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MEDICAL POLICY – 2.02.30

Transcatheter Mitral Valve Repair or Replacement

BCBSA Ref. Policy:	2.02.30
Effective Date:	Oct. 1, 2024
Last Revised:	Sept. 10, 2024
Replaces:	N/A

RELATED MEDICAL POLICIES:

7.01.131 Transcatheter Pulmonary Valve Implantation

7.01.132 Transcatheter Aortic-Valve Implantation for Aortic Stenosis

Select a hyperlink below to be directed to that section.

Clicking this icon returns you to the hyperlinks menu above.

Introduction

The heart has four chambers, two upper and two lower. The mitral valve is between the upper and lower left chambers. After blood has been pumped from the upper left chamber to the lower left chamber, the mitral valve closes. The mitral valve is made up of small pieces of tissue called leaflets. If the leaflets don't close properly when the left lower chamber pumps blood out to the body some of the blood can leak back into the upper left chamber. This is known as mitral valve regurgitation. Medication can be used to help manage the symptoms of mitral valve regurgitation. Open heart surgery is a treatment option. If a person is too sick for surgery, a nonsurgical procedure may be used to place a clip to close the leaky mitral valve. In this procedure, a long, hollow tube (a catheter) is threaded through a specific vein into the heart. The catheter then becomes the pathway for getting the clip to the mitral valve. Imaging is used to make sure the device is correctly placed. If the valve stops working, it can be replaced in some people. This policy describes when transcatheter mitral valve repair or replacement is considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Service	Medical Necessity
Transcatheter mitral valve repair	**Transcatheter mitral valve repair (TMVR) using a device approved by the US Food and Drug Administration (i.e. MitraClip, PASCAL) for use in mitral valve repair may be considered medically necessary for individuals with symptomatic, primary mitral regurgitation who are considered at prohibitive risk for open surgery.** **Prohibitive risk for open mitral valve repair surgery may be determined based on:** • The documented presence of a Society for Thoracic Surgeons predicted mortality risk of 12% or greater (See **Related Information**) **AND/OR** • The documented presence of a logistic EuroSCORE of 20% or greater **Transcatheter mitral valve repair with a device approved by the US Food and Drug Administration (i.e. MitraClip) may be considered medically necessary for individuals with heart failure and moderate-to-severe or severe* symptomatic secondary mitral regurgitation despite the use of maximally tolerated guideline-directed medical therapy (**See Appendix**)** **Note:** ***** Moderate to severe or severe MR may be determined by: • Grade 3+ (moderate) or 4+ (severe) MR confirmed by echocardiography • New York Heart Association (NYHA) functional class II, III, or IVa (ambulatory) despite the use of stable maximal doses of guideline-directed medical therapy and cardiac resynchronization therapy (if appropriate) administered in accordance with guidelines of professional societies.
Transcatheter mitral valve replacement	**Transcatheter mitral valve-in-valve replacement (TMViVR) with a device approved by the US FDA (i.e. Edwards SAPIEN3)**

Service	Medical Necessity
	is considered medically necessary for individuals when all of the following conditions are present: • Failure (stenosed, insufficient, or combined) of a surgical bioprosthetic mitral valve **AND** • New York Heart Association heart failure class II, III, or IV symptoms (see **Definition of Terms**) **AND** • The individual is not an operable candidate for open surgery, as documented by at least 2 cardiovascular specialists (including a cardiac surgeon) **OR** ○ Is an operable candidate but is considered at increased surgical risk for open surgery, as documented by at least 2 cardiac specialists (including a cardiac surgeon) **OR** ○ Is considered at increased surgical risk for open surgery (e.g., repeat sternotomy) due to a history of congenital vascular anomalies **AND/OR** • Has a complex intrathoracic surgical history, as documented by at least 2 cardiovascular specialists (including a cardiac surgeon) **Transcatheter mitral valve repair is considered investigational in all other situations.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Name of the Food and Drug Administration (FDA) approved device to be used • Documentation that individual has symptomatic primary mitral regurgitation **AND** • The individual is at greater risk for open mitral valve repair surgery based on: ○ The documented presence of a Society for Thoracic Surgeons predicted mortality risk of 12% or greater

Documentation Requirements

AND/OR

- The documented presence of a logistic EuroSCORE of 20% or greater

OR

- Documentation that individual has heart failure and moderate-to-severe or severe symptomatic secondary MR despite the use of maximally tolerated guideline-directed medical therapy including the guideline-directed medical therapy that has been trialed and failed

OR

- Documentation that individual requires transcatheter mitral valve in valve replacement

AND

- Has failure (stenosed, insufficient, or combined) of a surgical bioprosthetic mitral valve

AND

- Has New York Heart Association heart failure class II, III, or IV symptoms

AND

- Is not an operable candidate for open surgery, as documented by at least 2 cardiovascular specialists (including a cardiac surgeon)

  OR

  - Is an operable candidate but is considered at increased surgical risk for open surgery, as documented by at least 2 cardiac specialists (including a cardiac surgeon

  OR

  - Is considered at increased surgical risk for open surgery (e.g., repeat sternotomy) due to a history of congenital vascular anomalies

AND/OR

- Is considered at increased surgical risk for open surgery (e.g., repeat sternotomy) due to a history of congenital vascular anomalies

Coding

Code	Description
CPT	
0345T	Transcatheter mitral valve repair percutaneous approach via the coronary sinus
0483T	Transcatheter mitral valve implantation/replacement (TMVI) with prosthetic valve; percutaneous approach, including transseptal puncture, when performed
0484T	Transcatheter mitral valve implantation/replacement (TMVI) with prosthetic valve; transthoracic exposure (e.g., thoracotomy, transapical)

Code	Description
0544T	Transcatheter mitral valve annulus reconstruction, with implantation of adjustable annulus reconstruction device, percutaneous approach including transseptal puncture (e.g. Edwards Cardioband Mitral Valve Reconstruction System or Carillon Mitral Contour System)
33418	Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed; initial prosthesis (e.g. MitraClip Delivery System or PASCAL Precision Transcatheter Valve Repair System)
33419	Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed; additional prosthesis(es) during same session (List separately in addition to code for primary procedure) (e.g. MitraClip Delivery System or PASCAL Precision Transcatheter Valve Repair System).

Related Information

Definition of Terms

New York Heart Association (NYHA) Classification:

Class I No symptoms and no limitation in ordinary physical activity, e.g., shortness of breath when walking, climbing stairs etc.
Class II Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
Class III Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g., walking short distances (20–100 m). Comfortable only at rest.
Class IV Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients

The FDA definition of high risk for open surgery is:

- Society of Thoracic Surgeons (STS) predicted operative risk score of 8% or higher; or
- Judged by a heart team, which includes an experienced cardiac surgeon and a cardiologist, to have an expected mortality risk of 15% or higher for open surgery.

Evidence Review

Description

Transcatheter mitral valve repair (TMVR) is an alternative to surgical therapy for mitral regurgitation (MR). MR is a common valvular heart disease that can result from a primary structural abnormality of the mitral valve (MV) complex or a secondary dilatation of an anatomically normal MV due to a dilated left ventricle caused by ischemic or dilated cardiomyopathy. Surgical therapy may be underutilized, particularly in individuals with multiple comorbidities, suggesting that there is an unmet need for less invasive procedures for MV repair. These devices, MitraClip and PASCAL, have approval from the US Food and Drug Administration for the treatment of severe symptomatic MR due to a primary abnormality of the MV (primary MR) in individuals considered at prohibitive risk for surgery. MitraClip is also approved for individuals with heart failure and moderate-to-severe or severe symptomatic secondary MR despite the use of maximally tolerated guideline-directed medical therapy. The Edwards SAPIEN 3 transcatheter heart valve has been approved by the US Food and Drug Administration for transcatheter mitral valve-in-valve replacement (TMViVR) in individuals with a failing surgical bioprosthetic mitral valve who are at high or greater risk for repeat surgery.

Background

Mitral Regurgitation

Epidemiology and Classification

Mitral regurgitation (MR) is the second most common valvular heart disease, occurring in 7% of people older than age 75 years and accounting for 24% of all individuals with valvular heart disease.[1-2] MR with accompanying valvular incompetence leads to left ventricular (LV) volume overload with secondary ventricular remodeling, myocardial dysfunction, and left heart failure. Clinical signs and symptoms of dyspnea and orthopnea may also be present in individuals with valvular dysfunction.[3] MR severity is classified as mild, moderate, or severe disease on the basis of echocardiographic and/or angiographic findings (1+, 2+, and 3-4+ angiographic grade, respectively).

Individuals with MR generally fall into two categories — primary (also called degenerative) and secondary (also called functional) MR. Primary MR results from a primary structural abnormality

in the valve, which causes it to leak. This leak may result from a floppy leaflet (called prolapse) or a ruptured cord that caused the leaflet to detach partially (called flail).[4] Because the primary cause is a structural abnormality, most cases of primary MR are surgically corrected. Secondary MR results from left ventricular (LV) dilatation due to ischemic or dilated cardiomyopathy. This causes the mitral valve (MV) leaflets not to coapt or meet in the center.[3] Because the valves are structurally normal in secondary MR, correcting the dilated LV using medical therapy is the primary treatment strategy used in the US.

Standard Management

Surgical Management

In symptomatic individuals with primary MR, surgery is the main therapy. In most cases, MV repair is preferred over replacement, as long as the valve is suitable for repair and personnel with appropriate surgical expertise are available. The American College of Cardiology and the American Heart Association have issued joint guidelines for the surgical management of MV, which are outlined in **Table 2**.[5]

The use of standard open MV repair is limited by the requirement for thoracotomy and cardiopulmonary bypass, which may not be tolerated by elderly or debilitated individuals due to their underlying cardiac disease or other conditions. In a single-center evaluation of 5737 individuals with severe MR in the US, Goel et al (2014) found that 53% of individuals did not have MV surgery performed, suggesting an unmet need for such individuals.[6]

Isolated MV surgery (repair or replacement) for severe chronic secondary MR is not generally recommended because there is no proven mortality reduction and an uncertain durable effect on symptoms. Recommendations from major societies[7,8] regarding MV surgery in conjunction with coronary artery bypass graft surgery or surgical aortic valve replacement are weak because the current evidence is inconsistent on whether MV surgery produces a clinical benefit.[9,10,11,12]

Transcatheter Mitral Valve Repair

Transcatheter approaches have been investigated to address the unmet need for less invasive MV repair, particularly among inoperable individuals who face prohibitively high surgical risks due to age or comorbidities. MV repair devices under development address various components of the MV complex and generally are performed on the beating heart without the need for cardiopulmonary bypass.[1,13] Approaches to MV repair include direct leaflet repair[14], repair of the

mitral annulus via direct annuloplasty, or indirect repair based on the annulus' proximity to the coronary sinus. There are also devices in development to counteract ventricular remodeling and systems designed for complete MV replacement via catheter.

Direct Leaflet Approximation

Devices currently approved by the FDA for transcatheter mitral valve repair (TMVR) undergo direct mitral leaflet repair (also referred to as transcatheter edge-to-edge repair). Of the TMVR devices under investigation, the MitraClip, has the largest body of evidence evaluating its use; it has been in use in Europe since 2008.[14] The MitraClip system is deployed percutaneously and approximates the open Alfieri edge-to-edge repair approach to treating MR. The delivery system consists of a catheter, a steerable sleeve, and the MitraClip device, which is a 4-mm wide clip fabricated from a cobalt-chromium alloy and polypropylene fabric. MitraClip is deployed via a transfemoral approach, with trans-septal puncture used to access the left side of the heart and the MV. Placement of the MitraClip leads to coapting of the mitral leaflets, thus creating a double-orifice valve.

The PASCAL (PAddles Spacer Clasps ALfieri) Mitral Repair System (Edwards Lifesciences) is also a direct coaptation device and works in a similar manner to the MitraClip system.[15] PASCAL has been in clinical use since 2016 and was approved for use in Europe in 2019.[16] The delivery system consists of a 10-mm central spacer that attaches to the MV leaflets by 2 paddles and clasps.

Other Mitral Valve Repair Devices

Devices for TMVR that use various approaches are in development. Techniques to repair the mitral annulus include those that target the annulus itself (direct annuloplasty) and those that tighten the mitral annulus via manipulation of the adjacent coronary sinus (indirect annuloplasty). Indirect annuloplasty devices include the Carillon Mitral Contour System (Cardiac Dimension) and the Monarc device (Edwards Lifesciences). The CE-marked Carillon Mitral Contour System is comprised of self-expanding proximal and distal anchors connected with a nitinol bridge, with the proximal end coronary sinus ostium and the distal anchor in the great cardiac vein. The size of the connection is controlled by a manual pullback on the catheter. The Carillon system was evaluated in the Carillon Mitral Annuloplasty Device European Union Study (AMADEUS) and the follow-up Tighten the Annulus Now study, with further studies planned.[17] The Monarc system also involves two self-expanding stents connected by a nitinol bridge, with one end implanted in the coronary sinus via the internal jugular vein and the other in the great

cardiac vein. Several weeks after implantation, the biologically degradable coating over the nitinol bridge degrades, allowing the bridge to shrink and the system to shorten. It has been evaluated in the Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for the Treatment of Mitral Regurgitation (EVOLUTION I) trial.[18]

Direct annuloplasty devices include the Mitralign Percutaneous Annuloplasty System (Mitralign) and the AccuCinch System (Guided Delivery Systems), both of which involve transcatheter placement of anchors in the MV; they are cinched or connected to narrow the mitral annulus. Other transcutaneous direct annuloplasty devices under investigation include the enCorTC device (Micardia), which involves a percutaneously insertable annuloplasty ring that is adjustable using radiofrequency energy, a variation on its CE-marked enCor$_{SQ}$ Mitral Valve Repair System, and the Cardioband Annuloplasty System (Valtech Cardio), an implantable annuloplasty band with a transfemoral venous delivery system.

Transcatheter Mitral Valve-in-Valve Replacement

Mitral valve-in-valve replacement is a minimally invasive procedure designed to treat patients with failing surgical bioprosthetic mitral valves who are at high risk for complications with repeat open-heart surgery. The Edwards SAPIEN 3 Transcatheter Heart Valve received FDA approval in June 2017 (PMA #P140031) for patients with a failing surgical bioprosthetic mitral valve who are at high or prohibitive risk for repeat surgery. The procedure involves deploying the replacement valve within the failing bioprosthetic valve using a catheter-based transapical or transseptal approach. Once in position, the replacement valve is expanded, pushing the leaflets of the failing bioprosthetic valve aside and taking over the valve function.

Medical Management

The standard treatment for individuals with chronic secondary MR is medical management. Individuals with chronic secondary MR should receive standard therapy for heart failure with reduced ejection fraction; standard management includes angiotensin converting enzyme inhibitor (or angiotensin II receptor blocker or angiotensin receptor-neprilysin inhibitor), β-blocker and mineralocorticoid receptor antagonist, and diuretic therapy as needed to treat volume overload.[3,4] Resynchronization therapy may provide symptomatic relief, improve LV function, and in some individuals, lessen the severity of MR.

Summary of Evidence

For individuals who have symptomatic primary mitral regurgitation (MR) and are at prohibitive risk for open surgery who receive transcatheter mitral valve repair (TMVR) using MitraClip or PASCAL, the evidence includes a noninferiority randomized controlled trial (RCT) and single-arm prospective cohort with historical cohort and registry studies. The relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The primary evidence includes the pivotal EVEREST II HRR and EVEREST II REALISM studies, the Transcatheter Valve Therapy Registry study, and the CLASP IID/IIF study. Studies evaluating MitraClip have demonstrated that MitraClip implantation is feasible with a procedural success rate greater than 90%, 30-day mortality ranging from 2.3% to 6.4% (less than predicted Society of Thoracic Surgeons (STS) mortality risk score for MR repair or replacement; range, 9.5%-13.2%), postimplantation MR severity grade of 2+ or less in 82% to 93% of individuals, and a clinically meaningful gain in quality of life (5-point to 6-point gains in SF-36 scores). At one year, freedom from death and MR more than 2+ was achieved in 61% of individuals but the one-year mortality or heart failure hospitalization rates remain considerably high (38%). Conclusions related to the treatment effect on mortality based on historical controls cannot be made because the control groups did not provide unbiased or precise estimates of the natural history of individuals eligible to receive MitraClip. Given that primary MR is a mechanical problem and there is no effective medical therapy, an RCT comparing TMVR with medical management is not feasible or ethical. The postmarketing data from the US is supportive that MitraClip surgery is being performed with short-term effectiveness and safety in a select patient population. The CLASP IID/IIF randomized cohort demonstrated that PASCAL is noninferior to MitraClip in safety and effectiveness for individuals with primary MR at prohibitive surgical risk, and the single-arm registry cohort demonstrated that PASCAL is safe and effective in individuals with complex mitral valve (MV) anatomy precluding the use of MitraClip. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure and symptomatic secondary mitral regurgitation (SMR) despite the use of maximally tolerated guideline-directed medical therapy who receive TMVR using MitraClip, the evidence includes a systematic review, two RCTS, and multiple observational studies. The relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The trials had discrepant results potentially related to differences in primary outcomes. The larger trial, with individuals selected for nonresponse to maximally tolerated therapy, found a significant benefit for MitraClip up to 5 years compared to medical therapy alone, including benefits in overall survival and hospitalization for heart failure. Improvements in MR severity, quality of life measures, and functional capacity persisted to 36 months in individuals who received TMVR. The systematic review confirmed the benefit of

MitraClip found in the larger RCT but had important methodological limitations. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have symptomatic primary or secondary MR and are surgical candidates who receive TMVR using MitraClip, the evidence includes a systematic review, one RCT and a retrospective comparative observational study in individuals aged ≥75 years. The relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The RCT found that MitraClip did not reduce MR as often or as completely as the surgical control, although it could be safely implanted and was associated with fewer adverse events at one year. Long-term follow-up from the RCT showed that significantly more MitraClip individuals required surgery for MV dysfunction than conventional surgery patients. For these reasons, this single trial is not definitive in demonstrating improved clinical outcomes with MitraClip compared with surgery. Additional RCTs are needed to corroborate these results. The observational study in individuals aged ≥75 years found that although MitraClip was associated with improved one-year survival and a lower rate of all acute complications compared with surgical repair, it had lower five-year survival and greater MR recurrence. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have symptomatic primary or secondary MR who receive TMVR using devices other than MitraClip or PASCAL, the evidence includes a randomized study, nonrandomized prospective studies, and noncomparative feasibility studies. The relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The randomized, sham-controlled trial for the indirect annuloplasty device Carillon offers promising safety data, however further studies are needed to determine efficacy and long-term outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have valve dysfunction and mitral stenosis or regurgitation after prior bioprosthetic mitral valve replacement, who are at a high or prohibitive risk for redo surgical mitral valve replacement (rSMVR), and who receive a transcatheter mitral valve-in-valve replacement (TMViVR) using an FDA-approved device, the evidence includes two meta-analyses, eight comparative retrospective cohort studies, and nine observational studies. Relevant outcomes are OS, morbid events, functional outcomes, and treatment-related morbidity. The meta-analyses had mixed early-term findings, with one observing a benefit for in-hospital mortality favoring TMViVR over rSMVR, but at 30 days, 1-year, and 2-year follow-up, no difference between groups in OS was observed in either review. Both analyses found that complications of stroke, renal dysfunction, vascular complications, pacemaker implantation, and

bleeding were more common in the rSMVR group. The comparative studies generally found that mortality was equivalent or favored TMViVR through 1-year follow-up; however, several studies that reported longer-term outcomes observed that the trend in mortality was reversed with numerically higher rates in the TMViVR group. TMViVR was associated with a shorter hospital or ICU stay than rSMVR. Several adverse events (acute kidney injury, cardiac arrest, cardiogenic shock, major bleeding, pacemaker implantation, pneumonia, sepsis, stroke, and vascular complications) were more commonly reported in the rSMVR group compared to TMViVR. These results were supported by observational data, which provided data on mortality, functional outcomes, and complications through up to 7 years post-implantation. The evidence base is limited primarily by the lack of experimental studies, but assigning patients who are at high or prohibitive risk for open surgery to rSMVR is ethically prohibitive so retrospective comparisons will likely continue to represent the best available evidence for this intervention. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02444338	A RandomizEd Study of tHe MitrACliP DEvice in Heart Failure Patients With Clinically Significant Functional Mitral Regurgitation (RESHAPE-HF)	505	Apr 2024 (completed)
NCT04009434	Treatment of Concomitant Mitral Regurgitation by Mitral Valve Clipping in Patients With Successful Transcatheter Aortic Valve Implantation	1162	Aug 2023 (unknown status)
NCT01626079[a]	Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (The COAPT Trial) and COAPT CAS (COAPT)	614 in COAPT and 162 in COAPT CAS	July 2024 (5-year follow-up per protocol)[b]

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT04198870[a]	Percutaneous MitraClip Device or Surgical Mitral Valve REpair in PAtients With PrImaRy MItral Regurgitation Who Are Candidates for Surgery (REPAIR MR)	500	Feb 2032
NCT05090540	Transcatheter Edge to Edge Mitral Valve Repair Versus Standard Surgical Mitral Valve Operation for Secondary Mitral Regurgitation	600	Mar 2025
NCT05051033	Percutaneous or Surgical Repair In Mitral Prolapse And Regurgitation for >65 Year-Olds (PRIMARY)	450	Jan 2032
NCT05021614[a]	Evaluation of the Efficacy and Safety of the Transcatheter Mitral Valve Repair System in Patients With Moderate and Above Degenerative Mitral Regurgitation at High Surgical Risk	150	Sep 2027
NCT04734756[a]	A Prospective, Multicenter, Objective Performance Criteria Study to Evaluate the Safety and Effectiveness of Dragonfly Transcatheter Mitral Valve Repair System for the Treatment of Degenerative Mitral Regurgitation (DMR) Subjects	120	May 2027
NCT04733404[a]	A Prospective, Multicenter, Objective Performance Criteria Study to Evaluate the Safety and Effectiveness of Dragonfly Transcatheter Mitral Valve Repair System for the Treatment of Functional Mitral Regurgitation (FMR) Subjects	120	Sep 2027
NCT04430075[a]	Transcatheter Repair of Mitral Regurgitation With Edwards PASCAL Transcatheter Valve Repair System: A European Prospective, Multicenter Post Market Clinical Follow-Up (PMFC)	500	Jun 2028
NCT03706833[a]	Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial (CLASP IID/IIF): A Prospective, Multicenter, Randomized, Controlled Pivotal Trial to Evaluate the Safety and Effectiveness of Transcatheter Mitral Valve Repair With the Edwards PASCAL Transcatheter Valve Repair System Compared to Abbott MitraClip in Patients With Mitral Regurgitation	1275	Jan 2028
NCT05332782	Outcomes of Patients tReated with Mitral Transcatheter Edge-to-edge Repair for Primary Mitral Regurgitation Registry (PRIME-MR)	2000	Jan 2026
NCT05496998[a]	Transcatheter Mitral Valve Replacement With the Medtronic IntrepidTM TMVR Transfemoral System in	360	Nov 2026

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Patients With Severe Symptomatic Mitral Regurgitation - APOLLO-EU Trial		
NCT05417945[a]	A Prospective, Multicenter Study to Evaluate the JensClip Transcatheter Valve Repair System	124	Dec 2024
NCT05455489	GISE Registry of Transcatheter Treatment of Mitral Valve Regurgitation With the MitraClip G4	264	Aug 2029
NCT03271762	Multicentre and Randomized Study of MITRACLIP® Transcatheter Mitral Valve Repair in Patients With Severe Primary Mitral Regurgitation Eligible for High-risk Surgery	330	May 2027
NCT04402931	Randomized Trial of Transcatheter Valve-in-Valve Intervention vs Redo Surgery for the Treatment of Structural Mitral Bioprosthetic Dysfunction	150	Dec 2031
NCT03193801	PARTNER 3 Trial - SAPIEN 3 Transcatheter Heart Valve Implantation in Patients With a Failing Mitral Bioprosthetic Valve	53	Aug 2031

NCT: national clinical trial

[a] Denotes industry-sponsored or cosponsored trial. [b] Primary results have been published; long-term follow-up ongoing.

Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or the National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that

are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology and American Heart Association

In 2020, the American College of Cardiology and American Heart Association presented updated expert consensus on the management of mitral regurgitation (MR).[92] The recommendations are as follows: "At present, transcatheter mitral repair using an edge-to-edge clip device can be considered for the treatment of patients with primary MR and severe symptoms who are felt to be poor surgical candidates. Surgical or transcatheter treatment for secondary MR is undertaken only after appropriate medical and device therapies have been instituted and optimized, as judged by the multidisciplinary team with input from a cardiologist with experience managing heart failure and MR."

Also in 2020, the American College of Cardiology and American Heart Association released updated guidelines on the management of valvular heart disease.[5] The guidelines state that TMVR is of benefit to individuals with severely symptomatic primary MR who are at high or prohibitive risk for surgery, and to a subset of individuals with secondary MR who remain severely symptomatic despite guideline-directed management and therapy for heart failure. Individuals who have prosthetic valve stenosis are recommended to be offered revision surgery, but for severely symptomatic patients who are at high risk for surgery, a transcatheter aortic valve-in-valve procedure may be reasonable (B level of evidence, moderate class of recommendation); no recommendation is given regarding mitral valve-in-valve procedures. Relevant recommendations on interventions for primary and secondary MR are shown in **Table 2**.

Table 2. Recommendations on Interventions for Primary and Secondary MR

Recommendation	COR	LOE
Primary MR		
In symptomatic patients with severe primary MR (Stage D), mitral valve intervention is recommended irrespective of LV systolic function	1 (Strong)	B-NR[1]
In asymptomatic patients with severe primary MR and LV systolic dysfunction (LVEF <60%, LVESD >40 mm) (Stage C2), mitral valve surgery is recommended	1 (Strong)	B-NR[1]

Recommendation	COR	LOE
In patients with severe primary MR for whom surgery is indicated, mitral valve repair is recommended in preference to mitral valve replacement when the anatomic cause of MR is a degenerative disease, if a successful and durable repair is possible	1 (Strong)	B-NR[1]
In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF >60% and LVESD >40 mm) (Stage C1), mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1% when it can be performed at a Primary or Comprehensive Valve Center	2a (Moderate)	B-NR[1]
In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF >60% and LVESD <40 mm) (Stage C1) but with a progressive increase in LV size or decrease in EF on ≥3 serial imaging studies, mitral valve surgery may be considered irrespective of the probability of a successful and durable repair	2b (Weak)	C-LD[2]
In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, TEER is reasonable if mitral valve anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year	2a (Moderate)	B-NR[1]
In symptomatic patients with severe primary MR attributable to rheumatic valve disease, mitral valve repair may be considered at a Comprehensive Valve Center by an experienced team when surgical treatment is indicated, if a durable and successful repair is likely	2b (Weak)	B-NR[1]
In patients with severe primary MR where leaflet pathology is limited to less than one half the posterior leaflet, mitral valve replacement should not be performed unless mitral valve repair has been attempted at a Primary or Comprehensive Valve Center and was unsuccessful	3: Harm (Strong)	B-NR[1]
Secondary MR		
In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal GDMT for HF (Stage D), TEER is reasonable in patients with appropriate anatomy as defined on TEE and with LVEF between 20% and 50%, LVESD <70 mm, and pulmonary artery systolic pressure <70 mmHg	2a (Moderate)	B-R[3]
In patients with severe secondary MR (Stages C and D), mitral valve surgery is reasonable when CABG is undertaken for the treatment of myocardial ischemia	2a (Moderate)	B-NR[1]
In patients with chronic severe secondary MR from atrial annular dilation with preserved LV systolic function (LVEF >50%) who have severe persistent symptoms (NYHA class III or IV) despite therapy for HF and therapy for associated AF or other comorbidities (Stage D), mitral valve surgery may be considered	2b (Weak)	B-NR[1]
In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent severe symptoms (NYHA class III or IV) while on optimal GDMT for HF (Stage D), mitral valve surgery may be considered	2b (Weak)	B-NR[1]
In patients with CAD and chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) (Stage D) who are undergoing mitral valve surgery because of severe	2b (Weak)	B-R[3]

Recommendation	COR	LOE
symptoms (NYHA class III or IV) that persist despite GDMT for HF, chordal-sparing mitral valve replacement may be reasonable to choose over downsized annuloplasty repair		
Intervention for Prosthetic Valve Stenosis		
In patients with symptomatic severe stenosis of a bioprosthetic or mechanical prosthetic valve, repeat surgical intervention is indicated unless the surgical risk is high or prohibitive	1 (Strong)	B-NR1
For severely symptomatic patients with bioprosthetic aortic valve stenosis and high or prohibitive surgical risk, a transcatheter ViV procedure is reasonable when performed at a comprehensive valve center	2a (Moderate)	B-NR1
For patients with significant bioprosthetic valve stenosis attributable to suspected or documented valve thrombosis, oral anticoagulation with a VKA is reasonable	2a (Moderate)	B-NR1

Source: Adapted from Otto et al (2020)[5]

[1]Moderate, nonrandomized; [2]Limited data; [3]Moderate, randomized.

AF: atrial fibrillation; CABG: coronary artery bypass graft; CAD: coronary artery disease; COR: class of recommendation; EF: ejection fraction; GDMT: guideline-directed medical therapy; HF: heart failure; LOE: level of evidence; LV: left ventricular; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameters; MR: mitral regurgitation; MV: mitral valve; NYHA: New York Heart Association; TEE: transesophageal echocardiogram; TEER: transcatheter edge-to-edge repair; ViV: valve-in-valve; VKA, vitamin K antagonist.

American College of Cardiology, American Association for Thoracic Surgery, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

The American College of Cardiology, American Association for Thoracic Surgery, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons (2014) issued a position statement on transcatheter therapies for mitral regurgitation (MR).[93] This statement outlined critical components for successful transcatheter MR therapies and recommended ongoing research and inclusion of all individuals treated with transcatheter MR therapies in a disease registry.

The European Society of Cardiology and the European Association for Cardio-Thoracic Surgery

The European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) issued guidelines on the management of valvular heart disease in 2022.[8] A new position on the management of prosthetic valve dysfunction was issued, stating, "Transcatheter

valve-in-valve implantation in the mitral and tricuspid position may be considered in selected patients at high risk for surgical intervention." This recommendation was given a class IIb recommendation, indicating that there is conflicting evidence about the usefulness or efficacy of this treatment, with the opinion being supported by less well-established evidence.

National Institute for Health and Care Excellence

The NICE guideline on heart valve disease management (2021) makes the following recommendations related to TMVR:[94]

- "1.5.10 - Consider transcatheter edge-to-edge repair, if suitable, for adults with severe primary mitral regurgitation and symptoms, if surgery is unsuitable.
- 1.5.14 - Consider transcatheter mitral edge-to-edge repair for adults with heart failure and severe secondary mitral regurgitation, if surgery is unsuitable and they remain symptomatic on medical management."

Another NICE guideline was issued in 2021 on the use of transapical transcathter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis:[95],

- "1.1 - Evidence on the safety of transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis is adequate and shows some serious but well recognized complications. Evidence on its efficacy is limited in quality. So, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research."
- "1.4 - Patient selection should be done by a multidisciplinary team which must include interventional cardiologists experienced in the procedure, cardiac surgeons, an expert in cardiac imaging, and where appropriate, a cardiac anaesthetist and a specialist in medicine for older people. The multidisciplinary team should determine the risk level for each patient and the device most suitable for them."
- "1.6 - The procedure is technically challenging and should only be done in specialized centers, and only by clinical teams with special training and experience in complex endovascular cardiac interventions, including regular experience in transcatheter valve implantation procedures. Centers doing these procedures should have cardiac surgical support for emergency treatment of complications and subsequent patient care."
- "1.7 - NICE encourages further research into transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis. Studies should

include details on patient selection, type and size of valve used, functional outcomes (New York Heart Association functional class, mitral valve regurgitation), quality of life, patient reported outcome measures, survival and complications. Studies should report long term follow up of clinical outcomes and valve durability. NICE may update this guidance on publication of further evidence."

Medicare National Coverage

The Centers for Medicare & Medicaid Services issued a national coverage decision for the use of TMVR in 2015, which was updated in 2021.[96]

The Centers for Medicare & Medicaid Services determined that it would cover TMVR under Coverage with Evidence Development for the treatment of symptomatic moderate-to-severe or severe functional (secondary) MR or significant symptomatic degenerative (primary) MR when all of the following conditions are met:

1. "The procedure is furnished with a [TMVR] system that has received FDA [Food and Drug Administration] premarket approval (PMDA).
2. The patient (preoperatively and postoperatively) is under the care of a heart team...
3. Each patient's suitability for surgical mitral valve repair, [TMVR], or palliative therapy must be evaluated, documented…
4. An interventional cardiologist or cardiac surgeon from the heart team must perform the mitral valve [TMVR]...
5. Mitral valve [TMVR] must be furnished in a hospital with appropriate infrastructure and experience...
6. The heart team and hospital are participating in a prospective, national, audited registry...
7. The registry shall collect all data necessary and have a written executable analysis plan..."

Regulatory Status

In October 2013, the MitraClip Clip Delivery System (Abbott Vascular) was approved by the FDA through the premarket approval process for treatment of "significant symptomatic mitral regurgitation (MR ≥3+) due to primary abnormality of the mitral apparatus (degenerative MR) in

patients who have been determined to be at a prohibitive risk for mitral valve surgery by a heart team."[19]

In June 2017, the Edwards SAPIEN 3 Transcatheter Heart Valve received FDA approval through the premarket approval process for the treatment of patients with a "failing surgical bioprosthetic mitral valve who have been determined to be at high or greater risk for open-heart surgery by a heart team."

In March 2019, the FDA approved a new indication for MitraClip for "treatment of patients with normal mitral valves who develop heart failure symptoms and moderate-to-severe or severe mitral regurgitation because of diminished left heart function (commonly known as secondary or functional mitral regurgitation) despite being treated with optimal medical therapy. Optimal medical therapy includes combinations of different heart failure medications along with, in certain patients, cardiac resynchronization therapy and implantation of cardioverter defibrillators."

In September 2022, the FDA approved the PASCAL Precision Transcatheter Valve Repair System through the premarket approval process for treatment of "significant, symptomatic mitral regurgitation (MR ≥3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team."[20]

FDA product code for MitraClip and PASCAL: NKM.

FDA product code for Edwards SAPIEN 3: NPV

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Appendix

Figure 1

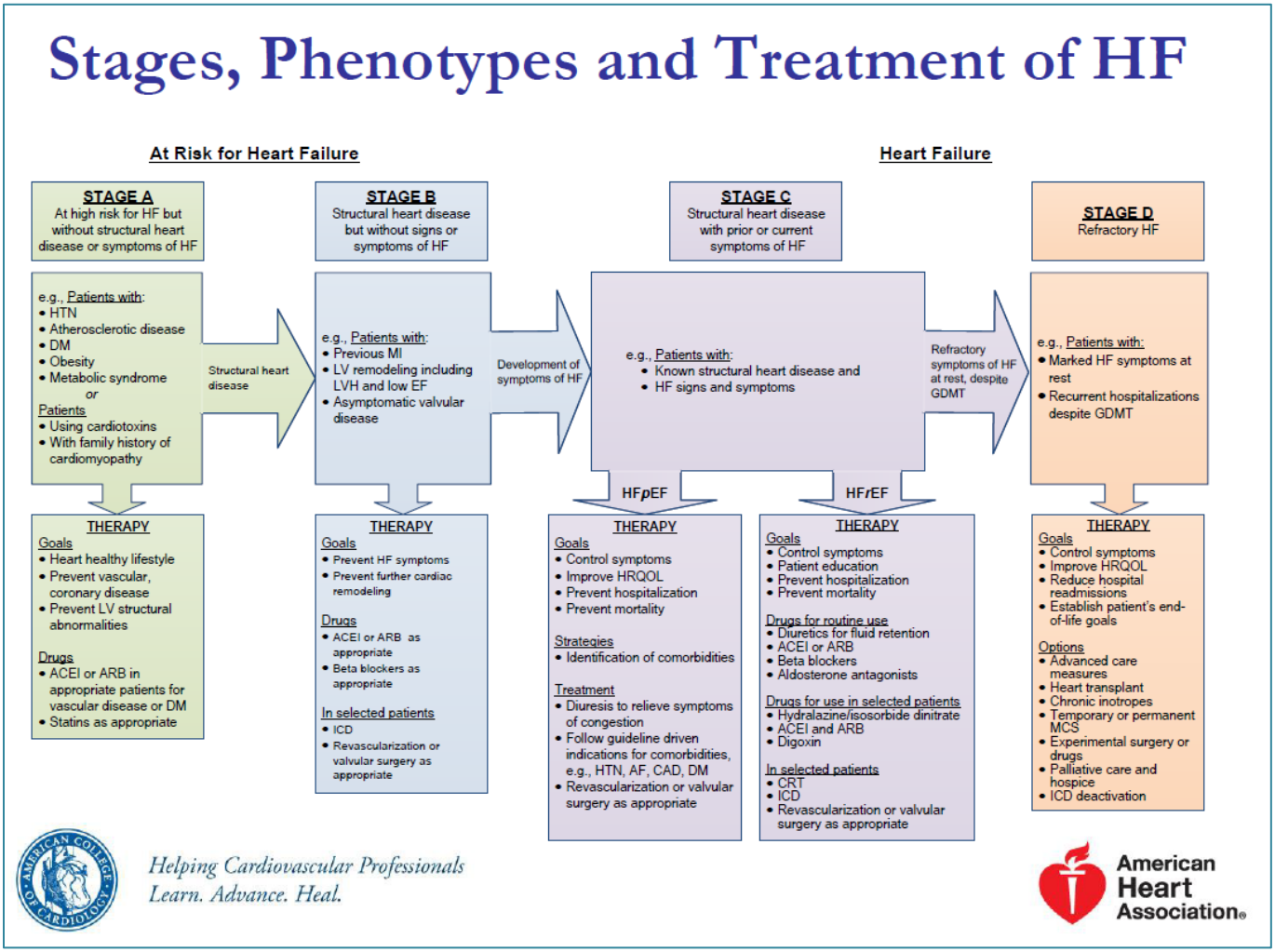
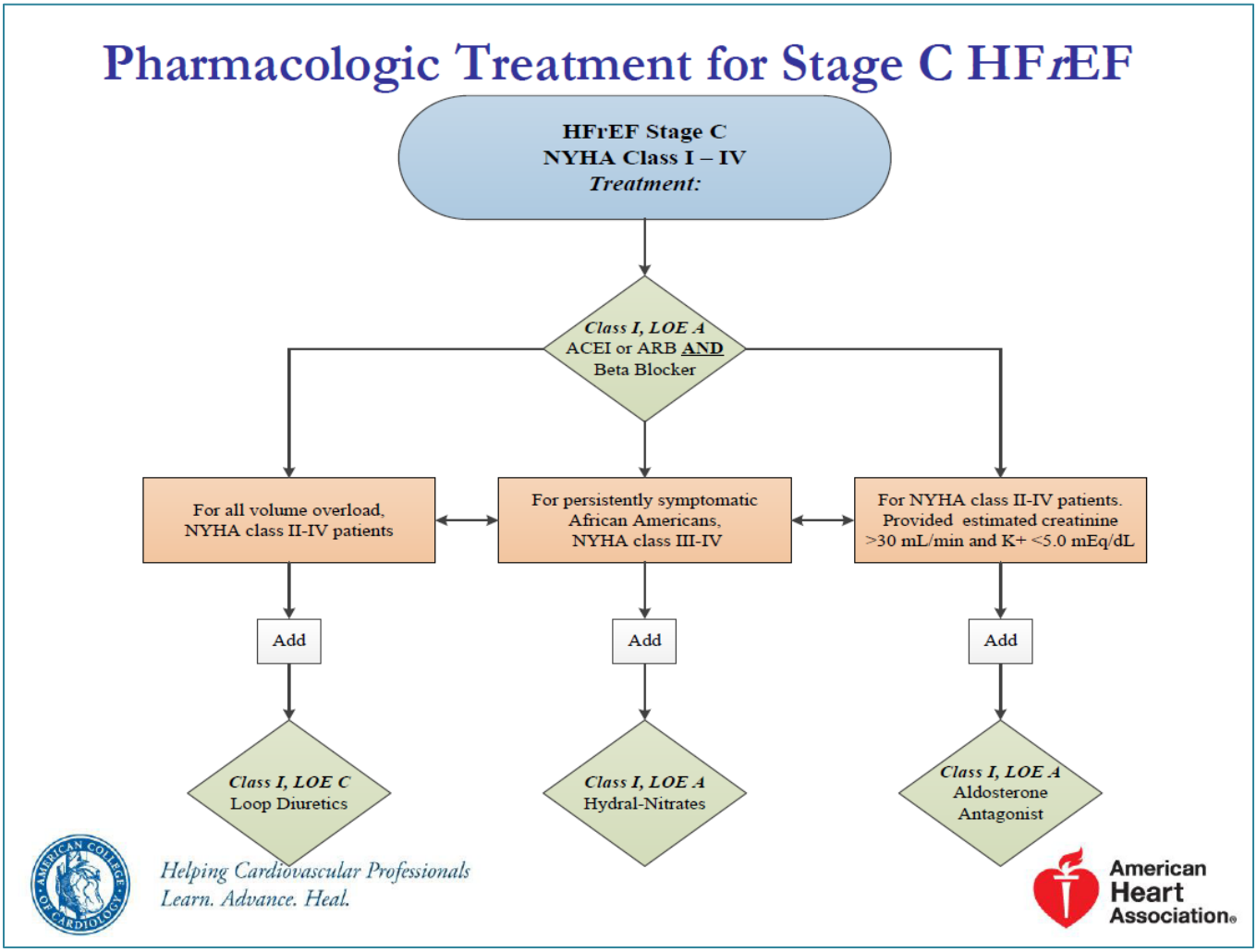

Stages, Phenotypes and Treatment of HF
At Risk for Heart Failure
Heart Failure
STAGE A
At high risk for HF but without structural heart disease or symptoms of HF
STAGE B
Structural heart disease but without signs or symptoms of HF
STAGE C
Structural heart disease with prior or current symptoms of HF
STAGE D
Refractory HF
e.g., Patients with:
• HTN
• Atherosclerotic disease
• DM
• Obesity
• Metabolic syndrome
or
Patients
• Using cardiotoxins
• With family history of cardiomyopathy
Structural heart disease
e.g., Patients with:
• Previous MI
• LV remodeling including LVH and low EF
• Asymptomatic valvular disease
Development of symptoms of HF
e.g., Patients with:
• Known structural heart disease and
• HF signs and symptoms
Refractory symptoms of HF at rest, despite GDMT
e.g., Patients with:
• Marked HF symptoms at rest
• Recurrent hospitalizations despite GDMT
HFpEF
HFrEF
THERAPY
Goals
• Heart healthy lifestyle
• Prevent vascular, coronary disease
• Prevent LV structural abnormalities
Drugs
• ACEI or ARB in appropriate patients for vascular disease or DM
• Statins as appropriate
THERAPY
Goals
• Prevent HF symptoms
• Prevent further cardiac remodeling
Drugs
• ACEI or ARB as appropriate
• Beta blockers as appropriate
In selected patients
• ICD
• Revascularization or valvular surgery as appropriate
THERAPY
Goals
• Control symptoms
• Improve HRQOL
• Prevent hospitalization
• Prevent mortality
Strategies
• Identification of comorbidities
Treatment
• Diuresis to relieve symptoms of congestion
• Follow guideline driven indications for comorbidities, e.g., HTN, AF, CAD, DM
• Revascularization or valvular surgery as appropriate
THERAPY
Goals
• Control symptoms
• Patient education
• Prevent hospitalization
• Prevent mortality
Drugs for routine use
• Diuretics for fluid retention
• ACEI or ARB
• Beta blockers
• Aldosterone antagonists
Drugs for use in selected patients
• Hydralazine/isosorbide dinitrate
• ACEI and ARB
• Digoxin
In selected patients
• CRT
• ICD
• Revascularization or valvular surgery as appropriate
THERAPY
Goals
• Control symptoms
• Improve HRQOL
• Reduce hospital readmissions
• Establish patient's end-of-life goals
Options
• Advanced care measures
• Heart transplant
• Chronic inotropes
• Temporary or permanent MCS
• Experimental surgery or drugs
• Palliative care and hospice
• ICD deactivation
Helping Cardiovascular Professionals
Learn. Advance. Heal.
American Heart Association.

Figure 2



Source: https://www.heart.org/idc/groups/heart-public/@wcm/@mwa/documents/downloadable/ucm_489089.pdf Now archived.

History

Date	Comments
09/08/14	New Policy. Policy created with literature review through June 4, 2014. Transcatheter mitral valve repair considered investigational for all indications.
01/12/15	Coding update. New CPT codes 33418-33419, effective 1/1/15, added to policy; codes 0343T and 0344T deleted 12/31/14 noted on policy.

Date	Comments
12/08/15	Annual Review. Added policy statement that Transcatheter mitral valve repair with the MitraClip is now medically necessary to treat degenerative mitral regurgitation when criteria are met. (Previously considered Investigational). Updated Policy Guidelines, with clarification about documented presence of risk score from one of the stated tools in the prohibitive risk definition. Added FDA indications for use. Policy updated with literature review through June 1, 2015; references added. Policy statement changed as noted. Codes 0343T and 0344T removed as deleted from codebook effective 12/31/14.
02/01/16	Coding update. Added 93799.
08/01/16	Annual Review, approved July 12, 2016. Policy updated with literature review through March 30, 2016; references 25, 29, 31, 37, and 41 added. Policy statements unchanged.
10/21/16	Minor formatting edit. Restored reference hyperlinks.
08/01/17	Annual Review, approved July 11, 2017. Policy moved into new format. Policy updated with literature review through March 23, 2017; references 27-28 and 36 added. "Cleared" changed to "approved" in the medically necessary policy statement.
01/23/18	Coding update, added CPT codes 0483T and 0484T (new codes effective 1/1/18).
08/01/18	Annual Review, approved July 13, 2018. Policy updated with literature review through March 2018; references 29, 34-35, and 53 added. In the policy degenerative mitral regurgitation was replaced with primary mitral regurgitation and functional mitral regurgitation was replaced with secondary mitral regurgitation including the policy statement to be in consistent with language used in the guidelines. Data from FDA documents were added. Removed CPT code 93799.
07/01/19	Coding update, added CPT code 0544T (new code effective 7/1/19).
08/01/19	Annual Review, approved July 11, 2019. Policy updated with literature review through March 2019, references 50-51 added. Regulatory Status section updated with new indication. Policy statement added; transcatheter mitral valve repair with an FDA-approved device considered medically necessary for patients with heart failure and secondary mitral regurgitation despite the use of maximally tolerated guideline-directed medical therapy. Information regarding optimal medical therapy added. Removed CPT 0483T and 0484T.
04/01/20	Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020.
06/26/20	Policy will remain active and will no longer be deleted effective July 2, 2020.
07/02/20	Minor update. Related policy 7.01.132 removed; this policy is deleted and replaced with InterQual criteria.
01/01/21	Annual Review, approved December 1, 2020. Policy updated with literature review through March 23, 2020; references added. Policy statements unchanged.

Date	Comments
08/01/21	Annual Review, approved July 9, 2021. Policy updated with literature review through March 30, 2021; references added; guidelines section updated. Policy statements unchanged.
08/01/22	Annual Review, approved July 11, 2022. Policy updated with literature review through March 16, 2022; references added to review of evidence for 'Other Transcatheter Mitral Valve Repair Devices'; guidelines section updated. Minor editorial refinements to policy statements; intent unchanged.
08/01/23	Annual Review, approved July 10, 2023. Policy updated with literature review through March 13, 2023; references added. Policy statements unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/24	Coding update. Added descriptions in parenthesis for CPT codes 0544T, 33418 and 33419.
10/01/24	Annual Review, approved September 10, 2024. Policy updated with literature review through March 6, 2024; title changed to 'Transcatheter Mitral Valve Repair or Replacement'; new indication for transseptal valve-in-valve replacement considered medically necessary when criteria are met; references added. Added CPT codes 0483T and 0484T.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.