% of patients submitted to TMVR *versus* 73% of surgical patients (p=0.007). Mortality rates at 12 months were similar between groups (6%). However, the need for surgical correction of mitral valve dysfunction was greater in the

Source: adapted from Nombela-Franco L, Urena M, Ribeiro HB, Rodés-Cabau J. Advances in percutaneous treatment of mitral regurgitation. Rev Esp Cardiol (Engl Ed). 2013;66(7):566-82. <https://doi.org/10.1016/j.rec.2013.02.014>. Figura 1; Classification of percutaneous therapies for the treatment of mitral regurgitation; p. 567.² MT: minitoracotomía; SC: seno coronario; TA: transapical; TF: transfemoral; TP: transpericárdico; TS: transeptal.

*Devices approved for clinical use by the European Union; † devices first used in human beings in experimental settings; ‡ devices in preclinical phase.

ViV: valve-in-valve; CS: coronary sinus; TF: transfemoral; TS: transeptal; TA: transapical.

Figure 1. Different transcatheter therapies for mitral valve repair and replacement.

Source: copyright Abbott.

Figure 2. MitraClip® system based on the Alfieri procedure.¹⁰

Table 1. Features associated with success in clip-based transcatheter mitral valve repair

Feature	Favorable	Less favorable or unfavorable
Location of leaflet pathology	Noncommissural pathology (middle or medial and lateral segments)	Commissural segment, leaflet perforation or cleft
Calcification	No or minimal calcification	Severe leaflet calcification or calcium in area of leaflet grasping zone Severe annular calcification
Mean mitral valve gradient	Transmitral gradient <4mmHg	Mitral stenosis (rheumatic or calcified; mean gradient >5mmHg)
MVA	≥4cm ²	<4cm ²
Grasping zone length	>10mm	<7mm
Primary MI	Flail width <15mm Flail gap <10mm Single segment pathology Normal leaflet thickness	Flail width >15mm and flail gap Multisegment pathology, highly mobile flail leaflet and multiple ruptured chords Severely and diffusely thickened (5mm in diastole) and redundant leaflets (Barlow's type); LVEDD >55mm
Secondary MI	Coaptation depth <11mm; coaptation length >2mm	LVEDD >70mm

Source: adapted from Bonow RO, O'Gara PT, Adams DH, Badhwar V, Bavaria JE, Elmariah S, et al. 2020 Focused Update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2020;75(17):2236-70.

Table 7: Feasibility of transcatheter edge-to-edge repair; p. 2259.²³

MVA: mitral valve area; MI: mitral insufficiency; LVEDD: left ventricle end-diastolic diameter.

TMVR with clip relative to the surgery arm (20% and 2% respectively; $p<0.001$). At 1 year, the incidence of 3+ or 4+ MI was higher in the TMVR with clip as compared to the surgery arm (17% and 4%, respectively; $p=0.01$). At 5-year follow-up, mortality rates were similar between groups.¹¹ The primary safety endpoint of the study included severe adverse events at 30 days and was in favor of the TMVR with clip arm (TMVR, 15%, and surgery arm, 48%; $p<0.001$) due to the greater need of transfusion of one or more red blood cell units in surgical patients (13%

versus 45%; $p=0.01$). Surgical morbidity rates as per Society of Thoracic Surgeons (STS) were 9% and 2% (surgical and TMVR patients respectively; $p=0.02$). The main conclusion of the EVEREST II trial was that, although percutaneous repair with clip was less effective in reducing mitral regurgitation compared to conventional surgery, the procedure was safer and led to similar clinical improvement, in spite of greater need for reintervention, particularly in the first 6 months.¹¹ Major findings of the EVEREST II trial are summarized in table 2.

Table 2. Primary efficacy endpoint at 12 months and severe adverse events in the EVEREST II trial

Event	Mitral clip	Surgery	p-value
Primary efficacy endpoint at 12 months			
Survival free from death, mitral surgery or MI $\geq 3+$ or 4+	100 (55)	65 (73)	0.007
Death	11 (6)	5 (6)	1.00
Mitral valve surgery	37 (20)	2 (2)	<0.001
MI grade 3+ or 4+	38 (21)	18 (20)	1.0
Adverse event at 30 days			
Any severe event except transfusion	9 (5)	9 (10)	0.23
Death	2 (1)	2 (2)	0.89
Second mitral valve surgery	0	1 (1)	0.4
Stroke	2 (1)	2 (2)	0.89
Blood transfusion ≥ 2 units	24 (13)	42 (45)	<0.001

Source: adapted from Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fain PS, et al.; EVEREST II Investigators. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364(15):1395-406. Table 2; primary efficacy end point at 12 months and major adverse events at 30 days in the intention-to-treat population; p. 1402.¹²
Results expressed as n (%).
MI: mitral insufficiency.

The EVEREST II trial and several other global registries have shown that mitral clips can be used effectively in individuals with functional or degenerative MI. Therapeutic benefits of this intervention are reduced mitral regurgitation and improved functional class after implantation, which translate into better quality of life and less need for readmission due to HF. Especially in the functional or secondary MI population, the number of treated patients in the EVEREST II trial was small. Still, a subanalysis of this study revealed similar reduction in mitral regurgitation in a small group of patients with functional MI treated surgically or with MitraClip®.¹² Specific, well-designed randomized trials comparing TMVR with clip and optimized medical management alone, for example, were still lacking.

RECENT TRIALS ADDRESSING MITRACLIP® USE IN SECONDARY OR FUNCTIONAL MITRAL INSUFFICIENCY

Given the limited outcomes of surgical treatment for secondary/functional MI,^{3,13} and the lack of randomized trials comparing TMVR with clip and optimized medical management, findings of two important randomized trials have been recently published.

The first trial (MITRA-FR - Percutaneous Repair with the MitraClip® Device for Severe Functional/Secondary Mitral Regurgitation) included 304 patients with functional MI and HF with reduced (15% to 40%) left ventricle ejection

fraction (LVEF) submitted to optimal medical treatment (OMT) and cardiac resynchronization therapy (if indicated).¹⁴ Patients were randomized (1:1) to MitraClip® or OMT alone. The procedure was associated with low rates of complication and high efficacy. Upon discharge, 91.9% of patients had MI ≤ 2 . However, there were no significant differences between groups regarding the composite primary endpoint of death or unplanned HF readmission within 12 months (54.6% *versus* 51.3%, intervention and conservative management group, respectively). All-cause mortality rates of 24.3% and 22.4% and HF readmission rates of 48.7% and 47.4% (intervention and conservative management group, respectively) were also reported (Figure 3). Equivalent and significant New York Heart Association (NYHA) functional class improvement was also noted in both groups at 12 months. Randomized design with 99% follow-up on the primary endpoint and funding by

Source: translated and adapted from Obadia JF, Messika-Zeitoun D, Leurent G, Lung B, Bonnet G, Piriou N, et al.; MITRA-FR Investigators. Percutaneous repair or medical treatment for secondary mitral regurgitation. *N Engl J Med*. 2018;379(24):2297-306. Figure 2; Kaplan-Meier Estimates of Survival without a Primary Outcome Event; p. 2304.¹⁴ Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, et al.; COAPT Investigators. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med*. 2018;379(24):2307-18. Figure 1A; Primary effectiveness and safety end points and death; p. 2314.¹⁵

Figure 3. Primary endpoints of the MITRA-FR (A) and COAPT (B) trials comparing percutaneous intervention with MitraClip® and medical management alone in patients with secondary or functional mitral insufficiency.

the French government (French Ministry of Health and Research National Program) are the major strengths of this trial. Nonetheless, large amounts of echocardiographic and functional status data were missing at the 12-month follow-up. Subgroup analyses revealed consistent findings in several pre-specified subgroups.

The COAPT trial (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) is another important study. This trial included 614 patients (almost twice as many as the MITRA-FR trial) with moderate or severe functional ischemic (60.7%) or non-ischemic (39.3%) MI, who were symptomatic in spite of OMT and cardiac resynchronization therapy, as per the guidelines.¹⁵ Patients were randomized to MitraClip® procedure (n=302) or OMT alone (n=312). Heart failure readmission rates at 2 years (primary endpoint) were significantly lower in the MitraClip® relative to the OMT only group (35.8% and 67.9% respectively; RR=0.53; 95%CI 0.40-0.70; p<0.001). In the MitraClip® arm, the number needed to treat (NNT) in order to reduce readmission rates at 2 years was only 3.1 (95%CI 1.9-7.9) (Figure 2). All-cause mortality rates at 2 years were also significantly lower in the MitraClip® as compared to the OMT alone group (29.1% versus 46.1%; RR=0.62; 95%CI 0.46-0.82; p<0.001), yielding a NNT of only 5.9 patients treated to prevent one death at 2 years (95%CI 3.9-11.7). The rate of freedom from device-related complications at 12 months (primary safety endpoint) was only 96.6%. Significant (p<0.01) improvement in quality of life and functional capacity and significantly (p<0.01) reduced MI and left ventricular diameter (left ventricular end-diastolic diameter) were also reported.¹⁵

The different outcomes between these two important contemporary trials addressing the use of TMVR with MitraClip® in functional or secondary MI are worthy of consideration. Deeper and detailed analysis of each of these studies raises several questions which may help clarify these differences, as summarized in table 3. Firstly, sample size (304 versus 614 patients) and follow-up time to primary endpoint assessment (12 versus 24 months) differed widely, so that the COAPT trial included twice the number of patients followed for twice as long. Also, the primary endpoint in the COAPT trial accounted for all HF admissions (including recurrent events), whereas the primary endpoint in the MITRA-FR trial comprised all-cause mortality or unplanned HF admission. As for inclusion criteria, different definitions of mitral regurgitation were adopted, the MITRA-FR trial enrolling patients with less severe MI (effective regurgitant orifice area >20mm² and/or regurgitant volume >30mL in the MITRA-FR trial versus >30mm² and >45mL in the COAPT trial). The MITRA-FR trial also included patients with more advanced HF (LVEF ranging from 15% to 40% and 20% to 50%, MITRA-FR and COAPT trial, respectively) and larger left ventricle. This translated into larger left ventricles (mean end-diastolic volume index of 135mL/m² versus 101mL/m²) and less severe MI (effective regurgitant orifice area of 31±10mm² versus 41±15mm²) in the MITRA-FR compared to the COAPT trial. With regard to implantation techniques, good success rates were reported in the MITRA-FR trial relative to previous observational studies. However, even better rates with less periprocedural complications were reported in the COAPT trial. Enrollment strategies also differed. In the COAPT trial, a central eligibility committee examined the

Table 3. Differences between the MITRA-FR and the COAPT trial

	MITRA-FR (n=304)	COAPT (n=614)
MI grade of severity for enrollment in trial	European guideline criterion: EROA >20mm ² or RV >30mL/beat	American guideline criterion: EROA >30mm ² or RV >45mL/beat
LVEF, %	15-40	20-50
EROA, mean±SD	31±10mm ²	41±15mm ²
LVEDV, mean±SD	135±35mL/m ²	101±34mL/m ²
Baseline and follow-up clinical management	Patients receiving medications for HF at baseline, practice-based adjustments accepted over the course of follow-up	Trial committee confirmed patients were taking maximum tolerated doses of medications for HF; few adjustments required over the course of follow-up
Acute outcomes: no clip/MI ≥3+, %	9/9	5/5
Periprocedural complications, %*	14.6	8.5
MI ≥3+ with MitraClip® at 12 months, %	17	5

*Periprocedural complication definition adopted in the MITRA-FR trial: device deployment failure, hemorrhage requiring transfusion or vascular complication requiring surgery, cardiogenic shock requiring inotropic medication, cardiac embolisms including gas embolism or stroke, tamponade, urgent cardiac surgery, interatrial septal lesion or interatrial communication.

MI: mitral insufficiency; EROA: effective regurgitant orifice area; RV: regurgitant volume; LVEF: left ventricle ejection fraction; SD: standard deviation; LVEDV: left ventricle end-diastolic volume; HF: heart failure.

current medical management of each patient prior to enrollment. Medical management was optimized prior to actual enrollment and few changes were made over the course of follow-up. In contrast, a more inclusive enrollment strategy was adopted in the MITRA-FR trial and changes in medical management according to real world practices were accepted. This may have translated into improvements observed in the control arm of the latter trial. Whether or not the above-mentioned differences impacted the results of both trials is not completely defined yet.

Another recent important concept formulated to explain differences between both trials is the occurrence of disproportionate MI (Figure 4).¹⁶ Patients with severe left ventricle dysfunction may be further categorized according to MI severity, and whether it is proportionate or disproportionate to the degree of ventricular dysfunction (Figure 4).¹⁷ Medical management aimed at decreasing left ventricular volume overload (such as neurohormonal blockers) are effective in proportionate MI but no so much in disproportionate MI. In contrast, procedures aimed at improving mitral valve function (such as cardiac resynchronization and mitral valve repair) are effective in patients with disproportionate MI. This is yet another potential partial explanation for outcome differences between the MITRA-FR and COAPT trials.

Source: Grayburn PA, Sannino A, Packer M. Proportionate and disproportionate functional mitral regurgitation: a new conceptual framework that reconciles the results of the MITRA-FR and COAPT trials. *JACC Cardiovasc Imaging*. 2019;12(2):353-62.¹⁷ <https://doi.org/10.1016/j.jcmg.2018.11.006>. Figure 2; Relationship between EROA and LVEDV illustrating domains that define disproportionately severe, proportionately severe, and nonsevere functional mitral regurgitation; p. 357. CRT: cardiac resynchronization therapy.

Figure 4. Procedures aimed at transcatheter mitral valve repair should be indicated for patients with disproportionate mitral insufficiency relative to ventricular dysfunction severity (orange-colored region) rather than for those with proportionate or non-severe mitral insufficiency (grey and blue regions, respectively). The equation for the proportional relation corresponds to effective regurgitant orifice area divided by left ventricle end-diastolic volume (ratio=0.13-0.14).^{16,17}

ONGOING STUDIES

Two other ongoing trials addressing TMVR MitraClip® in patients with functional MI may contribute with additional data about this therapy, namely the RESHAPE-HF2 (A Clinical Evaluation of the Safety and Effectiveness of the MitraClip System in the Treatment of Clinically Significant Functional Mitral Regurgitation; NCT02444338) trial comparing MitraClip® and OMT alone in 420 patients, and the MATTERHORN (A Multicenter, Randomized, Controlled Study to Assess Mitral vAlve reconsTrucTion for advancEd Insufficiency of Functional or iscHemic ORiGiN; NCT02371512) trial comparing MitraClip® and surgical treatment (mitral valve repair or replacement) in 210 patients.

NOVEL TRANSCATHETER MITRAL VALVE REPAIR TECHNOLOGIES

Transcatheter mitral valve repair has revolutionized MI treatment over the last few years. However, advancements and improvements are important and always desirable. Novel devices are currently available worldwide and may be implemented in routine practice in the near future. As shown in figure 5, novel devices, such as the MitraClip®

	MitraClip 3 rd generation NTR/XTR	MitraClip 4 th generation NT/XT/NTW/XTW	Edwards - Pascal
Number of sizes	2	4	1
Grasping width	4mm	4mm - G4 NT; G4 XT 6mm - G4 NTW; G4 XTW	7mm
Clip arm length	9mm - NTR 12mm - XTR	9mm - G4 NT; G4 NTW 12mm - G4 XT; G4 XTW	9mm
Independent grasping	No	Yes	Yes
Spacer	No	No	Yes - 10mm
Left atrium pressure monitoring	No	Yes	Yes
sheath size	24Fr	24Fr	22Fr

Source: Grasso C, Popolo Rubbio A. The PASCAL transcatheter mitral valve repair system for the treatment of mitral regurgitation: another piece to the puzzle of edge-to-edge technique. *J Thorac Dis*. 2017;9(12):4856-59.¹⁹ Praz F, Braun D, Unterhuber M, Spirito A, Orban M, Brugger N, et al. Edge-to-edge mitral valve repair with extended clip arms: early experience from a multicenter observational study. *JACC Cardiovasc Interv*. 2019;12(14):1356-65.²⁰ Praz F, Spargias K, Chrissoheris M, Büllesfeld L, Nickenig G, Deuschl F, et al. Compassionate use of the PASCAL transcatheter mitral valve repair system for patients with severe mitral regurgitation: a multicentre, prospective, observational, first-in-man study. *Lancet*. 2017;390(10096):773-80.²¹

Figure 5. Major features of novel transcatheter mitral valve repair devices with clip, including the third (NTR and XTR) and fourth (G4 NT, NTW, XT and XTW) generations MitraClip®, as well as the Edwards Pascal devices.

NTR, the MitraClip® XTR and the Edwards Pascal TMVR systems are being incorporated. The MitraClip® NTR is a third-generation device incorporating important changes, primarily in the delivery system, for easier navigation and clip positioning in the mitral valve through the left atrium. It also includes grippers made of nitinol wire for easier grasping of valve leaflets. In the XTR version, 3mm longer arms allow leaflet grasping even in cases with more challenging anatomy. A fourth-generation MitraClip® device (G4 - NT/XT/NTW/XTW) shall be available in the near future. This version offers 9- and 12-mm long arms and wider arm width range (4 to 6mm).¹⁸ This system also allows independent grasping of the anterior and posterior leaflets and continuous left atrial pressure monitoring. The Edwards Pascal system comprises a simplified left atrium navigation system consisting of a 10-mm central spacer to achieve MI reduction. This system also allows independent grasping of mitral leaflets and continuous left atrial pressure monitoring.¹⁹

A recent study investigated MitraClip® XTR in 107 patients (mean age, 76±9 years; 69% males) with functional (n=53; 50%), primary (n=40; 37%) or mixed etiology (n=14; 13%) MI. Of 102 patients (95.3%) who survived the procedure and were discharged with no need for surgery, 95 (93%) had MI ≤2+ and 79 (77%) MI ≤1+. Mean transmitral gradient increased from 1.9±1.0mmHg to 3.5±1.8mmHg upon hospital discharge (p<0.001). The mean number of clips per patient was 1.5±0.6 and 46 patients (43%) required multiple devices. Clip detachment, leaflet injury and conversion to open surgery were reported in four, two and four cases, respectively. Overall procedural success rate was 93%.²⁰

Another recent study evaluated the Pascal device in 23 patients (median age of 75 years) with moderate or severe MI. Patients received at least one Pascal device and residual MI <2+ was achieved in 22 (96%) cases. A second clip was required in six (26%) cases. The procedure was technically

successful in 22 (96%) patients and successful outcome at 30 days was reported in 18 (78%) cases.²¹

COMMENTS

According to guidelines provided by the major national and international societies, transcatheter mitral valve repair with clip is indicated for patients with moderate or severe mitral insufficiency (NYHA functional class III or IV dyspnea) who remain symptomatic in spite of optimized medical management, but are high-risk patients for conventional mitral valve surgery due to comorbidities (Figure 6).^{22,23} Life expectancy >1 year and favorable anatomy are other important criteria. Tridimensional transesophageal echocardiographic monitoring by a specialist is highly recommended to monitor the procedure. This procedure should be carried out by trained interventional cardiologists specialized in transcatheter procedures and the indication should be supported by a multidisciplinary team (clinical cardiologist, cardiovascular imaging specialist, cath lab specialist and surgeon). Recent randomized trials addressing MitraClip® use in patients with functional mitral insufficiency suggest this therapy is actually effective in reducing mitral insufficiency in properly selected patients, with favorable anatomy, and should be performed by experienced operators and with high levels of precision, in order to control symptoms, improve patient quality of life, enhance left ventricular remodeling and, eventually, decrease mortality. Long-term follow-up on the COAPT and MITRA-FR trials and the ongoing RESHAPE-HF2 and MATTERHORN trials may contribute with additional information to further consolidate this intervention as an important therapeutic alternative for mitral valve disease. Finally, the results obtained with novel mitral clip devices (MitraClip®

		Surgical risk	
		Not high	High or prohibitive
Cause of MR	Primary	Surgical repair <ul style="list-style-type: none"> - Class I guideline for surgical repair - Repair success dependent on anatomy and surgeon - Referral for repair generally advised - Post-procedural MR associated with impaired survival in some studies 	Transcatheter repair <ul style="list-style-type: none"> - Class IIb guideline for transcatheter repair - Clinical and anatomic criteria for eligibility - ~90% have MR reduction, with ~65% having residual MR grade ≤1+
	Secondary	Surgical repair or replacement <ul style="list-style-type: none"> - Class IIb for surgical intervention - Survival benefit of surgery uncertain - Multiple factors for strategy of replacement vs. repair - Consideration is adjunctive to OMT 	Transcatheter repair <ul style="list-style-type: none"> - No current interventional guideline recommendation - Consideration is adjunctive to OMT - Survival and symptom benefit in selected patients

Source: adapted from Sorajja P, Cavalcante JL, Gössl M. The need for transcatheter mitral valve replacement. J Am Coll Cardiol. 2019;73(11):1247-9. Figure 1; Current practice for nonmedical therapy in MR; p. 1248.22

MR: mitral regurgitation; OMT: optimal medical treatment.

Figure 6. Current recommendation for management of patients with mitral insufficiency according to recent studies.

NTR, MitraClip® XTR, MitraClip® G4 NTW and Edwards-Pascal) offering longer and wider arms, and allowing independent grasping of anterior and posterior leaflets, may translate into improved outcomes and greater benefits for patients.

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DISCLOSURE OF CONFLICTS OF INTEREST

Henrique Barbosa Ribeiro is proctor of MitraClip® (Abbott Vascular).

CONTRIBUTION OF AUTHORS

Conception and design of the study: HBR, FSBJ and AA; data collection: HBR, FSBJ and AA; data interpretation: HBR, FSBJ and AA; writing of the text: HBR, FSBJ and AA; approval of the final version to be published: HBR, FSBJ and AA.

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