Innovative Approaches to Mitral Valve Repair and Replacement

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Introduction

Minimally invasive valve surgery in its most comprehensive definition involves any procedure to replace or repair a heart valve without a full sternotomy. It is not a single approach but more of a constellation of different techniques and technologies that are specific to this type of procedure. They include various enhanced visualization or exposure devices and instrumentation, as well as modified perfusion techniques, used with the ultimate goal of minimizing surgical trauma by limiting the surgical incision. Types of access typically used include partial upper or lower sternotomy with a T or J transection of the sternum, and mini-thoracotomy approaches using videoscopic or robotic assistance or direct vision.

Reported advantages of these procedures over their open surgical analogues include shorter hospital and intensive care unit stays, less postoperative pain, a more cosmetically acceptable incision, lower thoracic wound infection rates, less use of blood products, better postoperative respiratory function, a more rapid return to baseline functional status, greater patient satisfaction, and lower hospital costs [1–4]. These advantages mimic those observed with minimally invasive techniques used in other fields. Concerns remain, however, that there is a tradeoff of limited exposure against safety, operative length—including cardiopulmonary bypass time and duration of cross-clamping (if used)—ability to adequately evacuate air from the heart, quality of valve repair, potential vascular and cerebrovascular complications, and a long learning curve.

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The recent development and implementation of transcatheter mitral valve (MV) replacement and repair technologies, while representing the pinnacle of minimally invasive ideals, will for the near future remain limited in scope because of the heterogeneity of the MV, technical challenges, and lack of long-term data regarding durability and results. Nonetheless, transvenous/transseptal access to the MV for deployment of a mitral clip has benefited a subset of patients. Newer technologies have been developed to access and repair the MV via a transapical approach. These transcatheter/transapical approaches have been named "micro" invasive procedures to differentiate them from techniques that require cardiopulmonary bypass (CPB). Less-invasive approaches, whether surgical or transcatheter, will continue to evolve and play a major role in cardiovascular therapies.

Evolution

Minimally invasive MV surgery has undergone an evolution of different techniques and philosophies. In this chapter, we review the evolution of the procedure, including the development of CPB techniques, surgical incisions, and approaches that have led the way to its current state. In addition, we review different techniques for replacing and repairing the MV in different disease states.

The first successful use of CPB by John Gibbon in 1953 paved the way to allowing correction of complex cardiac anomalies in a bloodless field [5]. The first documented minimally invasive approach to both aortic and mitral valve disease through a right parasternal incision is attributed to Cosgrove and colleagues in 1996 [6]. Concurrently, improvements were made to minimize the circulating blood volume through a bypass circuit, with the objective of diminishing the inflammatory reaction caused by CPB. Cannulas became smaller and longer and were manufactured with non-kinking materials to maximize flow dynamics. Application of carbon dioxide to displace the oxygen in the operative field has reduced the risk of air embolism. In addition, the advent and routine use of intraoperative transesophageal echocardiography (TEE) has

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aided in both confirming cannula placement and ensuring proper removal of air [7].

One of the most significant advances in the evolution of minimally invasive valve surgery is the development of alternative methods of establishing CPB. Because these procedures do not fully expose the heart, alternative techniques involving central aortic or peripheral cannulation via the femoral, subclavian/axillary, and/or jugular vessels were required. Additionally, many minimally invasive operations employ hybrid cannulation strategies involving both central and peripheral cannulation. These strategies can be used on an arrested, fibrillating, or even beating heart [8].

Several disadvantages of peripheral arterial cannulation have been documented, including elevated incidences of vascular complications and stroke [9–11]. However, results from several studies of large patient cohorts contradict these findings [12, 13]. In fact, outcomes have been similar whether central arterial or peripheral cannulation was used. Numerous variations of venous cannulation have been tried, as well. The application of vacuum-assisted drainage with a hard-shell reservoir has had a dramatic impact on venous drainage, augmenting the decompression of the right atrium and ventricle. Such drainage is performed directly via the right atrium or percutaneously from the femoral or internal jugular veins [14].

In a similar manner, cardioplegia solution can be administered either antegrade directly into the aorta or retrograde via the coronary sinus with either transjugular access or direct right atrial insertion. Additionally, extended-effect cardioplegia solutions have allowed surgeons to protect the heart for longer periods of time while performing complex valvular reconstructions.

In the beginning, minimally invasive MV operations were performed through a right parasternal incision. This required resecting the third and fourth costal cartilages, which led to significant chest-wall deformities and paradoxical chest-wall motion [15]. Thereafter, for many surgeons, ministernotomy with a T or L transection of the sternum in the fourth or fifth intercostal space became the incision of choice for minimally invasive mitral-valve repairs [16, 17]. This allows central cannulation and facilitates conversion to median sternotomy if necessary. Other incisions have included a right thoracotomy, right infra-axillary thoracotomy [18], transsternal approach [19], inverted T-sternotomy [20], and "V"-incision [1]. Today, a right mini-thoracotomy in the fourth or fifth intercostal space is the most widely used approach.

In addition, innovative technologies have been developed to facilitate minimally invasive cardiac surgery. The port-access, keyhole, or "Heart Port" method was one of the first to use aortic occlusion with an endoaortic balloon inserted through a peripheral artery, along with a retrograde cardioplegia catheter inserted through the right internal jugular vein [21]. An alternative method that is commonly used today is direct aortic clamping either via a separate port or directly through the incision [22].

In 1996, Carpentier described the use of 2-D video thoracoscopic assistance to improve visualization of the MV [23]. Shortly thereafter, a 3D version was developed to improve depth perception. In an attempt to further facilitate the procedure, a voice-activated robotic arm was attached to the scope (AESOP 3000, Computer Motion, Inc., CA, USA), allowing mitral surgery to be performed by a single surgeon [24].

In 1998, Carpentier also became the first surgeon to perform a MV operation using a robotic system, the Da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) [25]. This telemanipulator allowed the surgeon to sit at a console and remotely control surgical instruments in the operative field with 360 degrees of motion. Robotic surgical systems were met with great enthusiasm initially but were not widely adopted because they involved an extremely steep learning curve. In addition, operative times and costs are often greater for robotic surgery than for traditional sternotomy approaches, except at a few expert centers. Nonetheless, newer generations of the Da Vinci Surgical System have been developed, and other corporations—including Google, which has teamed up with Johnson & Johnson (Verb Surgical), Medtronic, and Cambridge Medical Robotics (Versius)—are now introducing their own versions of the robotic system.

Minimally Invasive Surgical Approaches for the Mitral Valve

The most common surgical approach to the MV is through a median sternotomy with central aortic and right atrial cannulation. The MV is exposed through the intra-atrial groove or the right atrium with either a transseptal exposure or a superior approach through the dome of the left atrium.

Less-invasive approaches to the MV have also been devised. The most common include a right mini-thoracotomy with direct visualization, video thoracoscopic visualization, and robotic surgical assistance. The most important considerations are that the patient's safety not be compromised and that the mitral repair be effective and durable.

Comorbidities and Anatomic Considerations

A complete history and physical exam to identify all comorbidities should be routine before any cardiac operation. In addition, computed tomography (CT) imaging can help to determine whether a patient is a good candidate for a minimally invasive approach. When such an approach is planned, careful screening is necessary for several pertinent comor-

bidities. Significant lung disease is of particular concern in minimally invasive surgery because this approach may require single-lung ventilation. Furthermore, lung dysfunction places the patient at risk for postoperative respiratory failure. Any patient with symptoms of obstructive lung disease or with a heavy smoking history should be considered for pulmonary function testing.

Any history of chest trauma, chest tube placement, empyema, or chest surgery should be elucidated, because existing adhesions or scarring can complicate efforts to obtain the necessary exposure of the heart. These pulmonary adhesions may require extensive dissection, potentially leading to lung injury. Interestingly enough, imaging cannot detect intraoperative adhesions that would potentially preclude a right mini thoracotomy approach.

If a chest radiograph shows the right border of the heart adjacent to the right border of the vertebral column, the heart might be displaced toward the left side of the chest. In addition, the surgeon should know if the patient has breast implants, as these can complicate placement of the atrial retraction system. Significant obesity or extensive chest-wall musculature can place the MV further away from the surgeon, also potentially compromising exposure.

Physical examination and a CT scan help identify congenital and traumatic chest-wall and skeletal deformities that can compromise exposure during minimally invasive mitral surgery. In these specific cases, preoperative screening can potentially prevent conversion by identifying aberrant or challenging anatomy.

Although the aforementioned barriers can potentially complicate minimally invasive right thoracotomy surgery, none of them definitively contraindicate it.

Peripheral vascular disease, aortic aneurysmal disease, and aortic calcification are also of particular concern. Minimally invasive surgery often involves cannulating the femoral vessels for retrograde arterial perfusion, as well as aortic occlusion with a cross-clamp or endoaortic balloon. Existing peripheral vascular disease may preclude safe aortic cross-clamping or peripheral cannulation, thereby placing the patient at risk for perioperative limb ischemia. A complete physical examination should be made of the femoral and peripheral pulses. Any abnormalities on examination or a history of prior vascular disease warrants additional testing. Noninvasive vascular screening can be a useful adjunct to the physical exam. A more detailed assessment is obtained with CT angiography of the chest, abdomen, and pelvis, including the femoral vessels. This scan can reveal vascular dissection, thrombus, aneurysmal dilation, and occlusive disease, all of which contraindicate minimally invasive surgery. Patients with an aortic diameter >4 cm may not be suitable candidates for endoaortic balloon occlusion. A calcified aorta does not contraindicate mitral surgery, but identifying it preoperatively enables the surgeon to be prepared to perform the procedure on a fibrillating heart if necessary. In addition, evaluating the venous phase on CT can help identify barriers to successful peripheral venous cannulation, especially for patients with a history of iliofemoral deep vein thrombosis or an inferior vena cava filter. Having such a filter does not definitively contraindicate femoral venous cannulation, but cannulation should be attempted with fluoroscopic guidance.

In addition, obesity and overlying pannus can interfere with femoral cannulation and place the patient at risk for infection. Evidence of fungal infection in the groin should prompt consideration of alternate cannulation sites.

Coronary artery disease, coexisting valvular disease, reduced left ventricular ejection fraction (LVEF), right ventricular dysfunction, and severe pulmonary hypertension are additional comorbidities that should be screened for. Echocardiography should be completed on all patients preoperatively and can identify many of these comorbidities. Left heart catheterization identifies coronary disease, potentially allowing hybrid approaches with percutaneous coronary intervention and, thereafter, valve surgery in selected patients. The American Heart Association (AHA) guidelines recommend left heart catheterization for male patients over 40 and postmenopausal women undergoing valvular surgery [26]. The need for concomitant coronary revascularization may be considered a relative contraindication to minimally invasive MV replacement unless the revascularization can be performed percutaneously. Concomitant tricuspid valve and even aortic valve surgery is not a contraindication. A minimally invasive approach through the right chest can incur longer ischemic times, which places patients with severely decreased LVEF, depressed right ventricular function, and severe pulmonary hypertension at high risk if the surgeons are inexperienced. In addition, topical cooling of the heart may not be possible with a minimally invasive approach.

The only definitive contraindication to a less-invasive approach is the inability to cannulate the patient safely. Although challenging to address, anatomical variants and associated comorbidities are not definitive contraindications to minimally invasive MV surgery.

Additional Considerations

Other important factors may influence patient selection for minimally invasive mitral surgery. For example, for most reoperative MV procedures, a minimally invasive approach should be considered. Performing the procedure through the right chest and avoiding a redo sternotomy limits the associated risk of iatrogenic injuries. In the majority of cases, a right chest approach provides a field with fewer adhesions. In addition, some patients with prior stroke, limited mobility, or increased frailty may benefit from the avoidance of a

sternotomy. Furthermore, many of the relative contraindications to minimally invasive surgery can be overcome with surgeon experience and modified operative techniques. Inserting transjugular retrograde coronary perfusion cannulas and pulmonary artery vents can augment cardiac protection and heart decompression in patients with existing coronary disease or aortic insufficiency. Retrograde cannulas can also be inserted directly into the right atrium from the operating port. Cold fibrillatory arrest may be an option for patients with extensive pericardial adhesions, aortic disease precluding cross-clamp or endoaortic balloon placement, or prior coronary artery bypass grafting. Hybrid approaches with percutaneous coronary intervention can further increase candidacy for these procedures. Mitral annular calcification adds significant complexity and thus can be considered a relative contraindication. The feared complication of atrioventricular disruption associated with mitral annular calcification is sometimes difficult to repair for even the most experienced limited-access surgeons. These features can be identified on both preoperative echocardiography and CT angiography. Not only should the pathology of the MV be considered, but any additional valve disease must be considered, as well. Aortic regurgitation is of particular interest, as it may complicate cardiac protection, arrest, and effective decompression and venting. As surgeon experience increases, more complex repairs, as well as concomitant procedures, can be completed with a minimally invasive platform.

Robotic Mitral Valve Surgery

Robotic mitral surgery is more technically challenging and takes longer to learn than other approaches. Patient setup in the operating room is largely the same as in other minimally invasive approaches. The trachea is intubated with either a double-lumen tube or a bronchial blocker. In some cases, a pulmonary EndoVent and transjugular retrograde cardioplegia cannula (Edwards Lifesciences, Irvine, CA, USA) are inserted. The patient is positioned with the right chest elevated by a scapula roll. The right arm hangs off the table with the elbow slightly flexed. Defibrillator pads are placed on the posterior and lateral thorax.

Robotic mitral operations usually require peripheral cannulation, usually via the femoral artery and vein, although in some cases, an additional venous cannula is inserted into the superior vena cava (SVC) through the right internal jugular vein. An endoscope port is placed in the fourth intercostal space (ICS), 2–3 cm lateral to the nipple. The right minithoracotomy working port (1.5-cm retractor) is placed in the fourth ICS as well, approximately 4 cm lateral to the camera. The left robotic arm enters through a port in the second ICS, halfway between the endoscope port and shoulder. The right robotic arm is placed in the sixth ICS in the region of the anterior axillary line. An atrial lift retractor is inserted through an additional port in the fourth ICS medial to the camera port. Aortic occlusion is performed with an endoaortic balloon catheter. In these cases, bilateral radial arterial lines are placed, and care is taken to avoid dampening of the pressures, which signals migration of the balloon and occlusion of the great vessels. If an endoaortic balloon is not used, a sixth incision or port is created in the second ICS, 10 cm posterior to the left robotic arm, for insertion of a transthoracic cross-clamp. Cardioplegia solution is delivered through the endoaortic balloon or, if the aorta is clamped externally, directly into the aortic root with a small cannula. Mitral repair techniques are similar for all minimally invasive approaches. Robotic assisted MV replacement is more challenging and should be reserved for the most experienced robotic surgeons. Suture management is challenging, and the working port needs to be large enough to permit passage of the prosthetic valve. Autoknotting devices may facilitate tying in these cases [27].

Endoscopic Mitral Valve Surgery

The intraoperative setup and patient positioning are essentially similar to those used in a robotic operation. A 4-cm working incision or port is made at the level of the fourth or fifth ICS, starting at the anterior axillary line, and thereafter a soft tissue retractor is placed. Rib spreading with an intercostal rib retractor is avoided in these procedures. Another incision is made at the level of the seventh ICS midaxillary line. Through this incision, a sump suction is tunneled and is subsequently inserted through the left atriotomy and into the left inferior pulmonary vein to help drain the pulmonary venous return. Carbon dioxide is infused into the operative field at 2–3 L/min. This facilitates evacuation of air from the heart. Peripheral cannulation is usually used with video endoscopic procedures. Aortic occlusion can be performed with an endoaortic balloon or direct external aortic clamping through a separate incision. Cardioplegia solution is administered through the endoballoon or a cardioplegia cannula inserted directly into the aortic root.

Once electromechanical arrest of the heart is established, a left atriotomy is performed. Cross-clamping, cardioplegia delivery, pericardiotomy, atriotomy, and closure can be performed with videoscopic assistance or direct vision. A 5-mm trocar is placed 1 intercostal space above and lateral to the working port. A 0° or 30° thoracoscope is inserted through the trocar to directly visualize the MV. After the left atriotomy, an atrial lift retractor is inserted through the working port and connected to a post inserted through a separate stab wound medial to the incision. Long-shafted, manually controlled instruments are inserted through the working port to

perform the mitral repair or replacement. Video endoscopic operations can be challenging and take time to learn [28].

Direct Vision Right Mini-Thoracotomy Mitral Valve Surgery

A single-lumen endotracheal tube is inserted, and double-lung ventilation is used throughout the operation. If visualization of the heart is impaired by the lungs, the lungs are temporarily deflated, or CPB can be instituted early.

Single-lung ventilation with a double-lumen endotracheal tube or bronchial blocker is not commonly performed unless significant pleural adhesions limit visualization and dissection. There are reported cases of unilateral re-expansion pulmonary edema secondary to single-lung ventilation [29, 30].

Transesophageal Echocardiography

Every patient should have a thorough intraoperative 2-D and 3-D TEE assessment. The size of the mitral annulus and anterior leaflet are measured. Left ventricular function is assessed. The MV is further interrogated. Atherosclerotic disease is assessed in the ascending and descending aorta; evidence of grade 4 or 5 free-floating atheroma in the descending aorta should preclude femoral cannulation and retrograde arterial perfusion. The venous cannula is positioned in the SVC under TEE guidance, using a bicaval midesophageal view at 80–100°. In patients with mild-to-moderate aortic insufficiency, TEE is used to obtain a midesophageal four-chamber view at 0° to guide placement of a retrograde cardioplegia cannula.

Intraoperative fluoroscopy can also be used to aid placement of the venous guide wire and cannula when the wire cannot be visualized by TEE. Intraoperative iliac and abdominal aortic angiograms with fluoroscopy are performed when there is uncertainty after insertion of the femoral arterial cannula, or when calcified plaques are encountered during cannulation.

Cannulation and Perfusion

A femoral platform is the access site of choice. Left femoral artery and vein cannulation are preferred because most patients undergo a cardiac catheterization via the right femoral artery. If the surgeon is not yet experienced with this technique, CT angiography should be performed routinely, especially if severe peripheral vascular disease is suspected.

Before cannulation, the patient is fully heparinized (3.3 mg/kg). A 2–3-cm longitudinal skin incision is made above the inguinal crease. In our practice, using this approach, along with limited dissection of the anterior aspect of the vessels, has decreased the incidence of seroma formation. Careful attention is paid to assessing the quality of the artery. The presence of a posterior horseshoe calcified plaque does not contraindicate cannulation, but circumferential calcification does. A purse string suture is placed on the anterior aspect of each vessel. A modified Seldinger technique is used for cannulation. A guide wire is advanced through the femoral artery and subsequently into the proximal descending aorta, and its position is verified by TEE. The wire should pass through without resistance. Thereafter, a cannula is inserted into the artery. The choice of cannula size depends on the patient's body surface area.

If there is any resistance when the cannula is advanced, an alternative access site should be chosen. Additionally, if there are any concerns, an intraoperative angiogram can be performed. If an alternative cannulation site is required, the right axillary artery is the next access point of choice. During axillary cannulation, intraoperative fluoroscopy and angiography are always performed. Because all female patients are positioned with the arm placed over the head, if peripheral vascular disease is present, the axillary artery is cannulated through the axilla. Central cannulation can also be performed, although this is more challenging because of the distance from the incision.

Venous Cannulation

Femoral venous cannulation is performed by using a Seldinger technique. A wire is passed through the femoral vein and into the SVC under TEE guidance. A 0° bicaval view is obtained for placement [31].

Thereafter, a 25 Fr venous cannula is advanced deep into the SVC. To obtain adequate venous drainage, the cannula should be in the SVC, and vacuum drainage should be applied. Vacuum assistance with 35 mmHg of negative suction is applied and increased to 65 mmHg if necessary. The application of negative pressure increases the formation of gaseous microemboli, although this has not been proven to be harmful [32]. Evidence suggests that surpassing 60 mmHg of negative pressure does not increase the incidence of neurological events [33].

There are also instances in which additional venous drainage is required because of right-sided distention or dislodgement of the venous cannula into the right atrium. It is crucial to have adequate decompression of the right side of the heart, because this can lead to postoperative heart failure.

Patient Selection

When compared with standard sternotomy MV surgery, minimally invasive MV surgery appears to benefit higher-risk

patients. These include patients more than 75 years old [2], obese patients (body mass index >30 kg/m^2) [4], patients with chronic obstructive pulmonary disease (COPD) [3], and patients with a low LVEF (<35%) [4].

Several series have demonstrated lower morbidity and mortality with minimally invasive MV procedures in these subsets of patients. Concomitant tricuspid and aortic valve surgery can also be performed. Unlike in minimally invasive AVR surgery, a saphenous vein bypass to the right coronary artery cannot be performed. On the other hand, reoperative MV surgery is feasible in patients with prior valve surgery or coronary revascularization via a right mini-thoracotomy approach [34]. Patients with CAD amendable to PCI can be offered a hybrid approach. A percutaneous intervention can be performed at any time before the minimally invasive valve procedure; in a select few patients, it can be performed afterward. Furthermore, a mini-thoracotomy approach can be offered to patients receiving dual antiplatelet therapy [35].

Surgical Technique

All male patients are positioned with the arm hanging slightly off of the operating table with a scapula roll allowing elevation of the right chest. Female patients are positioned with the scapula roll as well, although the right arm is positioned over the head and the breast is displaced medially to provide additional exposure. A 5–6-cm incision is made at the level of the fourth or fifth intercostal space. A soft-tissue retractor and a rib spreader provide additional exposure. Cardiopulmonary bypass is instituted, and the pericardium is opened and retracted with stay sutures. The aorta is clamped directly through the incision, and cardioplegia solution is administered into the aortic root. If there is mild-to-moderate aortic insufficiency, a retrograde cardioplegia cannula is inserted. Thereafter, an atrial lift retractor is inserted, and the MV is further exposed. If a concomitant ablation or ligation of the atrial appendage is required, it is performed before the MV operation begins. Carbon dioxide is infused into the operative field at a rate of 2 L/min. Infusing a greater volume of CO_2 will raise the patients' CO_2 level during CPB, and sweeping it off will be an arduous task for the perfusionist.

The MV repair or replacement proceeds in the usual fashion, although long-shafted surgical instruments are required. On completion, the left atriotomy is closed and pacing wires are placed on the inferior wall of the right ventricle. The cross-clamp is removed, and deairing is performed with an aortic root vent. Once TEE images confirm adequate air removal, valve function, and valve competency, the patient is weaned from CPB. After protamine is administered, the femoral arterial and venous cannulas are removed. A drain is placed in the pericardium and the right pleural cavity. An intercostal nerve block is performed, and the chest is closed in the usual fashion.

Mitral Valve: Introduction

Mitral valve disease represents the most common valvular disorder worldwide. Although mitral stenosis (MS) is on the decline because of earlier treatment of rheumatic fever, mitral regurgitation (MR) remains a more common valvular disease, especially in developed nations. In the United States, MR is the most frequent valvular disease; nearly 10% of MR patients aged 75 years or older have moderate-to-severe MR [36]. This equates to 4 million affected persons, with an estimated incidence of 250,000 new cases of severe MR per year [36, 37]. Medical therapy has a limited role in these patients' treatment; surgical repair and replacement are the mainstays of therapy [26].

However, a large discrepancy exists between patients who have MV disease and patients who undergo surgical therapy; 2009 data show that only 2% of this potential patient population was treated surgically [38–40]. The reasons for this disparity are multifold. Nearly 50% of symptomatic patients with severe MR are never referred for correction because they are deemed too high risk for surgery. Of the patients referred for surgery, only a fraction actually undergo it; the rest are not treated surgically because of age, comorbidities, or severe LV dysfunction [39]. Mitral regurgitation also has a variable natural history: some patients have stable, mild, or moderate MR for many years, while others' MR progresses over a variable time course.

Etiology and Classification of Mitral Regurgitation

The etiology of MR is multifaceted, with surgical therapy offering different results for MR of different causes. Mitral regurgitation can be classified as either primary (organic) or secondary (functional), depending on the abnormality that leads to the regurgitation, although its pathophysiology varies widely within each category. Differentiating between these two entities is crucial to choosing a therapeutic strategy and predicting its outcome. In addition, it is important to recognize that a single patient's MR can have multiple causes.

Primary or organic MR is an intrinsic valvular abnormality affecting components of the mitral apparatus (i.e., leaflets, annulus, chordae, or papillary muscles). Dysfunction of any of the structures of the MV leads to regurgitation of blood into the atrium during systole. The most common causes of primary MR are degenerative diseases: a variety of conditions that cause abnormalities of the connective tissue, leading to structural changes of the mitral apparatus. Myxomatous degeneration of the MV in its most extensive form is called Barlow disease. The mitral leaflets become thickened and redundant and commonly develop multisegmental prolapse due to a myxoid infiltra-

tion. The valves are typically large, with diffuse chordal elongation and rupture. Carpentier described a "forme fruste" of Barlow disease, understanding that many valves have some but not all of the disease's pathologic features, thus recognizing the spectrum of lesions [41, 42].

Another cause of degenerative MR is fibroelastic disease, in which there is a deficiency of connective tissue. This leads to a deficiency of collagen, elastins, and proteoglycans, causing a thinning of the leaflets. The majority of patients present with a normal-appearing annulus and valve segments with thin and elongated or ruptured chordae. Some patients present with isolated prolapsing segments of the leaflets, which can become thickened from myxoid deposition, but the mechanism of MR is usually rupture of thin chordae tendineae.

Additional causes of primary MR include other connective tissue disorders (Marfan syndrome, Ehlers-Danlos syndrome), osteogenesis imperfecta, pseudoxanthoma elasticum, endocarditis, rheumatic disease, and radiation- or drug-induced valvulopathy. Rheumatic disease is the most prevalent cause of primary MR in developing countries.

Secondary or functional MR is caused by ventricular dysfunction due to dilation, diffuse hypokinesis, or segmental damage secondary to ischemic disease or dilated cardiomyopathy. These changes in the sphericity of the ventricle displace the papillary muscles in an outward and/or apical direction and cause tethering of the leaflets, thus restricting closure during systole. Another, less common cause of functional MR occurs only with left atrial remodeling from atrial fibrillation. In these cases, annular enlargement leads to MR with preserved LV function. In both types of secondary MR, the mitral leaflets are usually structurally normal or nearly normal.

Furthermore, as disease progresses, causes can become mixed; for instance, severe untreated primary MR may lead to ventricular remodeling and associated secondary MR. Multiple causes can also arise concurrently (e.g., ischemic MR with combined degenerative MR), further complicating matters. Although surgical therapy has had good results in primary MR, results in secondary MR have been varied.

Mitral Valve Apparatus Structure and Function

A thorough understanding of MV apparatus structure and function is necessary to understand surgical and percutaneous approaches to MV repair and replacement and their potential advantages and disadvantages. One can conceive of the MV apparatus as being formed by four components: the annulus, leaflets, chordae tendineae, and papillary muscles [43, 44].

The annulus is an ellipsoid, asymmetrical structure that forms the outer perimeter of the MV apparatus. The anterior portion makes up approximately one-third of the annular circumference and consists of a fibrous portion that is in continuity with the aortic annulus [44]. The posterior portion makes up the remaining two-thirds of the annular circumference and is a dynamic structure. The apparatus contains an asymmetric bileaflet valve consisting of an anterior leaflet and a posterior leaflet. The anterior leaflet has greater leaflet length but has a narrower base than the posterior leaflet. The leaflets are demarcated by an anterolateral and posteromedial commissure [44]. The MV leaflets are attached to the papillary muscles via chordae tendineae or chords. Primary chords attach to the free edge of the leaflets, whereas secondary chords attach to the body of the leaflets. Chords to the anterior leaflet attach to the anterolateral papillary muscles, whereas posterior chords attach to the posterolateral papillary muscles. All of the papillary muscles are affixed to the LV wall.

Functionally, pre-closure of the MV leaflets begins after atrial contraction to approximate the anterior and posterior leaflets. Closure of the MV components relies on the position of the anterior leaflet and coaptation of the leaflets. During systole, when in proper position, the anterior leaflet forms a veil parallel to systolic flow in the LV outflow tract. Then, during coaptation of the leaflets, coaptation over the rough zones on the atrial surfaces of either leaflet creates high friction and resistance, producing strong shear forces. Posterior annular contraction increases this coaptation to facilitate competent closure. Improper valve coaptation or loss thereof due to disruption of any of these anatomic elements of the MV apparatus can result in MR.

Assessing the Mitral Valve

Classification of Mitral Valve Dysfunction

Carpentier's classification of leaflet dysfunction has allowed surgeons and cardiologists to describe valve disease in universal terms [45]. The classification is based on leaflet motion.

- Type I: normal leaflet motion (annular dilatation, leaflet perforation, cleft valve)
- Type II: excessive leaflet motion (prolapse, chordal elongation or rupture, papillary muscle elongation or rupture)
- Type III: restricted leaflet motion
- Type IIIa: leaflet thickening and/or retraction, chordal thickening and/or retraction, commissural fusion (during systole and diastole)
- Type IIIb: papillary muscle displacement and/or leaflet tethering (during systole only)

Table 8.1 further details this complex interplay of etiology, lesions, and function. In any given patient, multiple causes, lesions, and mechanisms of dysfunction may be present, which in turn may necessitate the use of multiple techniques and technologies for valve repair.

Table 8.1 Mitral regurgitation: causes, example lesions, and type of dysfunction

Mechanism of MR and type of dysfunction	Cause of mitral regurgitation (e.g., of lesion)	
	Ischemic	Nonischemic
Organic/primary		
Type I		• Infectious/endocarditis (perforation)
		• Degenerative (annular calcification)
		• Congenital (cleft leaflet)
Type II	Ruptured papillary muscle	• Infectious/endocarditis (ruptured chord)
		• Traumatic (ruptured chord)
		• Rheumatic (elongated chords)
		• Degenerative (billowing/flail leaflets)
Type IIIa		• Rheumatic (e.g., fibrotic chords)
		• Iatrogenic (radiation/drug)
		• Inflammatory (lupus, anticardiolipin, eosinophilic, fibrosis, endocardial diseases)
Functional/secondary		
Type I and Type IIIb	Functional ischemic MR	• Cardiomyopathy, myocarditis
		• LV dysfunction (any cause)

LV left ventricular, *MR* mitral valve regurgitation

Grading the degree of MR has its limitations, so a comprehensive process to obtain multiple measurements by transthoracic echocardiography (TTE), TEE, and Doppler color flow imaging is essential. A more comprehensive assessment should be made—with cardiac magnetic resonance imaging, if necessary—to further quantify the degree of MR and resolve any discrepancies in the echocardiographic findings.

In most cases, TTE can identify the mitral valve pathology. When additional information is required, TEE provides a more precise and detailed assessment of the MV. It has better spatial resolution, allowing more accurate MR quantification, especially with regard to jet color characteristics. In addition, 3-D visualization of the valve provides further confirmatory evidence of the mitral leaflet abnormality and delineates its exact location [46].

Identifying the cause of the MR is essential for the patient's preoperative and postoperative management, as well as for planning the operative strategy. Obtaining an echocardiogram while the patient is not under anesthesia is important because the loading conditions of the heart are not altered; the degree of regurgitation can be significantly reduced and therefore underestimated when the patient is under anesthesia. Assessing not only leaflet pathology but also the direction of the single or multiple regurgitant jets is also important in planning the operative strategy.

The quantitative assessment of the MV by echocardiography classifies the degree of regurgitation into four grades (I–IV). The degree of severity can be graded further by calculating the effective regurgitant orifice area (EROA), regurgitant volume, and regurgitant fraction. It is important to understand that the quantitative parameters used to assess of the severity of MR are different with degenerative and functional MV disease.

With MR, anatomic malcoaptation of the mitral leaflets occurs during systole, and this results in an effective regurgitant orifice (ERO) that allows abnormal flow from the LV into the left atrium (LA) during systole. The ERO is influenced by the pressure gradient between the LV and the LA and may be dynamic, depending on the cause of the MR [47]. Increased afterload or ventricular volume can increase ERO, whereas decreased afterload and improved contractility can reduce ERO [48]. The sum of the regurgitant flow through the ERO during systole is the regurgitant volume (RVol) accumulated in the LA. This RVol reenters the LV during the subsequent diastole, resulting in volume overload of the LA and LV and ensuing manifestations and consequences of disease. In acute MR, the LA is small and has low compliance; as a result, any amount of RVol increases LA pressure. For this reason, acute MR is often not well tolerated and results in significant symptoms and hemodynamic changes.

The hemodynamic responses of the heart to chronic, slowly progressive MR are different from those associated with acute MR. These responses to the excessive chronic volume overload caused by MR initially result in a chronic compensated stage of volume overload, which, if uncorrected, can progress to a decompensated stage with irreversible LV dysfunction. In chronic MR, the LA remodels to accommodate the RVol so that the LA pressure is maintained; for this reason, even severe MR may be tolerated hemodynamically and symptomatically for a long period, even years [49]. Thus, in the chronic compensated state, the LV is initially unloaded by the low-resistance runoff into the LA, which is then countered by an increase in LV size to maintain wall stress at normal levels [50, 51]. In the chronic compensated stage, LV enlargement is the chief compensatory mechanism, allowing a greater LV volume as a result of the MR while maintaining normal diastolic pressures. The chronic overload from this RVol eventually leads to LV hypertrophy and dilatation [52]. The LV end-diastolic volume, end-systolic volume, and wall stress all increase, causing the LV to become more spherical [53, 54].

In the chronic compensated state, adequate forward cardiac output and normal filling pressures are maintained. Sequelae of this pathophysiology, such as atrial fibrillation due to continued left atrial enlargement, and pulmonary hypertension due to continued pressure overload, are the presenting clinical phenomena for some patients. Diastolic dysfunction may also be present but is often difficult to diagnose and quantify; it may account for symptomaticity and reduced functional capacity in patients with normal systolic function [55, 56].

Many patients remain asymptomatic in this state, and normalized preload and wall stress sometimes help the LV maintain normal contractility. Patients can remain in a chronic compensated stage for years to decades after the onset of MR.

However, eventually, the consequence of these changes is progressive LV enlargement beyond the compensated stage; the ensuing ventricular dysfunction can be severe [56]. Progressive LV enlargement may be due to increased severity of MR, continued compensatory chamber enlargement, or both. The LV enlargement can exacerbate MR because of ventricular-valvular interdependence, resulting in a vicious cycle of worsening MR and LV dysfunction. Preload and afterload changes can make the degree of this LV dysfunction difficult to characterize [57]. Nevertheless, these cumulative effects can result in irreversible LV dysfunction, leading to decompensated MR, with an ensuing poor prognosis.

In *primary MR*, mild MR is defined as a mitral RVol <30 mL, a regurgitant fraction (RF) <30%, and an EROA <0.2 cm^2, whereas severe MR is defined as a RVol ≥60 mL with an RF ≥50% and an EROA ≥0.4 cm^2. Other indicators of severe MR include a vena contracta width ≥0.7 cm with a large central regurgitant jet occupying >40% of the LA area or with a wall-impinging jet of any size, as well as blunting of the systolic component with systolic flow reversal in the pulmonary veins. Additional supportive signs include a very dense, early-peaking triangular jet on a continuous-wave Doppler echocardiogram and a peak mitral inflow velocity >120 cm/s [58].

The 2014 AHA/American College of Cardiology (ACC) guidelines now classify primary MR into four grades: grade A, at risk of MR; grade B, progressive MR; grade C, asymptomatic severe MR; and grade D, symptomatic severe MR (Table 8.2). Patients at risk of MR are identified on echocardiography with mild valvular prolapse but normal coaptation, or mild valvular thickening and leaflet restriction. They have either no MR jet or a jet area <20% of the LA, with a vena contracta <0.3 cm. Mitral valve surgery is not indicated for patients at risk of MR [26].

Progressive, or grade B, MR is characterized by severe mitral prolapse with normal coaptation, rheumatic changes with leaflet restriction, and loss of coaptation, or by prior infective endocarditis. The central jet measures 20–40% of the LA or may be a late systolic eccentric jet. The vena contracta measures <0.7 cm and has a regurgitant volume of <60 mL, an RF <50%, and an EROA <0.4 cm^2. Concomitant MV repair is now a class IIa recommendation for patients with grade B MR undergoing cardiac surgery for other indications [26].

Asymptomatic severe MR, or grade C, can be characterized similarly to grade B, in that echocardiographic findings are consistent with rheumatic changes or prior infective endocarditis. Grade C severity is often distinguished from Grade B by prolapse with the loss of leaflet coaptation or a flail leaflet, or by thickening of the leaflets associated with radiation heart disease. Defining echocardiographic measurements are a central jet >40% of the LA, a holosystolic eccentric jet, vena contracta >0.7 cm, regurgitant volume >60 mL, RF >50%, and an EROA >0.4 cm^2. Class Ia indications for surgery for asymptomatic severe MR include LV dysfunction (defined by an LVEF of 30–60% or a LV end-systolic diameter >40 mm) and cardiac surgery for other indications, during which the MV can be repaired concomitantly. Current guidelines make a class IIa recommendation for repair for asymptomatic severe MR in patients with preserved LV function, for whom the likelihood of a successful and durable repair is >95%, with an expected mortality <1% when performed at a Heart Valve Center of Excellence [26].

Symptomatic severe MR, or grade D, is identified by the same anatomic findings and echocardiographic measurements used to identify asymptomatic MR. Symptoms of severe MR include decreased exercise tolerance and exertional dyspnea. Mitral valve surgery is a class I recommendation for patients with an LVEF >30% and symptomatic severe MR. In addition, considering MV surgery in patients with an LVEF <30% now carries a class IIb recommendation [26].

In *secondary MR*, the thresholds of 0.4 cm^2 or 60 mL/beat may still be considered severe on the basis of several arguments. A lower RVol might still represent significant overload for a compromised LV. Because the total cardiac output of the ventricle is generally lower than in primary MR with preserved LV function, the 60-mL threshold may not be reached despite a >50% RF. In addition, with secondary MR, the orifice is usually crescentic along the commissural line and may underestimate the orifice area when one uses the 2D PISA method (in contrast to 3D), which inherently assumes a hemispheric flow convergence [59].

The most recent (2017) guideline the ERO delineating "severe" MR was changed from 0.2 cm^2 to 0.4 cm^2 recognizing that LV volume interacted with orifice area in delineating severity. In the typically dilated LV in patients with MR, an ERO of 0.4 cm^2 is usually associated with a regurgitant fraction of 50% while in smaller LVs the ERO may be less than 0.4 and still be consistant with severe MR. Most importantly, no single parameter should ever be used to assess MR severity in either primary or secondary MR. Rather all parameters including physical examination should be integrated to arrive at an estimation.

Cardiac magnetic resonance (CMR) can be used not only to assess the cause but also, more importantly, to quantify the severity of MR. Use of CMR is indicated when echocardiographic and clinical findings do not agree. It is extremely useful for quantifying multiple or eccentric MR jets that are difficult to evaluate by echocardiography. In addition, CMR can assess cardiac size and function and LV scar burden, along with their interaction, in patients with secondary MR [60]. Most comparisons of CMR and TTE show concordance

Table 8.2 Stages of primary MR

Grade	Definition	Valve anatomy	Valve hemodynamics[a]	Hemodynamic consequences	Symptoms
A	At risk of MR	• Mild mitral valve prolapse with normal coaptation • Mild valve thickening and leaflet restriction	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.3 cm	• None	• None
B	Progressive MR	• Severe mitral valve prolapse with normal coaptation • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE	• Central jet MR 20–40% • LA or late systolic eccentric jet MR • Vena contracta <0.7 cm • Regurgitant volume <60 mL • Regurgitant fraction <50% • ERO <0.40 cm^2 • Angiographic grade 1–2+	• Mild LA enlargement • No LV enlargement • Normal pulmonary pressure	• None
C	Asymptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥ 60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3–4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension may be present at rest or with exercise • C1: LVEF >60% and LVESD <40 mm • C2: LVEF ≤60% and LVESD ≥40 mm	• None
D	Symptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥ 60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3–4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension present	• Decreased exercise tolerance • Exertional dyspnea

ERO effective regurgitant orifice, *IE* infective endocarditis, *LA* left atrium/atrial, *LV* left ventricular, *LVEF* left ventricular ejection fraction, *LVESD* left ventricular end-systolic dimension, *MR* mitral regurgitation

From Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, et al. 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. J Thorac Cardiovasc Surg. 2014;148:e1–e132. Reprinted with permission

[a]Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence

in evaluating the degree of primary MR, although not secondary MR [61, 62].

The 2017 AHA/ACC guidelines classify secondary MR into the same 4 classes as primary MR: grade A, at risk of MR; grade B, progressive MR; grade C, asymptomatic severe MR; and grade D, symptomatic severe MR. Patients at risk of secondary MR have normal valve leaflets, chords, and annular structure, with associated coronary disease or cardiomyopathy. Echocardiography reveals no MR jet or a jet <20% of the LA, and a vena contracta <0.3 cm. No intervention is recommended for patients at risk of secondary MR [26].

The most recent 2017 ACC/AHA guidelines used to describe secondary/functional MR are shown in Table 8.3.

Secondary progressive MR is identified by wall motion abnormalities on echocardiography, with mild tethering of the mitral leaflet or with annular dilation and loss of central coaptation of the leaflets. The EROA is <0.4 cm^2, regurgitant volume is <60 mL, and the RF is <50%. Mitral valve repair (not replacement) may be considered for secondary progressive MR in patients undergoing cardiac surgery for other indications (class IIb recommendation) [26].

Asymptomatic and symptomatic severe secondary MR are associated with regional wall motion abnormalities, LV dilatation with severe tethering of a mitral leaflet, or annular dilation with severe loss of mitral leaflet coaptation. The EROA is >0.4 cm^2, with a regurgitant volume >60 mL or an RF >50%. Asymptomatic patients may have symptoms due to coronary ischemia or heart failure, but these symptoms respond to revascularization and medical therapy. In contrast, patients considered symptomatic have heart failure symptoms that

Table 8.3 Stages of secondary MR

Grade	Definition	Valve anatomy	Valve hemodynamics[a]	Associated cardiac findings	Symptoms
A	At risk of MR	• Normal valve leaflets, chords, and annulus in a patient with coronary disease or cardiomyopathy	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.30 cm	• Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities • Primary myocardial disease with LV dilation and systolic dysfunction	• Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
B	Progressive MR	• Regional wall motion abnormalities with mild tethering of mitral leaflet • Annular dilation with mild loss of central coaptation of the mitral leaflets	• ERO <0.40 $cm^{2,b}$ • Regurgitant volume <60 mL • Regurgitant fraction <50%	• Regional wall motion abnormalities with reduced LV systolic function • LV dilation and systolic dysfunction due to primary myocardial disease	• Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
C	Asymptomatic severe MR	• Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet • Annular dilation with severe loss of central coaptation of the mitral leaflets	• ERO ≥0.40 $cm^{2,b}$ • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50%	• Regional wall motion abnormalities with reduced LV systolic function • LV dilation and systolic dysfunction due to primary myocardial disease	• Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
D	Symptomatic severe MR	• Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet • Annular dilation with severe loss of central coaptation of the mitral leaflets	• ERO ≥0.40 $cm^{2,b}$ • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50%	• Regional wall motion abnormalities with reduced LV systolic function • LV dilation and systolic dysfunction due to primary myocardial disease	• HF symptoms due to MR persist even after revascularization and optimization of medical therapy • Decreased exercise tolerance • Exertional dyspnea

2D 2-dimensional, *ERO* effective regurgitant orifice, *HF* heart failure, *LA* left atrium, *LV* left ventricular, *MR* mitral regurgitation, *TTE* transthoracic echocardiogram

From Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, et al. 2017 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 Practice Guidelines. JACC 2017 70:252–289. Reprinted with permission

[a]Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence

[b]The measurement of the proximal isovelocity surface area by 2D TTE in patients with secondary MR underestimates the true ERO due to the crescentic shape of the proximal convergence

persist after revascularization and do not respond to optimized medical therapy. These symptoms may include decreased exercise tolerance and exertional dyspnea. Mitral valve surgery is recommended for both asymptomatic and symptomatic severe secondary MR in patients undergoing coronary artery bypass grafting or AVR (class IIa). Mitral valve repair or replacement may be considered for symptomatic patients undergoing other cardiac operations (class IIb) [26].

Nonischemic functional MR is most often due to severe chronic LV volume overload with unknown or idiopathic causes. Other advanced valvular heart disease is the second most common cause. Functional MR can be found in 40% of patients with heart failure due to dilated cardiomyopathy [63]. Functional, ischemic MR is increasingly prevalent as the population ages and as more patients survive myocardial infarction and live with severe ischemic heart disease. Ischemic MR can result in changes in mitral annular geometry and regional and global LV geometry and function, abnormal leaflet motion, increased distance between papillary muscles, misalignment of papillary muscles, and apical tethering of the leaflets with restricted systolic leaflet motion and a typical Carpentier type IIIb pattern of dysfunction [64, 65]. Thus, ventricular dysfunction, whether the cause is ischemic or nonischemic, can cause or contribute substantially to the development of MR. Technologies aimed at ameliorating ventricular dysfunction may therefore be important in treating MR in such patients.

Mitral Valve Stenosis

Mitral valve stenosis is classified into stages similar to the grades used to classify MR: stage A, at risk of MS; stage B, progressive MS; stage C, asymptomatic severe MS; and stage D, symptomatic severe MS. Patients at risk of MS may have MV doming identified by echocardiography, but with normal transmitral velocities. No intervention is recommended at this stage [26].

Patients with progressive MS may have rheumatic changes with associated commissural fusion and diastolic doming. The planimetered valve area is <1.5 cm^2, transmitral flow velocities are increased, and the diastolic pressure half-time is <150 ms. In contrast, both asymptomatic and symptomatic severe MS are associated with similar anatomy on echocardiography but with a planimetered valve area <1.5 cm^2, a diastolic pressure half-time >150 ms, and elevated (>30 mmHg) pulmonary artery systolic pressures. Very severe MS is further characterized by MV areas <1 cm^2 and diastolic pressure half-times >220 ms. Symptoms associated with MS can include decreased exercise tolerance and exertional dyspnea [26].

For patients with mitral stenosis, percutaneous balloon commissurotomy is often the first-line therapy when anatomically feasible. Candidates for balloon commissurotomy must be free of moderate or severe MR and must have no left atrial thrombus. The AHA/ACC guidelines currently make a class I recommendation for percutaneous balloon commissurotomy in symptomatic patients with severe MS and favorable valve morphology. Furthermore, patients with asymptomatic severe or very severe MS may be considered for balloon commissurotomy. However, for patients with severe symptomatic MS who are not candidates for balloon commissurotomy or for whom it has failed, MV surgery is recommended. Additionally, concomitant MV surgery is recommended for patients with moderate or severe MS undergoing cardiac surgery for other indications. Lastly, MV surgery with ligation of the left atrial appendage can be considered for patients with severe MS who have recurrent embolic events while on anticoagulation [26].

The Current Treatment Paradigm—Natural History of MR and Timing of Surgical Therapy

Medical therapy offers little for the treatment of severe MR, so the current treatment paradigm relies primarily on surgical repair or replacement of the MV. To understand the role and timing of surgical intervention in this current treatment paradigm, one must first consider the risks and benefits of surgical intervention and understand the natural history of MR, and how the interplay of these factors determines the current surgical paradigm for MR.

Surgery for Mitral Regurgitation

Surgical therapy for MR can be broadly grouped into two categories: MV repair and MV replacement. These procedures pose a risk of morbidity and mortality that increases with worsening MR and LV dysfunction [66]. As a result, at later stages of MR, the risks associated with surgery may be prohibitively high, precluding safe surgical intervention. Therefore, one of the major goals in the current treatment paradigm is to identify cases of MR and intervene surgically before the patients become too sick to tolerate surgery and have a low likelihood of surviving the operation.

At the other end of the spectrum, with regard to patients with MR and healthy ventricles, surgery is offered only to patients for whom the potential benefits of surgical correction of MR outweigh the risks. In this regard, some patients with MR can be considered "too healthy" for surgery and are monitored for progression of the disease until they fall within the appropriate therapeutic window.

Further complexity arises when the choice is made between MV replacement and repair. Mitral valve replacement involves placing a prosthetic valve in the heart, incurring a lifelong risk of infection. One must also consider the durability of the prosthetic valve. Replacement valves can be broadly categorized into mechanical valves and bioprosthetic tissue valves. Mechanical valves are extremely durable and may last for the patient's lifetime, but they pose certain risks. These include valve thrombosis and resultant embolization, which can result in stroke or other embolic phenomena, as well as the risk of bleeding incurred by lifelong anticoagulation with warfarin to prevent such thrombosis. Mechanical valves can also fail by developing infra-annular pannus, which impairs leaflet function and reduces the effective orifice area.

Bioprosthetic valves do not necessitate systemic anticoagulation with warfarin and therefore do not pose the attendant risks. However, bioprosthetic valves have limited durability; their life span averages 10–20 years and is lower in younger patients. Significant bioprosthetic valve deterioration then results in the need for reintervention and redo valve replacement, which usually carries a higher risk of morbidity and morbidity than primary valve replacement.

In contrast, MV repair does not incur the device-related risks of anticoagulation and bioprosthetic valve deterioration, because the native valve remains in place [67, 68]. Furthermore, with contemporary valve repair, the chordal apparatus is maintained; studies show preservation of LV geometry and systolic function and also lower rates of late complications than with prosthetic MV replacement [69]. However, not all valves can be repaired, even at the best referral centers. In addition, the risks, benefits, durability, and complications of surgery must be balanced against the natural history of MR, to further elucidate the best timing for

surgery and to better identify patients for whom surgical intervention is appropriate.

Natural History of MR

The natural history of MR varies substantially with severity, cause, and symptomatology. When treatment options are considered for patients with MR, it is important to distinguish between patients with symptomatic versus asymptomatic disease, and among patients with mild-to-moderate, moderate-to-severe, and severe MR.

As much as 20% of the population has trivial or mild-to-moderate MR; however, most of these individuals are asymptomatic, and for many, their MR never becomes significant enough to warrant surgical intervention [70, 71]. Furthermore, MR can remain mild or mild-to-moderate for many years without any significant worsening, either hemodynamically or in terms of symptoms. Affected patients are monitored for the development of significant hemodynamic changes or symptoms.

Although the development of symptoms is an indication for surgical intervention, it is an unpredictable and unreliable indicator of progression to moderate-to-severe or severe MR, of a chronic compensated state of MR, or of transition to a decompensated state. For example, by the time significant dyspnea arises, there may already be significant irreversible ventricular dysfunction. Thus, most patients with MR will be monitored for the development of significant anatomic, echocardiographic, or hemodynamic changes that indicate worsening MR. However; even patients with significantly worsening MR can remain asymptomatic.

The natural history of asymptomatic, moderately severe MR is controversial. Initial studies suggested a benign prognosis, without death or deterioration of LV function for up to 5 years of follow-up, but a 10% average annual risk of symptom development leading to surgical correction was noted [72]. Subsequent studies have shown a 5-year combined incidence of 42% for the onset of atrial fibrillation, heart failure, or cardiovascular death [73].

As MR progresses to the severe stage, if left untreated, its natural history involves worsening clinical deterioration, morbidity, and substantial mortality risk. This holds true in both symptomatic and asymptomatic patients. Thus, it is clear that such patients should be considered for surgery; however, as described previously, these patients are at risk for significant LV dysfunction, which can be difficult to detect and which substantially increases the likelihood of morbidity and mortality with operative intervention. Thus, patients who have developed severe LV dysfunction may be too sick for surgery and may thus fall out of the therapeutic window.

The end result of these considerations is summarized in Fig. 8.1, adapted from the 2017 ACC/AHA guidelines, describing recommendations for the timing of surgical intervention for MR.

Comorbidities

In addition to the risks and benefits of surgery and the natural history of MR itself, one must also consider comorbid conditions and the increased risks of morbidity, mortality, and complications they may pose. Two of the strongest risk factors for early mortality are age and NYHA functional class [66]. Continued heart failure is the main cause of death after surgical correction of MR [66]. Important predictors of late mortality after operation include advanced age, elevated serum creatinine level, elevated systolic blood pressure, coronary artery disease, advanced functional class heart failure, and echocardiographic evidence of reduced LVEF and worsening end-systolic dimension [66, 68, 74]. Renal failure or dysfunction, liver failure or dysfunction, a hostile chest due to prior sternotomy or radiation, COPD, prior stroke, endocarditis, and poor nutritional status are other factors and comorbidities that increase the risks associated with surgery and that may portend poorer outcomes. Thus, appropriate candidates for surgery are those patients who fall within the therapeutic window, and for whom the risks posed by comorbid conditions are low enough so as to not preclude surgical intervention.

Understanding this paradigm is important, as it lays the framework for understanding how emerging technologies for endovascular treatments—MV repair, MV replacement, and interventions to alleviate ventricular dysfunction—can alter the therapeutic window. This paradigm also informs what threshold levels of risk can be tolerated, and what threshold levels of benefit need to be exceeded, to ensure successful adoption of any given technique or technology.

Mitral Valve Repair

Despite the lack of randomized trials comparing MV repair and replacement in degenerative valve disease, comparative studies have demonstrated a survival advantage with MV repair [75–77]. In addition, repair preserves ventricular function and provides greater freedom from thromboembolic and anticoagulation-related events, as well as endocarditis.

The basic principles of any mitral repair include (1) reestablishing normal leaflet motion, (2) obtaining an adequate surface of leaflet coaptation, and (3) annular stabilization with a ring or band while maintaining an adequate mitral orifice size. To perform the most durable repair, the surgeon needs to be familiar with both the normal functional anatomy and the pathological anatomy as it relates to the lesions of the leaflets, leaflet motion, and annulus.

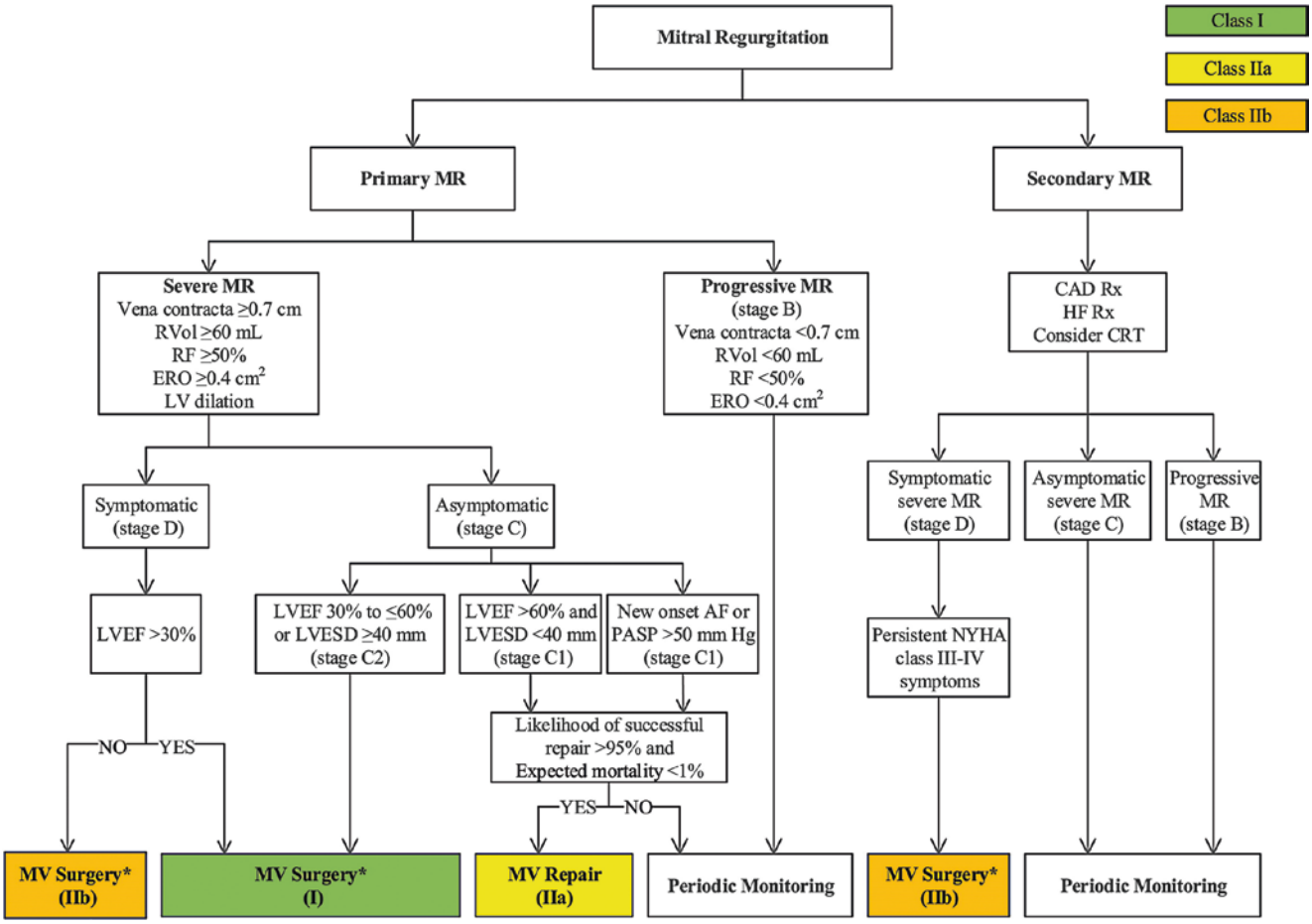

Fig. 8.1 Indications for surgery for mitral regurgitation. *AF* atrial fibrillation, *CAD* coronary artery disease, *CRT* cardiac resynchronization therapy, *ERO* effective regurgitant orifice, *HF* heart failure, *LV* left ventricular, *LVEF* left ventricular ejection fraction, *LVESD* left ventricular end-systolic dimension, *MR* mitral regurgitation, *MV* mitral valve, *MVR* mitral valve replacement, *NYHA* New York Heart Association, *PASP* pulmonary artery systolic pressure, *RF* regurgitant fraction, *RVol* regurgitant volume, *Rx* therapy. *Mitral valve repair is preferred over MVR when possible. From Nishimura et al. [26]

Repair techniques have evolved into three basic concepts. The first involves resectional techniques, which were popularized by Carpentier. This entails resecting abnormal leaflet tissue and later reconstruction. The second involves a "respect all, rather than resect" technique. With this approach, the free edges of the prolapsing leaflet segments are resuspended with artificial Gore-Tex neochords. Multiple variations of this approach have been described. The third concept combines the first 2: resecting all abnormal leaflet tissue, then using Gore-Tex neochords to address any remaining redundant leaflet tissue.

The edge-to-edge technique, which was popularized by Alfieri, has been used as both a primary repair strategy and a "bailout" technique. This technique provides a functional, as opposed to an anatomical, repair of the valve.

Carefully evaluating the valvular deformity by both preoperative and intraoperative echocardiography is essential. Thereafter, the surgeon must correlate these findings with the intraoperative valve analysis. Each of the leaflet segments, including commissures, chordae, and the subvalvular apparatus, as well as the annulus, must be carefully inspected. Many surgeons use P1 as a reference point to assess the degree of prolapse of the adjacent scallops because, in the majority of cases, P1 is free of disease. Others reject this concept and instead take a targeted approach to the valve by addressing the most significant lesion first and repairing additional defects thereafter. The surgeon must take into consideration the amount of leaflet tissue involved (volume) in relation to adjacent normal leaflet, the height of the affected leaflet, and the amount of support (chordae) that is lacking or in excess. Leaving the posterior leaflet too long (i.e., >1.5 cm) can lead to systolic anterior motion of the MV.

Today, more than 90% of cases of degenerative MV disease can be repaired at referral or expert centers. Furthermore, after surgeons obtain sufficient experience in minimally invasive surgery, essentially every repair technique can be

applied. Minimally invasive approaches to mitral surgery provide unimpeded, direct, and truly anatomic visualization of the MV. One must keep in mind that these approaches do not help surgeons to improve their competency with mitral repair techniques. Proficiency with a wide variety of mitral repair techniques is acquired with experience and repetition. A significant learning curve is associated with both mitral repair and minimally invasive access. Considering that among surgeons performing MV surgery, the median number of MV repairs per surgeon is 5 per year, proficiency in repair may be difficult to obtain. In addition, among all surgeons performing mitral surgery, the median MV repair rate is 41% [78]. Therefore, the concept of centers of excellence has been proposed in order to obtain the highest possible rate of durable repairs [79].

Furthermore, in 2008, 26% of Society of Thoracic Surgeons Adult Cardiac Surgery Database centers were performing a median of 3 less-invasive procedures per year [80]. Therefore, the necessary skillsets to perform complex MV repairs via a minimally invasive approach may be obtainable only at minimally invasive MV repair referral centers.

Mitral Valve Repair Techniques

Posterior Leaflet Prolapse or Flail

A P2 prolapse is the most common dysfunction seen in degenerative MV disease. A small segment of flailed or prolapsed leaflet can be managed with a limited triangular resection. In contrast, a broad scallop with a large area of prolapse or flailed segment can be addressed with a quadrangular resection. This can be performed along with a sliding or folding plasty. With larger resections, annular compression sutures can be considered, as well. An alternative approach is a butterfly resection of a broad P2 segment. In certain cases in which a limited triangular resection is performed and there is excess height in P2, a Gore-Tex chord can be added to avoid potential systolic anterior motion (SAM) of the MV. With excessive leaflet tissue, a larger quadrangular resection of P2 will help avoid SAM, as well.

Prolapse of P1 and P3 can be addressed with limited resection, depending on the thickness and amount of tissue on the affected scallop. Alternatively, a complete "respect rather than resect" approach can be taken by placing polytetrafluoroethylene (PTFE) artificial neochords. Several methods can be used. These include placing individual chords in the papillary muscles supported with or without pledgets, running one Gore-Tex suture through the papillary muscle and then into the leaflet and back multiple times, placing one small Gore-Tex loop in the papillary muscle and then passing multiple individual Gore-Tex sutures through the loop and into the leaflets as necessary, and using the multi-loop technique. This approach displaces the leaflets into the ventricle and establishes a new line of coaptation to simulate a Roman arch.

Anterior Leaflet Prolapse or Flail

Mild anterior leaflet prolapse usually does not need to be addressed and resolves once the annuloplasty is placed. For moderate or greater anterior prolapse or flail, placing artificial neochords is the most commonly used technique. Various methods have been described. Single or multiple Gore-Tex neochords can be placed from the papillary muscle to the free edge of the leaflet. It is important that the neochords cross neither the midline nor each other. The length of the leaflet can be determined by measuring the height of an adjacent normal native chordae or with the saline test after annuloplasty implantation. Another method involves using premeasured Gore-Tex loops. The length of these loops can be determined by measuring adjacent normal chordae intraoperatively or by measuring normal chordae with intraoperative TEE. These chordal loops for the anterior leaflet usually measure between 22 and 26 mm. Aggressively shortening the anterior leaflet can lead to residual MR and even SAM. Another reference point that can be considered for determining the chordal length is the annular plane; the free edge of the leaflet should reach the level of the annulus. Even with these methods, measuring an exact length can be challenging.

In addition, anterior leaflet secondary chords (which are usually the appropriate length) can be transferred to the free edge. These chords can serve as a guide to the proper length of an artificial neochord if one is needed for additional support.

Other, infrequently used alternative techniques include chordal transposition, which is effective but can potentially damage a normal posterior leaflet; this technique involves transposing a segment of normal posterior leaflet with native chordae of normal length to the affected segment of prolapsing anterior leaflet. Papillary muscle repositioning involves anchoring the fibrous head of the anterior papillary muscle to the posterior papillary muscle. Resecting the anterior leaflet is reserved for significant localized abnormalities of the leaflet, and resection is limited to no more than 10% of the leaflet.

Bileaflet Prolapse

Bileaflet prolapse can be treated with a combination of the previously described techniques. These are the most challenging of all repairs, as well as the least durable. Bileaflet

prolapse presenting with only a central jet identified by preoperative TEE can occasionally be addressed with only an annuloplasty ring that is sized to the annulus. Another approach to bileaflet prolapse is an Alfieri stitch (edge-to-edge repair) with the addition of an annuloplasty ring.

Commissural Prolapse

Limited commissural prolapse can be treated with a limited resection or folding plasty. With more extensive commissural prolapse secondary to leaflet destruction and chordal rupture, a quadrangular resection with annular plication can be performed. This procedure can be completed with a "magic stitch" to restore coaptation. In cases with more extensive involvement of the commissure, both A3 and P3 can be detached from the annulus after a quadrangular resection is performed. Annular plication and leaflet advancement are performed thereafter.

Patients with intact leaflets and elongated chordae can be treated with papillary muscle shortening or a papillary muscle sliding plasty. Another option is using artificial neochordae to reduce the height of the commissure.

Mitral Annular Calcification

Annular decalcification may be required to establish an adequate surface of leaflet coaptation in patients undergoing repair. The leaflet is detached from the annulus, and an attempt is made to resect the calcium bar en bloc. If this is not possible, fractional debridement with a rongeur can be performed, after which the leaflet is reattached. An ultrasonic debridement device can also facilitate the decalcification. Some cases may require patch repair of the atrioventricular groove to avoid a disruption. In cases of diffuse calcification, an alternative is to place annular sutures around the calcium and to modify the annuloplasty ring or band if necessary. Mitral annular calcification can pose a challenge, and the feasibility of repair may be limited.

Rheumatic Valvular Disease

In developing countries, attempts to repair a rheumatic valve in the earlier stages of the disease are complicated by the need for reoperation due to progressive distortion and fibrosis of the leaflets secondary to progression or recurrence of the rheumatic process. Replacement attempts are also plagued by several complications, as well as the risks associated with multiple operations, especially in young patients.

In developed countries, the disease process is different, and the leaflets undergo more of an advanced, end-stage histologic process that is unlikely to progress except for the development of calcium deposition. Annular dilatation is the cause of regurgitation in more than half of cases. Mitral repair is technically more feasible and yields better results in this group.

Repair for rheumatic mitral disease includes several techniques, ranging from commissurotomy, subvalvular chordal, and papillary muscle splitting to leaflet peeling and leaflet extension [81]. The initial step is to free the fused commissures and subvalvular apparatus by splitting the fused chords and papillary muscles. Shortened secondary chords are cut to free the leaflets even further. In some cases, even thickened restricted primary chords are transected and replaced with artificial Gore-Tex chords. The leaflets can be made more pliable by peeling off the inflammatory fibrotic layer and decalcification. When the leaflet and subvalvular mobilization are not enough to compensate for tissue retraction, performing leaflet augmentation techniques can increase the surface area of the leaflet, providing greater mobility and surface area for leaflet coaptation. Leaflet augmentation can be performed with autologous pericardium, bovine pericardium, or a collagen matrix, and on the anterior or posterior leaflet, or both leaflets. The leaflet extension technique also allows the insertion of a larger annuloplasty ring or band [81].

Annular Stabilization

Annular stabilization with a full ring or band is essential to the long-term durability of the repair. The choice between a full ring and a band is a topic of ongoing debate. The size of the annuloplasty is usually determined by the height of the anterior leaflet, although in cases of extreme myxomatous degeneration with voluminous leaflets and a very dilated annulus, a "true sized" annuloplasty is recommended. The annuloplasty restores the normal 4:3 ratio of the MV, increases the line of coaptation of the leaflets, and prevents annular dilatation. Some reports state that after a band is placed, the annulus between the trigones may continue to dilate and contribute to recurrent MR. On the other hand, others believe that a full ring can lead to mitral stenosis.

Edge-to-Edge

This technique, originally described by Alfieri [82], has been applied to degenerative disease with bileaflet prolapse, flail leaflet, and calcified annulus. The middle portion of each leaflet is identified by assessing the subvalvular apparatus with nerve hooks. Wide clefts are usually closed. The repair is completed by taking large bites through the rough zone of the leaflet tissue and suturing the free edge of A2 and P2 with

a running 4 or 5-0 Prolene suture. The running length is variable but commonly covers the whole length of the mid scallop. With flail segments other than A2 or P2, the location of the suture will correspond to the center of the flailed segment. An annuloplasty is performed at the end of the procedure [83].

The minimum ring or band size should be 32 mm. Failure to use annular stabilization will increase the failure rate. Mitral annular calcification also contributes to long-term failure.

Mitral Valve Replacement

Mitral valve replacement is reserved for patients with end-stage Barlow disease, previous failed attempts to repair the MV, a heavily calcified mitral annulus, or certain forms of rheumatic disease. The replacement procedure should spare the chords to maintain annular papillary continuity. The different options include preserving the posterior leaflet and chords and resecting the entire anterior leaflet; preserving the posterior leaflet and chords, then detaching the entire anterior leaflet from the annulus and incorporating it into the posterior suture line; preserving the posterior leaflet and chords and resecting only A1 and a portion of P2, leaving P3 intact; and resecting all leaflets and chords and resuspending the papillary muscles with Gore-Tex neochords, which are passed through the annulus and onto the sewing cuff of the valve (typically placed at 4 and 8 o'clock). In patients with mitral annular calcification, if sutures can be passed through the calcium, decalcification may be avoidable. If a large segment of calcium is present and precludes suture placement, the segment will need to be resected.

Some patients have valves that are not amenable to repair, so replacement is indicated. These include patients with irreparable complex valve disease, as well as elderly patients with multiple comorbidities, for whom the benefit of repair is outweighed by the risks. A good MV replacement is better than a bad MV repair.

Surgical Treatment of Functional Mitral Regurgitation

Annular Techniques

Secondary MR, also known as functional MR, is most often caused by ischemic or dilated cardiomyopathy. The MR is caused by changes in the LV that distort the valvular apparatus. Specifically, dilation of the LV results in inferior and lateral papillary muscle displacement, which ultimately leads to tethering of the valve leaflets and loss of central coaptation.

Left ventricular end-systolic volume index (LVESVI) can be used as a surrogate for LV dilation and remodeling associated with ischemic myocardial disease and is a predictor of poor prognosis in these patients. The principles of mitral valve surgery are to restore valve competence, reduce the LVESVI, and induce reverse remodeling of the LV, which may be associated with better outcomes [84]. For patients with secondary MR, the most commonly used technique is implanting a downsized annuloplasty ring [84–91].

However, the high recurrence rate of MR associated with repair, as compared to mitral valve replacement, has prompted further examination of the two approaches to secondary MR. Recently, the Cardiothoracic Surgical Trials Network conducted a randomized controlled trial of MV repair versus replacement for patients with severe ischemic MR. Unlike many of the previous studies, this trial showed no difference in overall LV remodeling or survival for patients who underwent repair versus replacement [92]. Furthermore, the rate of recurrence of moderate or severe MR was much higher with repair than with replacement (32.6% vs. 2.3%). On the other hand, patients who underwent repair but did not have recurrent MR had significant reverse LV remodeling. In addition, the absence of MR recurrence was associated with better quality of life. This finding prompted a search for predictors of recurrent MR in order to improve patient selection for MV repair.

A subgroup analysis by Kron and colleagues [93] identified only basal aneurysm as an independent risk factor for MR recurrence. This finding suggests that leaflet tethering plays a significant role in the recurrence of MR after repair. Other possible predictors include specific echocardiographic measurements, including leaflet tethering height, tenting area, coaptation distance, LVESVI, and ventricular sphericity index [89, 94–100]. Recently, follow-up studies have suggested that 3D echocardiography may be superior to 2D echocardiography at predicting MR recurrence [101]. In addition, a 3D echocardiography study identified a P3 tethering angle of 29.9° or larger as an independent risk factor for MR recurrence [102].

Subvalvular Techniques of Mitral Valve Repair for Ischemic Mitral Regurgitation

Chordal Cutting

The technique of chordal cutting typically focuses on anterior mitral leaflet tethering in functional MR (FMR). This attachment can cause an abnormal bend in the anterior mitral leaflet described as a "seagull wing" by Professor Alain Carpentier [103]. In theory, second-order chordal cutting should reduce the degree of leaflet tethering and increase leaflet mobility and coaptation height, thereby limiting the

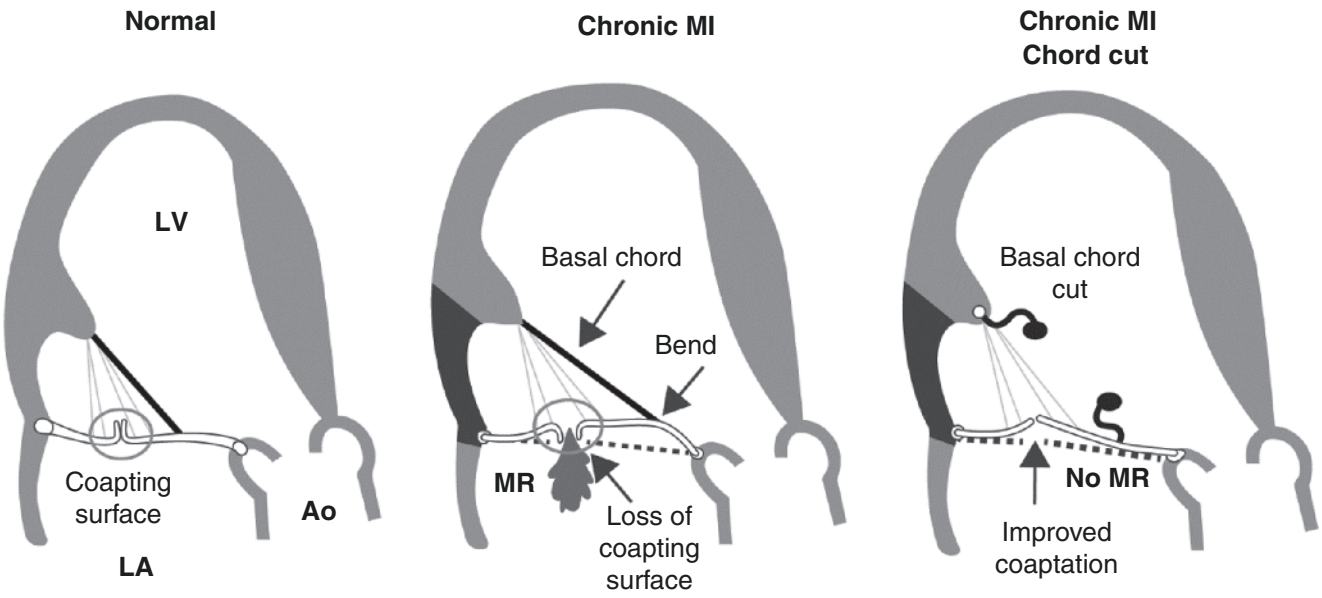

Fig. 8.2 Encircling the base of the papillary muscles with a Gore-Tex graft

degree of MR (Fig. 8.2). Chordal cutting can also be performed by dividing secondary chords to the posterior leaflet and to the commissure that arises from the papillary muscle or muscles affected by the infarcted myocardium [104]. To optimize visibility of the chords, this procedure is performed before the annuloplasty band is placed.

Compared with conventional MV repair, chordal-cutting MV repair has been associated with a reduced risk of recurrent MR because this repair produces greater reductions in tenting area and greater mobility of the anterior leaflet (as measured by a reduction in the distance between the free edge of the anterior MV leaflet and the posterior LV wall) without compromising postoperative LVEF [104].

Papillary Muscle Relocation

Papillary muscle relocation techniques for secondary MR are used to treat severe leaflet tethering and displacement of the coaptation point. One technique includes placing a 3-0 polypropylene suture through the posterior papillary muscle fibrous tip and then passing it through the adjacent mitral annulus just posterior to the right fibrous trigone [105]. After the mitral annuloplasty is performed, if the saline test reveals inadequate leaflet coaptation (typically in the P3 segment), the relocation suture is tightened, drawing the posterior papillary muscle tip closer to the annulus.

Another technique is the "ring plus string" repair [106, 107]. This technique is performed by anchoring a Teflon-pledgeted suture in the head of the posterior papillary muscle, then passing it through the fibrosa (midseptal annular saddle horn) under direct vision and exteriorizing it through the aortic wall underneath the commissure between the noncoronary and left coronary aortic cusps. The suture is then tied under echocardiographic guidance in the loaded, beating heart to reposition the displaced posterior papillary muscle toward the fibrosa. This technique has been refined to allow further reduction of the septal-lateral diameter after the loaded, beating heart is implanted with a DYANA nitinol-based dynamic annuloplasty device that can be deformed by activation with radiofrequency [108].

Papillary muscle relocation with a suture plus nonrestrictive mitral annuloplasty promotes a significant reversal of LV remodeling, a decrease in tenting area and coaptation depth, and less recurrent MR [109]. What remains to be seen is whether restrictive mitral valve annuloplasty produces better results than nonrestrictive annuloplasty. This raises the question of whether the annuloplasty technique or the subvalvular repair contributes more to the success of MV repair for FMR.

Papillary Muscle Approximation

Papillary muscle approximation (PMA) with a papillary muscle sling technique was first introduced to treat patients with ischemic LV dysfunction and FMR [110]. By restoring a more normal alignment between the mitral annulus and the laterally displaced papillary muscles, this technique could relieve the excess tethering on the mitral leaflets and significantly restore leaflet mobility. This method is performed by placing a 4-mm PTFE tube graft around the base of all the papillary muscles (Figs. 8.3 and 8.4). The graft is then progressively tightened until there is no gap between the bases of the two papillary muscles (Fig. 8.5). An annuloplasty ring that is "true sized" to the anterior leaflet is then placed (Fig. 8.6). This technique has been termed the "sling and ring" repair. It has been modified

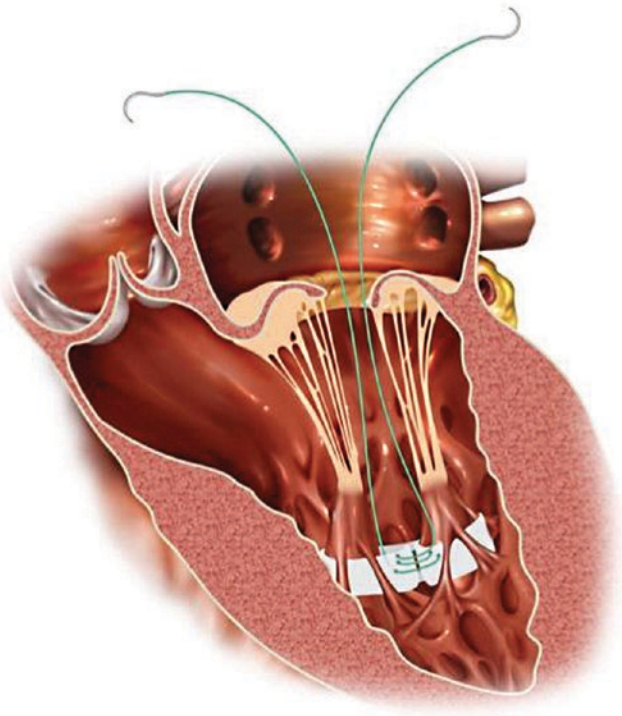

Fig. 8.3 Diagram showing sling around base of papillary muscles

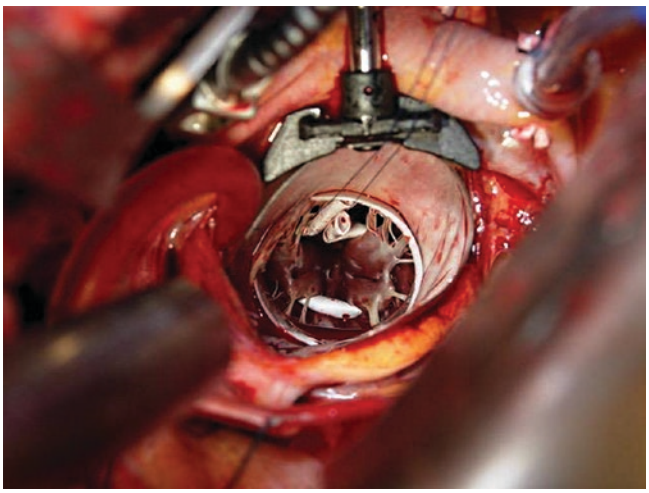

Fig. 8.4 Intraoperative photo of sling placed around the base of the papillary muscles

and performed safely in a minimally invasive fashion via a mini-right thoracotomy [111, 112].

The "sling and ring" repair has shown promise with regard to promoting LV remodeling and leaflet mobility by limiting the tethering secondary to displacement of the papillary muscles [110]. This anatomical correction can lead to improvements in ventricular diameter, LVEF, volume, and sphericity index.

A similar subvalvular approach to PMA consists of placing a single U-shaped stitch, reinforcing it with two patches

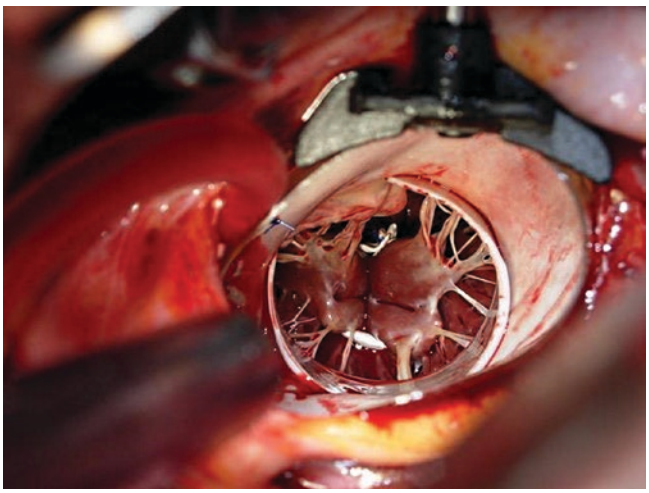

Fig. 8.5 Photo of PTFE graft tightly approximating the base of the papillary muscles

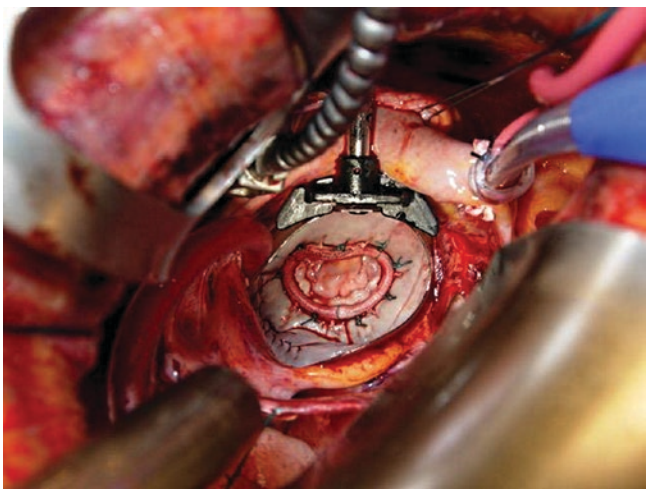

Fig. 8.6 Rigid annuloplasty ring, true sized to the anterior leaflet

of autologous pericardium, and passing it through the posterior and anterior papillary muscles [113]. This method of PMA lowers the rate of recurrent MR [113] and is believed to promote significant ventricular remodeling, reducing mean LVEDD and increasing mean LVEF [113]. This is consistent with the Cardiothoracic Surgery Network trial that showed that patients with more complex tethering may benefit from additional subvalvular procedures [92].

Surgical Ventricular Reconstruction

In certain populations, adding left ventriculoplasty to MV repair for FMR has been associated with more effective control of MR and further improvement of LVEF than restrictive mitral annuloplasty alone [114]. Surgical ventricular reconstruction (SVR) was first popularized for the management of heart failure with LV remodeling caused by coronary artery

disease, and SVR was shown to reduce LV volume, increase LVEF, and improve ventricular function [115, 116]. In the STICH trial, despite a significantly greater reduction in LV volume with SVR than with coronary artery bypass grafting alone, this improvement did not translate into a measurable survival benefit for patients [117].

An additional study has shown that when compared with annuloplasty alone, the addition of left ventriculoplasty significantly improved LVEF in patients with an enlarged LV (LVEDD >65 mm) and severe mitral tethering. There was also a nonsignificant trend toward greater improvement in MR grade when a left ventriculoplasty was performed [118].

Endovascular Devices for the Treatment of Mitral Regurgitation

In patients with severe MR, observational studies have demonstrated that surgery to repair or replace the MV was found to improve survival more effectively than medical therapy [119]. However, surgery can pose significant risks, including a 1–5% risk of mortality and a 10–20% risk of morbidities including stroke, reoperation, renal failure, and prolonged ventilation. Elderly patients and those with LV dysfunction are at even greater risk [120]. Even in patients with moderate-to-severe MR, and in asymptomatic patients, the risks posed by surgery are not trivial, which inspired the current paradigm of monitoring patients until symptom develop, MR or LV dysfunction worsens, or sequelae of MR arise such as atrial fibrillation or pulmonary hypertension—at which point the benefits of surgery justify the risks [119, 121]. In contrast, at experienced referral centers treating patients who have a >90% chance of successful repair, the benefits of surgery justify the risks for a broader range of indications, such that guidelines recommend considering MV repair even for asymptomatic patients with normal LV function [26].

The risks posed by surgery, combined with other factors such as patient preference for less-invasive therapies, the recent successes and rapid adoption of devices for transcatheter aortic valve replacement (TAVR), and the large, unmet clinical need for therapies for patients who are outside of the therapeutic window of surgery, have stimulated an explosion in the development of endovascular technologies for treating MR. Interest is especially great in therapies for high-risk patients deemed too sick for surgery.

Whereas TAVR for the treatment of aortic stenosis has enjoyed quick adoption and widespread success due to several factors (e.g., a singular pathophysiology of valve disease; the anatomy of the aortic annulus, which allows for precise stent-valve delivery; the ability to leverage conventional imaging techniques), the advancement of transcatheter MV interventions has been relatively slow. Endovascular therapy for MR poses far more complex challenges in terms of the anatomy, structure, and function of the MV apparatus, complex pathophysiological considerations, challenges in patient selection, imaging complexities, and comparison to gold-standard surgical approaches that include both repair and replacement. Nevertheless, a plethora of device technologies exist or are in development and the devices can be broadly categorized into repair and replacement devices.

Emerging Mitral Valve Repair Devices

Just as a variety of different surgical techniques exist to address and repair various lesions and associated dysfunction of the MV, a variety of devices are in development, largely mimicking surgical repair techniques, with the aim of producing results comparable to those of surgical repair but by a transvascular approach. Emerging devices can be categorized by where they are placed and their mechanism of action within the MV apparatus, including annulus-based devices, leaflet-based devices, chordal-based devices, and papillary muscle-based devices.

Annulus-Based Devices

Several device technologies are in development to replicate one of the mainstay techniques of surgical MV repair, namely mitral annuloplasty. These devices can be subdivided into direct and indirect annuloplasty devices. Direct annuloplasty devices seek to mimic surgical annuloplasty techniques; a variety of these devices are placed directly into the mitral annulus. Existing direct annuloplasty devices include the Edwards Cardioband device, the ValCare Amend device, the MitraSpan Transapical Segmented Reduction Annuloplasty (TASRA) device, and the Millipede Medical IRIS device.

Direct Annuloplasty Devices

Edwards Cardioband

The Edwards Cardioband system (Edwards Lifesciences) is an adjustable annuloplasty system that consists of a polyester sleeve implant with radiopaque markers spaced 8 mm apart. The sleeve is fastened to the mitral annulus with multiple repositionable and retrievable 6-mm anchors. The device uses a transfemoral implant delivery system and a 25 Fr transseptal steerable sheath (Fig. 8.7) [122].

A transseptal puncture is performed under TEE guidance, and an anchor is released close to the hinge of the leaflet and the anterior commissure. The implant is advanced until a radiopaque portion reaches the adjacent marker; the implant catheter is then navigated to each subsequent anchoring point along the posterior annulus until the tip reaches the last anchoring site. Thereafter, the implant is tightened to size with the adjustment tool, and the reduction of MR is assessed by TEE until the desired effect is obtained [122].

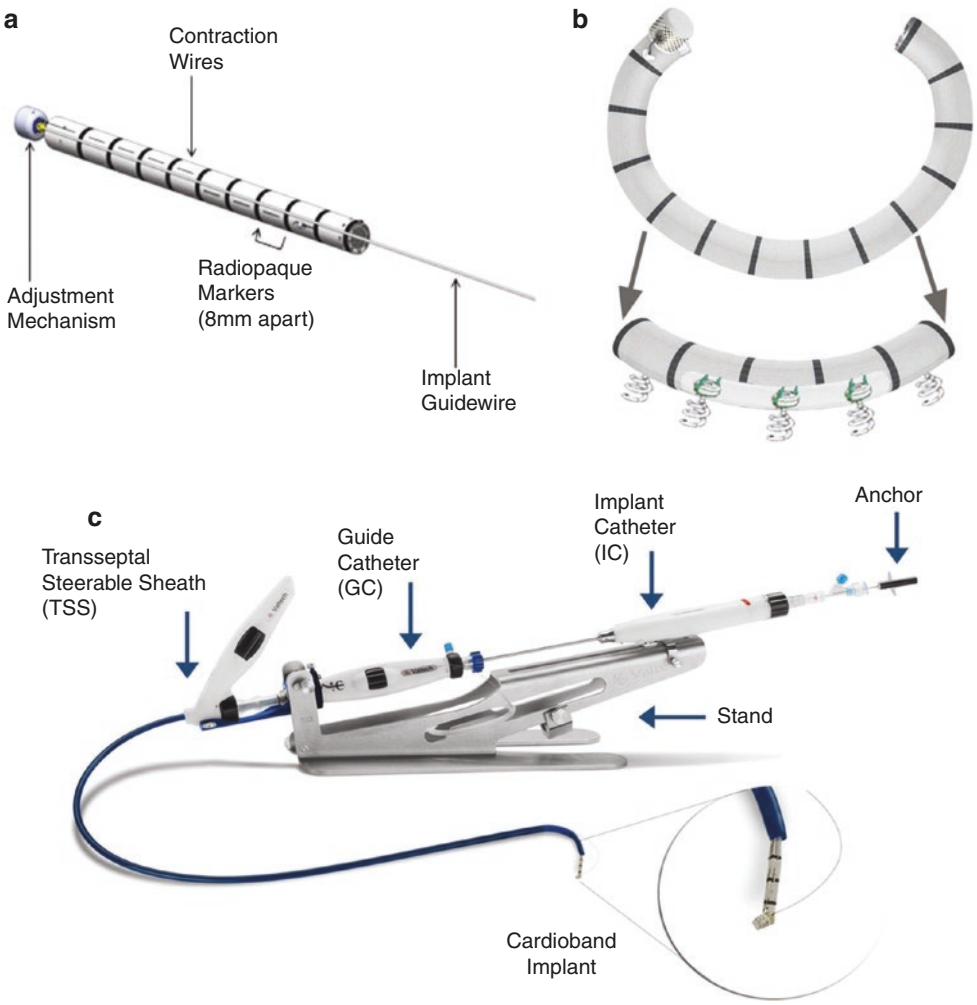

Fig. 8.7 Edwards Valtech Cardioband device, shown before (**a**) and after (**b**) implantation. (**c**) Cardioband delivery system. From Maisano et al. [122]. Reprinted with permission from Oxford University Press

Among 31 high-risk patients with symptomatic functional MR, procedural success was reported in all patients. A significant reduction in septolateral dimension was found in 29 patients, with no MR in 6 (21%), mild MR in 21 (72%), and moderate MR in 2 (7%). No procedural mortality was encountered, and in-hospital mortality was 6.5% (2/31); of note, neither death was procedure or device related. At 30 days, MR remained at 2+ or less in 22 patients (88%). Ongoing trials of the Cardioband device are described in Table 8.4 [122].

Valcare Amend Device

The Valcare Amend device is a D-shaped annuloplasty ring that is attached to the annulus with 12 independently deployed anchors positioned in 4 zones (Fig. 8.8). The posterior zones are anchored first and then pulled anteriorly to reduce the anterior-posterior dimension by 15–25%. The device is delivered by a transapical approach. The first human implantation was done in 2016 and reduced the patient's MR from severe (4+) to trace (1). Details of ongoing trials are listed in Table 8.5.

MitraSpan TASRA Device

The TASRA device (MitrasSpan Inc., Belmont, MA, USA), which is based on the concept of septal lateral annular cinching, is another direct annuloplasty device. The cinching device is delivered transapically with a low-profile (≤12-Fr) system. A suture is placed on both the anterior trigone and posterior mitral annulus, and the cinch device then compresses the annulus (Fig. 8.9).

Millipede Medical IRIS Device

Another device, the Millipede IRIS (Millipede Medical, Santa Rosa, CA, USA) seeks to replicate a semirigid, complete ring, using a zigzag-shaped nitinol frame that is placed in a supra-annular position. The delivery system uses a transseptal approach, and the device itself has anchors that attach the ring to the annulus. Collars on the peak of each zigzag contract or expand the ring when tightened or released to accomplish final sizing (Fig. 8.10) [123]. The first successful human implantation was completed in May 2017. Ongoing trial details are described in Table 8.6.

Table 8.4 Cardioband trials

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
REPAIR (transcatheteR rEPair of mitrAl Insufficiency with caRdioband system)	Prospective, multicenter, nonrandomized trial, 50 pts	1. Experimental: Device	1. Severe secondary MR (3+ to 4+) 2. Symptomatic MR (NYHA II–IVa) despite GDMT, including CRT if indicated 3. Transfemoral/ transseptal delivery feasible 4. Not offered surgery by local site heart team	1. LVEF <20% 2. LVEDD ≥7 cm 3. Heavily calcified 4. Significant CAD needing revascularization 5. Active endocarditis 6. Any endovascular or carotid intervention within 30 days, coronary within 3 months 7. Dialysis, liver disease 8. Life expectancy <12 months 9. PHtn >69 mmHg at rest 10. Right heart dysfunction 11. Bleeding or coagulation disorder 12. Prior MV repair 13. TIA or CVA within 3 months 14. Pregnancy 15. Hypersensitivity to nickel or chromium	1. Reduction in severity of MR by ≥1 on a 0–4 scale (30 days)	1. Change in 6MWD (6 months) 2. Change in MR severity (6, 12, and 24 months)	2 years	August 2019
ACTIVE—Edwards Cardioband system ACTIVE Pivotal Clinical trial	Global, multicenter RCT, 375 pts estimated	1. Experimental: Device 2. Comparator: GDMT	1. Clinically significant FMR 2. Symptomatic HF 3. Prior HF hospitalization within 12 months or elevated BNP	1. DMR 2. MAC impeding device 3. Other valve dx requiring intervention 4. Unfavorable anatomy 5. Life expectancy <12 months	1. Prevalence of MR ≤2+ 2. Time to cardiovascular death 3. Hospitalizations 4. 6MWD 5. KCCQ improvement	1. Rates of various adverse events (30 days) 2. NYHA improvement (1 year) 3. 6MWD improvement (1 year) 4. KCCQ improvement (1 year) 5. HF hospitalizations (1 year)	1 year	September 2024

6MWD 6-minute walk distance, *BNP* brain natriuretic peptide, *CAD* coronary artery disease, *CRT* cardiac resynchronization therapy, *CVA* cerebrovascular accident, *DMR* degenerative mitral regurgitation, *FMR* functional mitral regurgitation, *GDMT* goal-directed medical therapy, *HF* heart failure, *KCCQ* Kansas City Cardiomyopathy Questionnaire, *LVEDD* left ventricular end-diastolic dimension, *LVEF* left ventricular ejection fraction, *MAC* mitral annular calcification, *MAE* major adverse events, *MR* mitral regurgitation, *MV* mitral valve, *NYHA* New York Heart Association, *PHtn* pulmonary hypertension, *RCT* randomized, controlled trial, *TIA* transient ischemic attack

Fig. 8.8 Valcare Amend device. From https://www.medgadget.com/2016/06/amend-new-minimally-invasive-device-treating-mitral-regurgitation.html. Reprinted with permission from Valcare Medical

Indirect Annuloplasty Devices

Several device designs exist that seek to use the anatomical relationship of the coronary sinus to the mitral annulus to perform an indirect annuloplasty. The coronary sinus circumferentially tracks and surrounds the annulus along the posterior and posterolateral curvature of the heart. The devices are placed in the coronary sinus, and an attempt is made to reduce the annular size by tightening the sinus. Two such indirect annuloplasty devices, the Cardiac Dimensions Carillon system and the MVRx ARTO System, are described below.

Cardiac Dimensions Carillon System

The Carillon Mitral Contour system (Cardiac Dimensions Inc., Kirkland, WA, USA) is positioned in the coronary sinus to accomplish an indirect annuloplasty and treat functional MR. The device is a fixed-length, double-anchored nitinol structure whose distal anchor is deployed deep in the coronary sinus via a 9 Fr delivery catheter (Fig. 8.11) [124]. Traction is used to cinch the posterior periannular tissue and reduce the mitral annular circumference. When tissue plication is optimized as evidenced by a diminished degree of mitral regurgitation by TEE, the proximal anchor is deployed at the coronary sinus ostium. Angiography is performed before final release of the device, to ensure that the left circumflex coronary artery is unharmed.

The Carillon Mitral Annuloplasty Device European Union Study (AMADEUS) showed a modest (22%) reduction in MR at 6 months in 30 of the 48 patients enrolled. Similar results were shown in the Transcatheter Implantation of the Carillon Mitral Annuloplasty Device (TITAN) trial. The device was implanted successfully in 35 of 53 patients (68%), significantly reducing regurgitation and LV diastolic and systolic volumes. An additional study with the Carillon device is described in Table 8.7.

MVRx ARTO Device

Another device in development for treating FMR is the ARTO device (MVRx Inc., Belmont, CA, USA). This device employs magnet-tipped catheters positioned in the LA (through a transseptal puncture) and in the coronary sinus, which link on either side of the atrial wall behind the P2 segment of the posterior leaflet. The anchors are joined with a crossing wire to facilitate placement of a T-bar anchor in the coronary sinus. Another anchor is placed at the atrial septum at the site of transseptal puncture, and a linking suture is tensioned under TEE guidance until the anterior-posterior diameter of the mitral annulus is reduced sufficiently to reduce MR (Fig. 8.12) [125].

The first phase of the Mitral Valve Repair Clinical Trial (MAVERIC) of the ARTO device involved 11 patients with NYHA II–III symptoms and ≥2+ MR, for all of whom the risks of surgery were deemed prohibitively high by the heart team. Device implantation was successful in all 11 patients, with no procedural safety events and only 2 events at 30-day follow-up (1 pericardial effusion requiring drainage, and 1 asymptomatic device dislodgement). At 6 months, improvements were seen in MR grade, LV volumes, MR severity, regurgitant volumes, annular diameter, and functional status. The Phase II trial has yet to begin recruiting.

Leaflet-Based Devices

Several devices exist or are in development to correct leaflet disease or reapproximate leaflets in the manner of the Alfieri stitch. The most well known of these devices is the Abbott MitraClip, which is described elsewhere in this textbook. The success of the Abbott MitraClip has led to the development of other devices that work by leaflet coaptation, the best known of which is the Edwards PASCAL device.

Edwards PASCAL Device

The PASCAL device (Edwards LifeSciences) is another device that accomplishes leaflet coaptation. The device has a pair of paddles, placed 180° apart, which capture the edge of the anterior and posterior leaflet. A spacer in the middle is used to reduce the regurgitant orifice area, and the device allows independent leaflet grasping, giving it the potential for use in patients with more complex anatomy (Fig. 8.13) [123].

A multicenter prospective observational first-in-human compassionate use study is underway (Table 8.8). Preliminary (6-month) data show technical success in 28 of the first 29 patients, and less than one-quarter of patients required a

Table 8.5 Valcare Amend trials

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
AMEND™ Mitral Valve Repair System, Annuloplasty Ring Applied in a Transcatheter Method	Prospective, multicenter, single-arm, nonrandomized trial, 40 pts	1. Experimental: Device	1. Need for MV annuloplasty without need for concomitant CT surgery 2. NYHA ≥II 3. High risk for surgery	1. Major cardiac or noncardiac disease that incurs unacceptable risk 2. Life expectancy <12 months 3. Heavily calcified annulus/leaflets 4. Active infection or hx of endocarditis 5. Previous MV intervention 6. Drug/alcohol abuse	1. Freedom from MAE (30 days) 2. Technical success of implantation	1. Freedom from MAE at 6 months	6 months	December 2018

CT cardiothoracic, *hx* history, *MAE* major adverse events, *MV* mitral valve, *NYHA* New York Heart Association

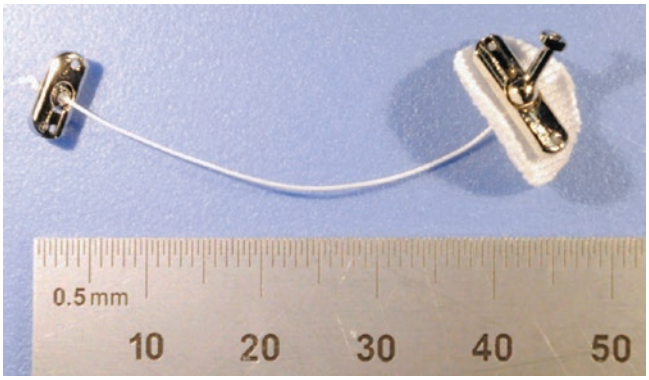

Fig. 8.9 MitraSpan Tasra device. Reprinted with permission from MitraSpan, Inc.

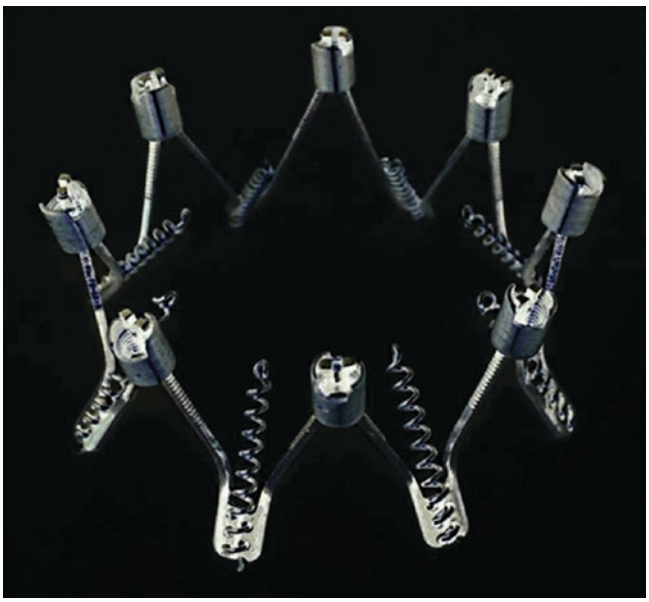

Fig. 8.10 Millipede IRIS Transcatheter Angioplasty Ring. From Sharma and Gafoor [123]. Reprinted with permission from Millipede Medical

second device implantation. Only 3 patients needed reintervention, and MR reduction and functional improvement were sustained; reverse LV remodeling was seen at 6 months, particularly in FMR patients.

Chordal Repair Devices

Numerous devices are being developed to repair chordal abnormalities. Prominent among these devices are the NEOCHORD DS1000 system, the Harpoon Medical Harpoon system, and the MISTRAL system.

NEOCHORD DS1000 System

The NEOCHORD DS1000 (NeoChord Inc., St. Louis Park, MN, USA) consists of expanded PTFE (ePTFE) sutures that are attached to the prolapsing mitral leaflet under echocardiographic guidance via an off-pump, transapical approach. Leaflets are grasped and pierced to allow fixation and retraction of the neochordae, and then are subsequently fixated at the LV apex (Fig. 8.14).

The initial Transapical Artificial Chordae Tendineae (TACT) trial involved 30 patients with severe MR due to isolated posterior leaflet prolapse. The procedure was successful in 26/30 patients, in whom at least one neochord was placed and MR was reduced from 3–4+ to ≤2+. This reduction in MR was maintained by 17/30 patients at 30 days. An ongoing trial with this device is described in Table 8.9.

Harpoon Medical Harpoon TSD-5 Device

Another device that also uses ePTFE chords, anchored to the prolapsed mitral leaflet via transapical access, is the Harpoon TSD-5 (Harpoon Medical, Baltimore, MD, USA). Under TEE guidance, the device is directed to the LV surface of the prolapsed leaflet, and the leaflet is perforated after it is stabilized and the device is actuated, perforating the leaflet with a needle that in turn is wrapped by ePTFE coils in a preformed knot. The needle is withdrawn, producing a double helix coiled knot on the atrial surface of the leaflet that secures the pair of ePTFE chords to the leaflet. Multiple devices can be deployed as needed before length is finally selected and the chords are tethered to the LV apex (Fig. 8.15). Initial data from 11 patients with severe MR for posterior leaflet prolapse show 100% procedural success, minimal postprocedural MR, and, at 1 month, mild MR and significant reductions in end-diastolic and left atrial volume. Trials have been planned for the Harpoon device.

Mitralix MISTRAL Device

Another device that reapproximates the chords is the transseptal 12-Fr MISTRAL device (Mitralix Ltd., Rehovot, Israel). This device consists of an atraumatic, spiral-shaped nitinol wire that pulls the chordae together.

Emerging Mitral Valve Replacement Devices

Although no device has yet been approved for transvascular MV replacement (TMVR), several promising devices are in development. Such TMVR devices have the potential to extend the therapeutic window into higher-risk, "too sick" patient populations, offering them relief of their MR with the potential for results comparable to those of surgical replacement with a bioprosthetic valve, but with fewer of the comorbidities associated with traditional surgery. In addition to extending the therapeutic window, TMVR devices have the potential to supplant traditional surgical valve replacement with a bioprosthetic valve for patients for whom this is the primary therapeutic option. Furthermore, TMVR devices hold an intriguing potential to treat secondary MR. Surgical

Table 8.6 Millipede IRIS trial

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
Annular Reshaping of the Mitral Valve for MR using the Millipede IRIS System	Prospective, multicenter, single-arm, nonrandomized trial, 30 pts	1. Experimental: Device	1. Severe symptomatic MR (ERO >0.2 cm^2 for secondary MR, ERO >0.4 cm^2 for primary MR) 2. LVEF >20% and <50% 3. NYSHA II–IVa 4. Normal CK-MB 5. LVESD <6.5 cm	1. PASP >70, RV dysfunction 2. HOCM, restrictive or constrictive HD 3. Hemodynamic instability 4. CABG, PCI, or carotid intervention within 30 days 5. Need for other CT surgery 6. LVEF <20% 7. CKD, multiple others	1. Acute safety, defined as incidence of adverse events (30 days)	1. Efficacy; echo-measured reduction in MR without significant MS (48 h)	30 days	December 2019

CABG coronary artery bypass grafting, *CKD* chronic kidney disease, *CKMB* creatine kinase-muscle/brain, *CT* cardiothoracic, *ERO* effective regurgitant orifice, *HD* heart disease, *HOCM* hypertrophic obstructive cardiomyopathy, *LVEF* left ventricular ejection fraction, *LVESD* left ventricular end-systolic dimension, *MR* mitral regurgitation, *MS* mitral stenosis, *NYHA* New York Heart Association, *PASP* pulmonary artery systolic pressure, *PCI* percutaneous coronary intervention, *RV* right ventricle/ventricular

results for secondary/functional MR are not as good as those for primary MR, and surgical repair with annuloplasty has been associated with a high recurrence rate of MR [92]. In such patients, a less invasive, less morbid, yet durable replacement option would be an attractive alternative.

However, the development of TMVR devices has been slow relative to the development of TAVR devices because of the complexity of the ventricular-valvular mitral apparatus, as well as the location and size of the MV. The mitral annulus is an amorphous, complex, and dynamic structure with an ellipsoid shape and variable calcification. The lack of a predominantly cylindrical structure (like the aortic valve annulus) with significant calcification has made deploying a stent-based valve prosthesis challenging in terms of anchoring and fixation, as well as properly aligning a newly placed endovascular prosthetic valve within the annulus. The pressure differential between the atrium and ventricle, which can be up to 3 times greater than that encountered in aortic valve delivery, further complicates matters. Furthermore, the large size of the mitral annulus, especially in patients with dilated ventricles, often necessitates the use of valves larger than 30 mm in diameter, making delivery of these devices challenging. This is especially true if a transfemoral/transseptal approach is used, because the size limitations of the right atrium, atrial septum, and LA would limit the maneuverability of such a device. For this reason, several valve devices are being developed to use a transapical approach. However, this approach carries an additional set of risks that have limited device development.

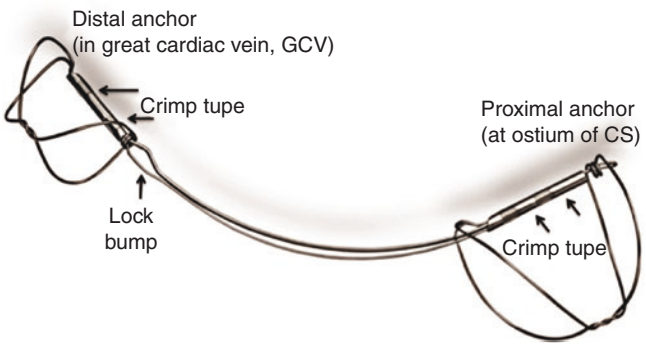

Fig. 8.11 Carillon device. The distal anchor is placed in the great cardiac vein, crimp tube, and lock bump (*left*), and the proximal anchor is placed at the ostium of the coronary sinus and the crimp tube (*right*). From Goldberg et al. [124]. Reprinted with permission from Europa Digital & Publishing

Broadly speaking, TMVR devices can be grouped according to their fixation method and their delivery approach. Delivery approaches can, in turn, be broadly categorized as transapical, transfemoral-transseptal, and transatrial. Currently, the majority of devices use a transapical approach, although future devices are being developed for a transseptal delivery approach. Fixation strategies differentiate valves into several different groups.

Wing- or Tab-Based Fixation Devices

Using wings or tabs that engage the native leaflets is the most common approach. These wings or tabs must capture healthy leaflets without becoming entangled in the chordae tendineae. This requirement may preclude or limit the use of these devices in patients with degenerative MR. These devices include the Edwards FORTIS, Neovasc Tiara, Edwards CardiAQ, and NaviGate devices.

Table 8.7 Carillon Mitral contour trial

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
CARILLON trial: Transcatheter treatment of FMR	Prospective, multicenter, multiple-arm, double-blind RCT, 400 pts	1. Experimental: Device 2. Comparator: GDMT for HF	1. Cardiomyopathy, NYHA II, III, or IV 2. FMR >2+ and ERO >0.2 cm^2 3. 6MWD 200–450 m 4. LVEF <50% 5. LVEDD >7 cm 6. Optimized on HF medications 7. Anatomy appropriate for implant	Many criteria; refer to trial	1. Freedom from MAE (12 months) 2. Hierarchical clinical composite (12 months) 3. Change in RVol (12 months)	1. Freedom from periprocedural MAE (30 days vs. discharge) 2. Freedom from MAE (12 months) 3. 6MWD (12 months) 4. LVESV (12 months) 5. KCCQ (12 months) 6. NYHA Class (12 months)	12 months	October 2025

6MWD 6-minute walk distance, *ERO* effective regurgitant orifice, *FMR* functional mitral regurgitation, *GDMT* goal-directed medical therapy, *HF* heart failure, *KCCQ* Kansas City Cardiomyopathy Questionnaire, *LVEDD* left ventricular end-diastolic dimension, *LVEF* left ventricular ejection fraction, *LVESV* left ventricular end-systolic volume, *MAE* major adverse events, *NYHA* New York Heart Association, *RVol* regurgitant volume

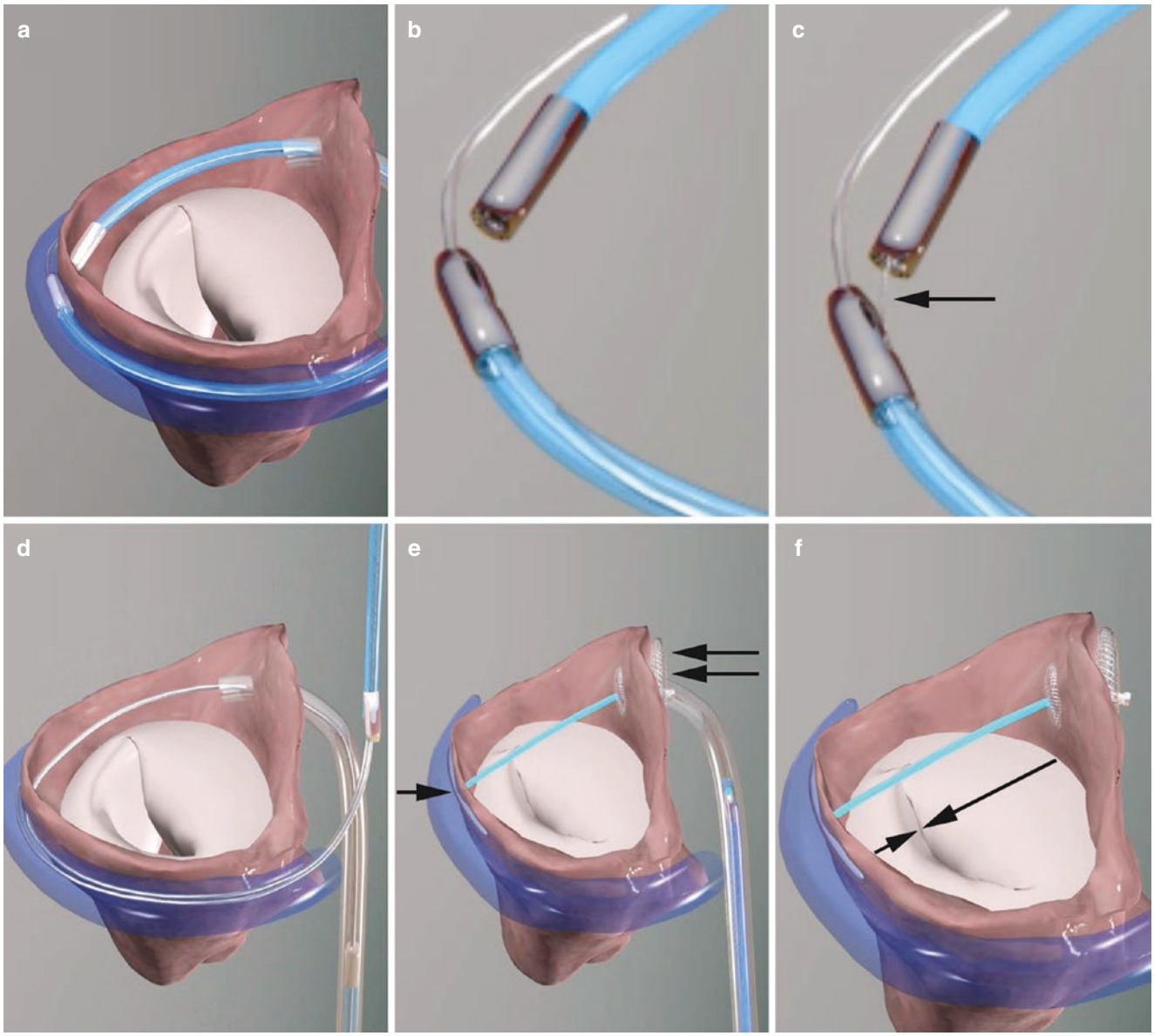

Fig. 8.12 ARTO device and implantation. (**a**) Great cardiac vein (GCV) and left atrial (LA) MagneCaths in position and magnetically linked behind the P2 segment of the posterior mitral leaflet. (**b**) Close-up of magnetically linked LA and GCV MagneCaths. Each magnetic catheter has a specific shape and lumen to direct and receive the crossing wire. (**c**) The crossing wire (*arrow*) is pushed from the GCV into the LA MagneCath. The MagneCaths are aligned to direct the wire safely from the GCV to the LA through the atrial wall. (**d**) After using an exchange catheter, the loop guidewire is placed across the left atrium. This guidewire directs the placement of the GCV anchor (T-bar, *single arrow*) and septal anchor (*double arrow*). (**e**) The Arto MVRx System in place before tensioning. (**f**) Tensioning of the bridge results in precise shortening of the mitral annulus anteroposterior diameter (*arrows*) and elimination of functional mitral regurgitation; once the final position is attained, the suture is cut and secured with a suture lock. From Erglis et al. [125]. Reprinted with permission from Europa Digital & Publishing

Edwards FORTIS Device

The Edwards Fortis TMVR device (Edwards LifeSciences) has a central cylindrical valve body composed of three pericardial leaflets sutured within a 29-mm diameter nitinol stent. It uses two paddles located in the outflow of the central valve body, allowing capture of the mitral leaflets to anchor the device. An additional atrial flange at the inflow point, made from nitinol struts covered with cloth, rests on the base of the LA and allows tissue endothelialization. The Fortis device is delivered through a 42 Fr transapical delivery system (Fig. 8.16) [126].

Twenty patients who were either inoperable or at high risk from conventional MV surgery and unsuitable for other transcatheter alternatives have received the FORTIS implant;

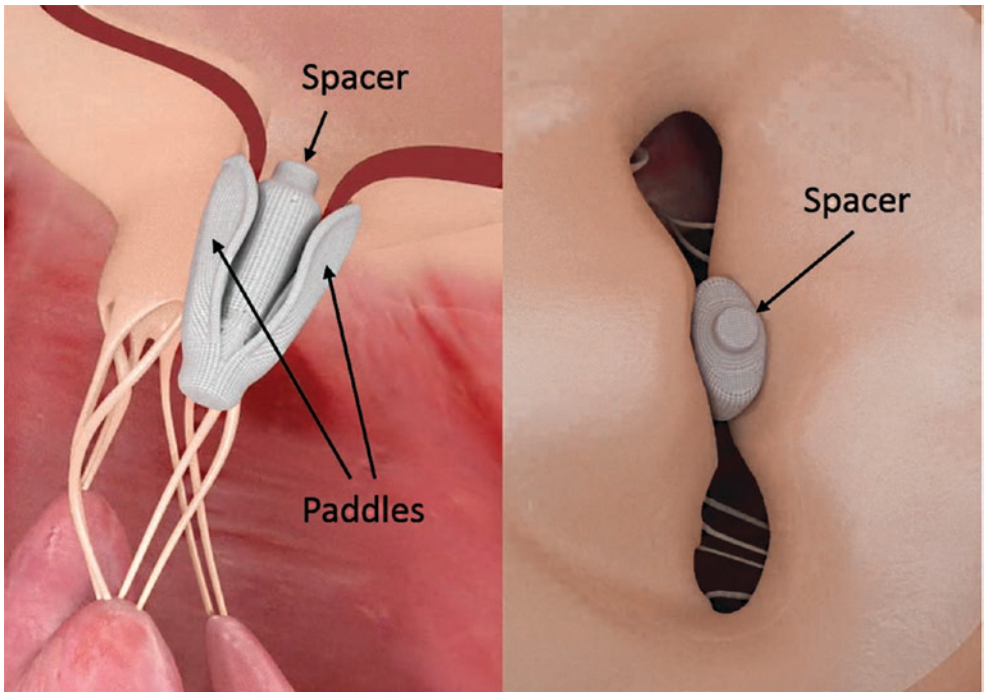

Fig. 8.13 Pascal device. The renderings show the device grasping leaflets in a cross-sectional view (*left*) and an atrial view (*right*). From Sharma et al. [123]. Reprinted with permission from Edwards Lifesciences

Table 8.8 CLASP study of the PASCAL device

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
CLASP Edwards PASCAL Transcatheter Mitral Valve Repair System Study	Prospective, multicenter, single-arm, open-label trial, 120 pts	1. Experimental: Device	1. NYHA II–IVa despite optimal medical therapy 2. Clinically significant MR 3. Candidacy for SMVR determined by heart team 4. Non-commissural primary regurgitant jet 5. MVA >4 cm^2	1. TEE failed or not possible 2. Unsuitable anatomy 3. MVA <4 cm^2 4. RV dysfunction or failure 5. Life expectancy <12 months	1. Composite of MAE (CV mortality, stroke, MI, new need for RRT, severe bleeding, reintervention for device complications) (30 days)	1. MR reduction (30 days–1 year) 2. All-cause mortality (30 days–1 year) 3. Recurrent HF hospitalization (30 days–1 year) 4. Change in 6MWD (6 months, 1 year)	1 year	August 2021

6MWD 6-minute walk distance, *CV* cardiovascular, *HF* heart failure, *MAE* major adverse events, *MI* myocardial infarction, *MR* mitral regurgitation, *MVA* mitral valve area, *NYHA* New York Heart Association, *RRT* renal replacement therapy, *RV* right ventricle/ventricular, *SMVR* surgical mitral valve repair, *TEE* transesophageal echocardiography

13 of these patients' results have been made available [127]. The procedure was successful in 10 patients. Two patients were converted to surgery, one because of device malposition and one because the balloon system became entangled in the chords before implantation. Incomplete posterior leaflet capture resulted in partial device migration and death for 1 patient on day 4. Four patients died in the hospital, and eight survived beyond 30 days. All FORTIS implants under all protocols have been voluntarily put on hold because of evidence of thrombosis.

Neovasc Tiara Device

The Neovasc Tiara (Neovasc Inc., Richmond, BC, Canada) consists of a D-shaped, self-expanding nitinol frame with a trileaflet bovine pericardial valve. It has a full atrial skirt and three ventricular anchors, one anterior and two posterior, that

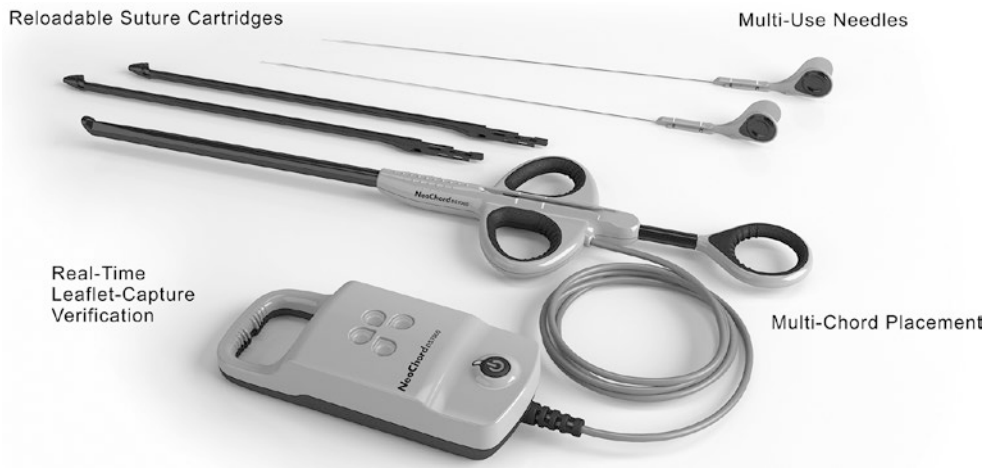

Fig. 8.14 NeoChord DS100 device with suture cartridges, multi-use needles, delivery instrument, and leaflet capture verification monitor. Reprinted with permission from NeoChord, Inc.

affix the valve to the fibrous trigone and the posterior annulus [128]. The valve currently is manufactured in two sizes, 35 and 40 mm, and the transapical delivery system is 32 Fr and 36 Fr, respectively (Fig. 8.17) [129]. The current status of ongoing trials involving the Tiara device is listed in Table 8.10.

Edwards CardiAQ Device

Another device system that uses fixation to the native valve leaflets via wings or tabs is the Edwards CardiAQ system (Edwards Lifesciences). The device is a self-expanding, nitinol frame with a trileaflet bovine pericardial valve. The frame has opposing anchors that secure the device in the annulus, and it possesses foam-covered ventricular anchors that engage the subvalvular apparatus. A polyester fabric skirt helps minimize paravalvular regurgitation. The device uses supra-annular positioning to reduce the risk of LV outflow tract obstruction, and it does not require rotational alignment [129, 130] (Fig. 8.18).

It uses a 33 Fr delivery system and can be deployed via a transapical or a transfemoral-transseptal approach. Two trials have been withdrawn and one trial was terminated to allow further design validation and testing of the valve; one trial remains ongoing and is described in Table 8.11.

"Valve and Dock" Fixation Devices

In the valve and dock approach to device fixation, a docking device is fixated to the mitral position; subsequently, a valve is docked inside this device. The Caisson TMVR and MValve devices both use this system.

Caisson TMVR Device

The Caisson TMVR device (Caisson Interventional LLC, Maple Grove, MN, USA) uses a valve and dock fixation method and is fully retrievable. The device has two components: a D-shaped, self-expanding nitinol anchor, and a self-expanding, nitinol-framed, trileaflet porcine pericardial valve. The device can be delivered through a transfemoral-transseptal approach with a 31 Fr delivery system (Fig. 8.19) [129]. The design of the Percutaneous Mitral Valve Replacement EvaLuation Utilizing IDE Early Feasibility Study (PRELUDE) of this device is summarized in Table 8.12.

MValve Device

Another novel device that uses this valve and dock approach is the MValve transcatheter mitral replacement system (MValve Technologies Ltd., Herzliyya, Israel). The device is deployed in two steps: A proprietary valve support/dock is deployed in and around the native mitral annulus, and a commercial transcatheter valve is deployed within the dock to replace the MV (Fig. 8.20) [129]. The device is designed to replicate existing valve-in-valve approaches by creating an annular dock inside the existing mitral annulus, within which any commercial valve can be placed.

Left Ventricular Tethering

Tethering to the LV is an approach wherein fixation of the valve relies on an additional anchor on the LV wall, near the apex. One concern posed by this approach is that it places an abnormal compressive load on the LV in patients who already have a compromised LV. The Abbott Tendyne valve uses this approach.

Abbott Tendyne Mitral Valve System

The Abbott Tendyne system (Abbott Vascular, Santa Clara, CA, USA) uses a transapical, fully repositionable and recapturable trileaflet porcine pericardial valve that is sewn inside two self-expanding nitinol stents. The outer stent is available in various sizes and is D-shaped to conform to the native mitral annulus. The inner circular frame has a large (>3.0 cm^2) effec-

Table 8.9 NeoChord DS1000 system trial

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
ReChord: Randomized trial of the NeoChord DS1000 system vs. open surgical repair	Prospective, multicenter, multiple-arm, open-label RCT, 585 pts	1. Experimental: Device 2. Comparator: SMVR	1. Candidate for SMVR w/ CPB 2. Grade III moderate or Grade IV severe DMR 3. Isolated segmental prolapse of A2 or P2 segment 4. Anterior leaflet ≥65% of AP distance 5. Anatomic and general suitability	1. Prior MV surgery 2. Concomitant cardiac procedures 3. Other cardiac procedures within 3 months	1. Proportion of patients free of MAE as compared with control group (30 days) 2. Proportion of patients free of Grade II, III, or IV MR, MV replacement, or MV reintervention compared with control group (30 days)	None	1 year	July 2025

AP anterior-posterior, *CPB* cardiopulmonary bypass, *DMR* degenerative mitral regurgitation, *MAE* major adverse events, *MV* mitral valve, *RCT* randomized, controlled trial, *SMVR* surgical mitral valve repair

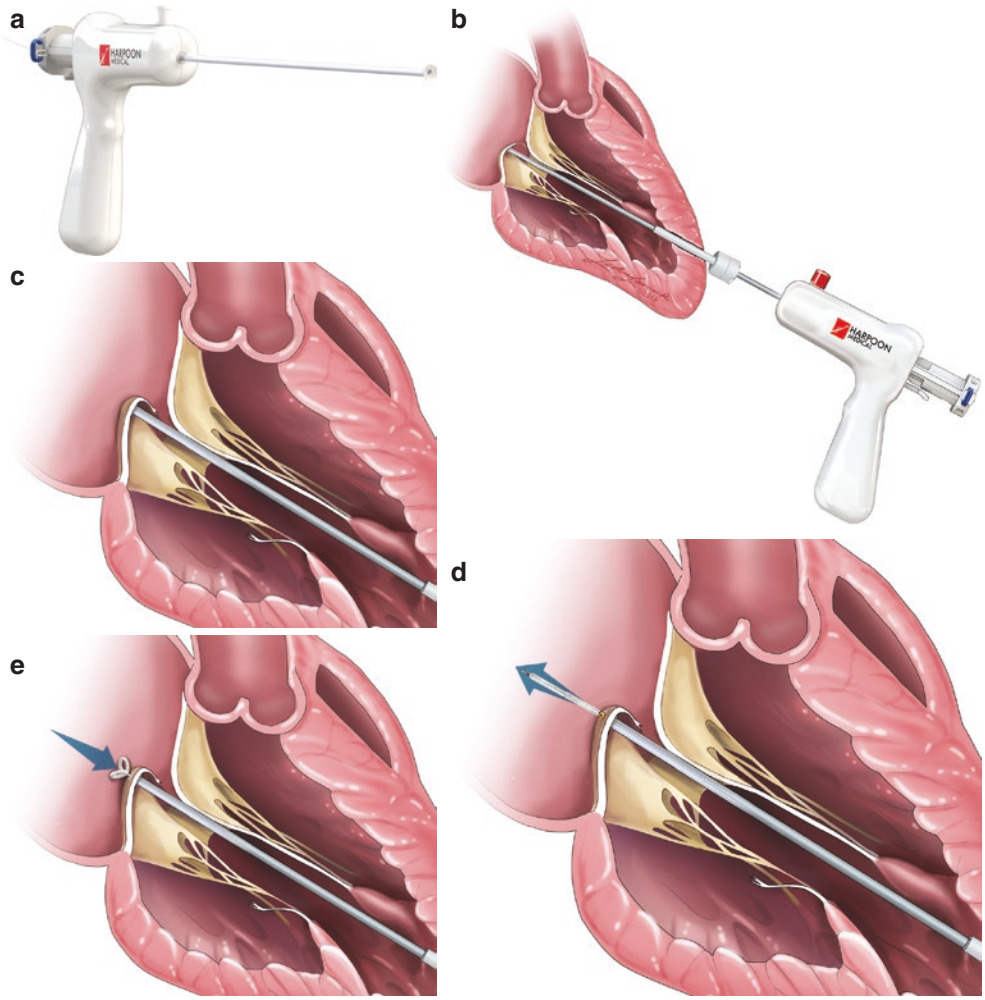

Fig. 8.15 Use of the Harpoon TSD-5 device for chordal repair in the mitral valve. (**a**) The Harpoon TSD-5. (**b**) Harpoon device inserted into left ventricle and directed toward and into contact with mitral leaflet. (**c**) Close-up view of Harpoon device in contact with mitral leaflet with ruptured chord. (**d**) Close-up view showing perforation of mitral leaflet with device needle and preformed PTFE chords. (**e**) Close-up view of deployed PTFE chords in knot configuration, secured to leaflet. Chords are then measured to appropriate length and anchored to LV apex. Images courtesy of Edwards Lifesciences LLC

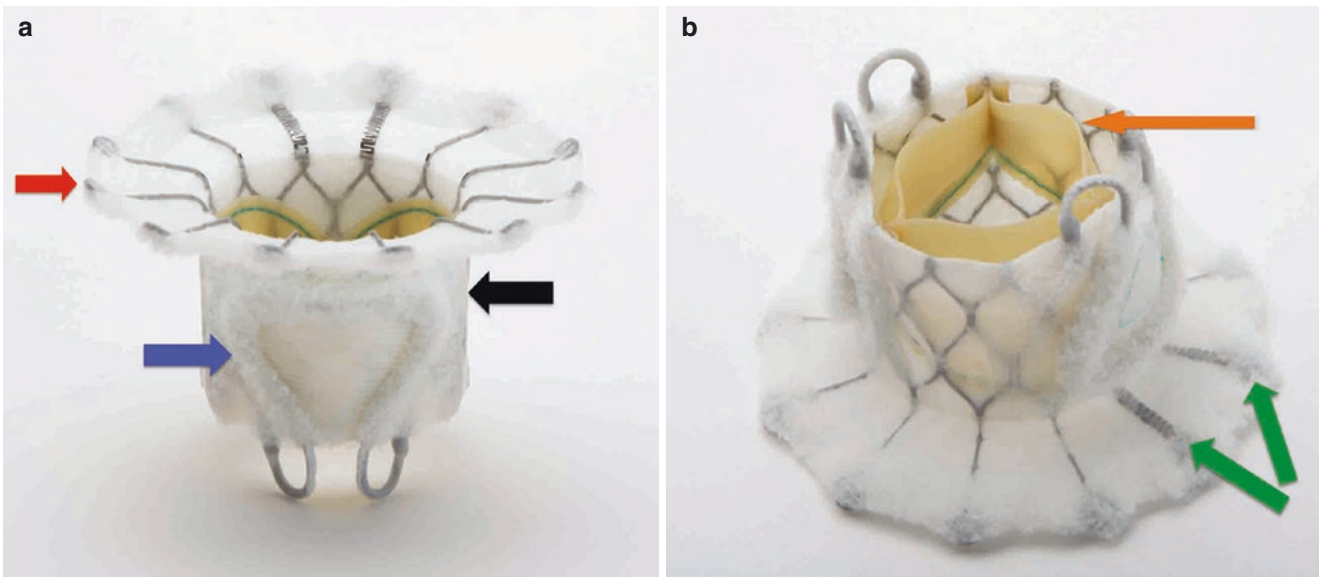

Fig. 8.16 Fortis device. (**a**) Side profile highlighting atrial flange (*red arrow*), body of valve (*black arrow*), and one of two paddles (*blue arrow*). (**b**) Side profile highlighting bovine pericardial leaflets (*orange arrow*) and flexible struts (*green arrow*), which align with the A2 segment of the mitral valve. From Bapat et al. [126]. Reprinted with permission from Europa Digital & Publishing

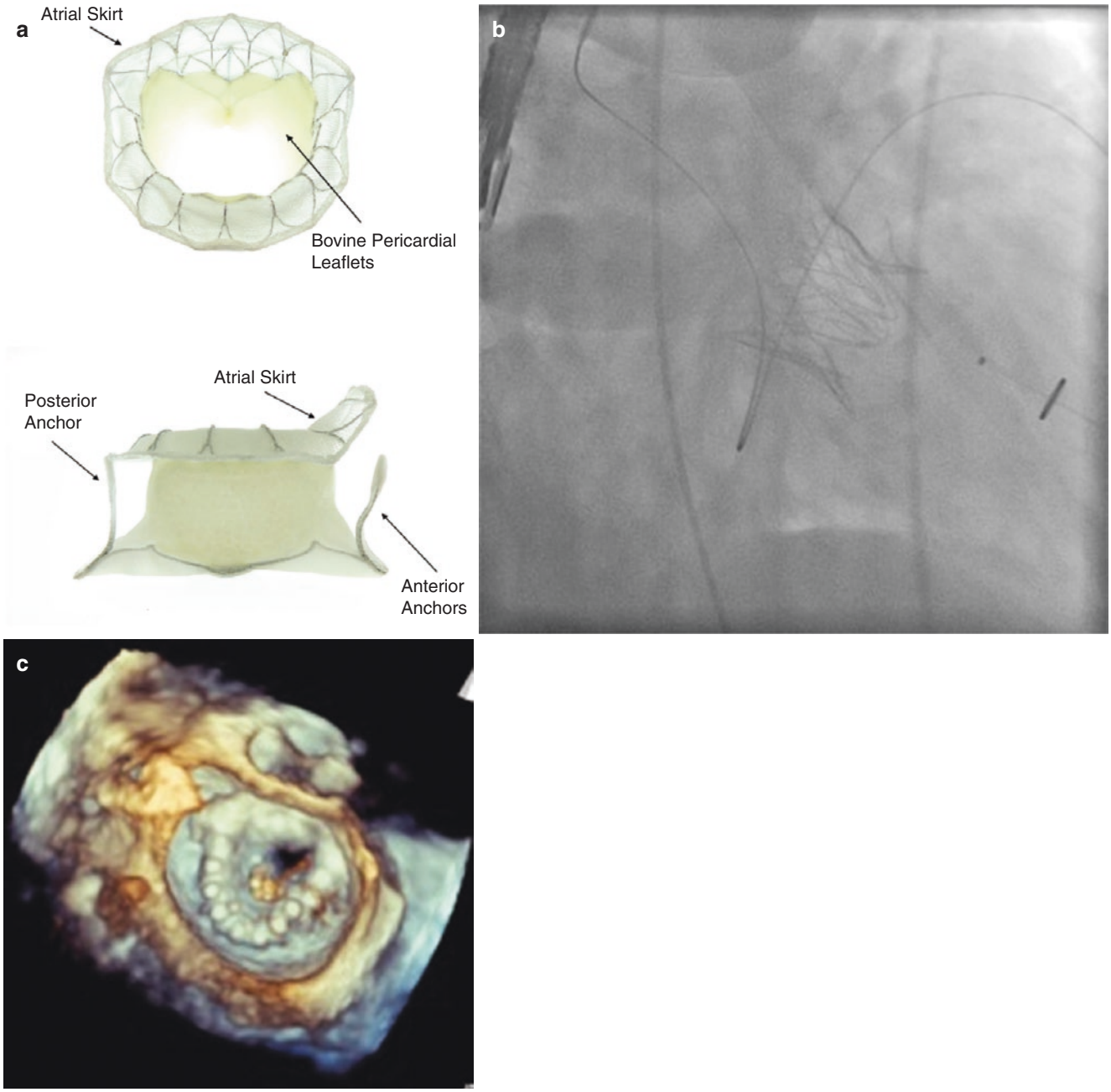

Fig. 8.17 Tiara device. (**a**) Valve prosthesis. (**b**) Valve prosthesis under fluoroscopy. (**c**) 2D TEE images of device. From Reguiero et al. [129]. Reprinted with permission from Elsevier

tive orifice area. The valve is tethered to the LV apex with an LV apical tethering system, which is designed to reduce paravalvular regurgitation and facilitate apical closure.

The device uses a 34 Fr transapical delivery sheath. The valve is positioned above the annulus, and the D-shaped outer stent is oriented such that the straight side and atrial cuff are aligned with the aortomitral continuity and the aorta. The valve is then retracted backwards into the mitral annulus with tactile guidance, and positioning is confirmed with echocardiography and fluoroscopy. Then the apical pad is positioned over the LV apical tether, and a tension gauge is used to adjust tension to keep the valve in a stable position (Fig. 8.21) [131].

An initial global feasibility study of 30 patients with grade 3/4 MR showed successful implantation in 28/30 patients, no residual MR in 26 patients, and only mild central MR (1+) in 1 patient at 30 days. At follow-up, 21 patients (75%) had NYHA Class I–II symptoms and improvement in LV end-diastolic volume index. Table 8.13 describes an ongoing trial of the Abbott Tendyne system.

Table 8.10 Neovasc Tiara trials

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
TIARA-I	Multicenter, single-arm, prospective study, 30 pts	1. Experimental: TMVR	1. Severe symptomatic MR (Stage D) 2. High surgical risk for open MV surgery 3. Meets anatomical eligibility criteria for available sizes 4. NYHA Class III–IV	1. Operable DMR per heart team 2. Prohibitive risk, deemed too frail, or listed for transplant 3. Unsuitable cardiac structure 4. Prior stroke within 4 weeks 5. Need for coronary revascularization 6. hx of or active endocarditis 7. Renal insufficiency (Cr >2.5 mg/dL)	1. Freedom from all-cause mortality and MAE: disabling stroke, MI, renal failure necessitating dialysis, life-threatening bleeding, cardiac surgical or transcatheter reintervention (30 days or discharge, whichever is later)	1. All-cause mortality, stroke, MI, renal failure, bleeding, reintervention (30, 90, 180 days, annually to 5 years) 2. Device- and procedure-related MAE (30 days) 3. Progression of HF (1 year) 4. Procedural success (post-procedure, then annually for 5 years) 5. NYHA class, 6MWD, functional performance (up to 5 years) 6. Survival (1 year)	5 years	August 2023
TIARA-II	Global, multicenter, single-arm, prospective safety and performance study	1. Experimental: TMVR	1. Severe symptomatic MR (Stage D) 2. High surgical risk for open MV surgery 3. Meets anatomical eligibility criteria for available sizes 4. NYHA Class III–IV	1. Frailty (per objective criteria) 2. Previous CT surgery 3. Unsuitable anatomy 4. Untreated CAD 5. Chronic dialysis 6. Pregnancy 7. Bleeding or coagulation disorder 8. Active infection 9. Life expectancy <1 year	1. Freedom from all-cause mortality (30 days) 2. Freedom from major adverse events (30 days) 3. Reduction of MR to optimal or acceptable (30 days)	1. Freedom from all-cause mortality (up to 5 years) 2. Freedom from MAE (up to 5 years) 3. Technical success 4. Procedural success (30 days) 5. Device success (up to 5 years) 6. NYHA Class (up to 5 years) 7. 6MWD (up to 5 years) 8. KCCQ (up to 5 years) 9. Hemodynamic performance (up to 5 years) 10. Patient success (1 year)	Up to 5 years	January 2024

6MWD 6-minute walk distance, *CAD* coronary artery disease, *Cr* creatinine, *CT* cardiothoracic, *DMR* degenerative mitral regurgitation, *HF* heart failure, *hx* history, *KCCQ* Kansas City Cardiomyopathy Questionnaire, *MAE* major adverse events, *MI* myocardial infarction, *MR* mitral regurgitation, *MV* mitral valve, *NYHA* New York Heart Association, *TMVR* transcatheter mitral valve replacement

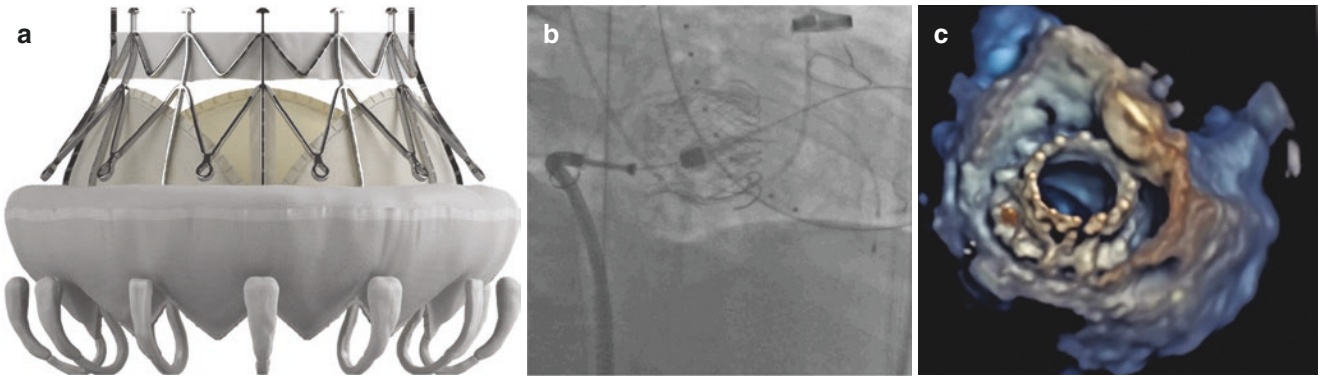

Fig. 8.18 CardiAQ device. (**a**) Valve prosthesis. (**b**) Valve prosthesis under fluoroscopy. (**c**) 2D TEE images of device. From Reguiero et al. [129]. Reprinted with permission from Elsevier

Table 8.11 Edwards CardiAQ trials

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
CardiAQ-Edwards TMVR Early Feasibility Study	Prospective, multicenter, single-arm, nonrandomized trial, 30 pts	1. Experimental: TMVR	1. Clinically significant, symptomatic MR 2. High risk for open-heart surgery 3. Meets anatomical criteria	1. Unsuitable anatomy 2. Inoperable patient	1. Safety assessed by freedom from device or procedure-related adverse events (30 days)	1. NYHA functional class (up to 5 years) 2. 6MWD (up to 5 years) 3. Reduction in MR grade (up to 5 years)	5 years	June 2022

6MWD 6-minute walk distance, *MR* mitral regurgitation, *NYHA* New York Heart Association, *TMVR* transcatheter mitral valve replacement

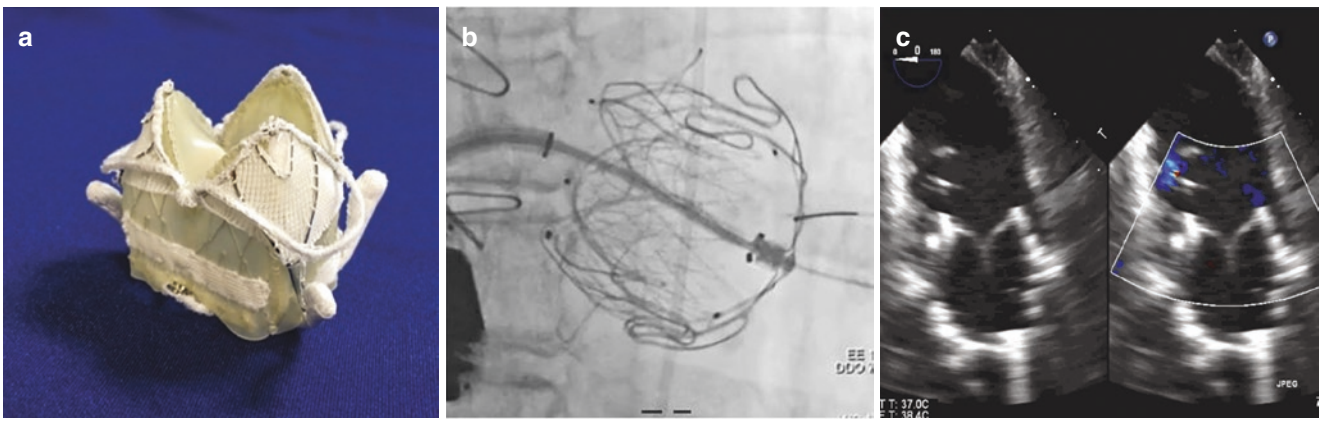

Fig. 8.19 Caisson TMVR device. (**a**). Valve prosthesis. (**b**) Valve prosthesis under fluoroscopy. (**c**) 2D TEE images of device. From Reguiero et al. [129]. Reprinted with permission from Elsevier

Clamping or Rivet Mechanisms for Annular Fixation

Yet another approach uses a clamping or rivet mechanism to surround the annulus and enable fixation. This approach may work well for certain anatomical situations, such as regurgitant MVs with an hourglass shape (i.e., a large LA and LV), but not in situations such as degenerative mitral disease in which the downstream flange of the clamp does not have a "lip" of tissue to engage. The NaviGate and HighLife valves use this approach.

Table 8.12 PRELUDE trial of Caisson TMVR

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
Caisson TMVR system early feasibility study (PRELUDE)	Prospective, multicenter, single-arm, nonrandomized trial, 20 pts	1. Experimental: TMVR	1. Severe MR 2. High risk for open-heart surgery 3. NYSHA II–IVa or HF	1. Unsuitable anatomy 2. LVEDD >7 cm 3. LVOT obstruction 4. Severe RV dysfunction 5. Stroke within 90 days 6. TIA or MI within 30 days	1. Number of pts without MAE (30 days)	1. Number of pts with technical success (intraoperative) 2. Number of living, stroke-free pts with device success (30 days)	30 days	December 2023

LVEDD left ventricular end-diastolic dimension, *LVOT* left ventricular outflow tract, *MAE* major adverse events, *MI* myocardial infarction, *MR* mitral regurgitation, *NYHA* New York Heart Association, *RV* right ventricle/ventricular, *TIA* transient ischemic attack, *TMVR* transcatheter mitral valve replacement

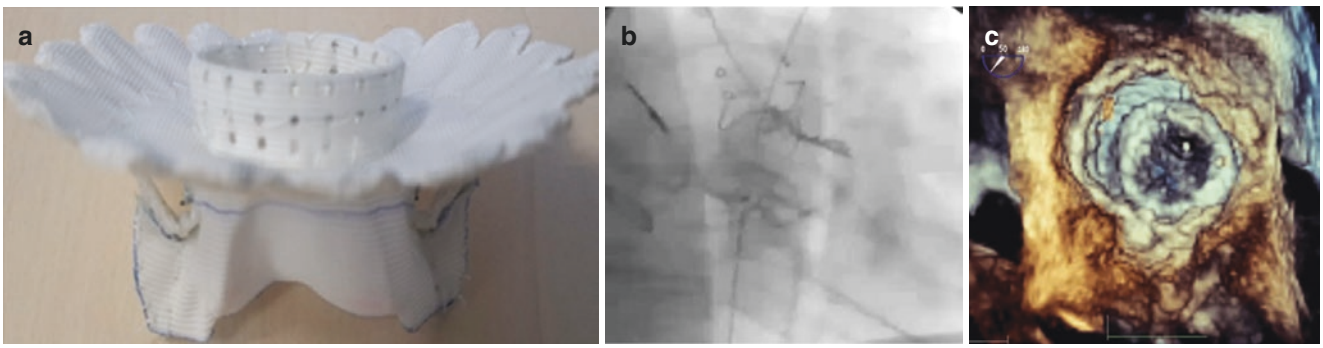

Fig. 8.20 MValve device. (**a**) Valve prosthesis. (**b**) Valve prosthesis under fluoroscopy. (**c**) 2D TEE images of device. From Reguiero et al. [129]. Reprinted with permission from Elsevier

Fig. 8.21 Tendyne System. Mitral valve prosthesis (*right*) and left ventricular apical tethering device (*left*). From Perpetua and Reisman [131]. Reprinted with permission from Europa Digital & Publishing

NaviGate Cardiac Structures NaviGate Mitral Valved Stent

The NaviGate Mitral Valved Stent (NaviGate Cardiac Structures Inc., Lake Forest, CA, USA) consists of a self-expanding nitinol frame with a truncated cone. Its low profile height (21 mm) allows delivery into the heart while reducing the risk of protrusion into the atrium or ventricle. The device employs two rows of annular winglets that anchor the device to the annulus. It is available in three sizes (30/36, 30/40, and 33/44 mm) and can be delivered via transseptal, transatrial, or transapical routes with a 30 Fr system (Fig. 8.22) [132]. Early feasibility trials have been planned with this device for use in both tricuspid and mitral valve positions.

HighLife Device

With the HighLife TMVR System (HighLife SAS, Paris, France), a loop is advanced via the aortic valve, and a subannular implant is delivered via an 18 Fr femoral arterial sheath to form a loop implant in a subannular position. Transatrial or transapical delivery is then used to deliver a trileaflet bovine pericardial valve within a nitinol frame, which has a preformed annular groove to allow seating within the initially placed loop implant. The bioprosthesis expands inside the loop, and the shape of the bioprosthesis prevents migration within the ventricle (Fig. 8.23) [133]. The design of the HighLife system trial is described in Table 8.14.

Dynamic Cork Effect

The last approach uses a dynamic cork effect. In this mechanism, variable degrees of radial stiffness along the height of the structure enable the valve to compress to fit the annulus but stay larger in diameter downstream of the annulus, acting as a "cork" during systole without dilating the annulus. An advantage of this design is a high degree of adaptability to the ovoid or kidney-bean shape of the MV annulus without the need for rotational alignment. Such a design may work well in treating both degenerative and functional mitral regurgitation, but it does have some downsides. Two concen-

Table 8.13 Abbott Tendyne trial

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
Expanded clinical study of the TENDYNE Mitral Valve System	Prospective, multicenter, single-arm, nonrandomized trial, 110 pts	1. Experimental: TMVR	1. Severe MR, primary or secondary 2. High risk/ unsuitable for open-heart surgery 3. NYSHA II–IVa	1. Severe MAC or MS 2. Chest condition precluding transapical access 3. Prior surgical or interventional treatment of mitral or aortic valves	1. Safety assessed by freedom from device- or procedure-related adverse events (30 days) 2. Performance assessed by freedom from device malfunction (30 days)	None	30 days	May 2018

MAC mitral annular calcification, *MR* mitral regurgitation, *MS* mitral stenosis, *NYHA* New York Heart Association, *TMVR* transcatheter mitral valve replacement

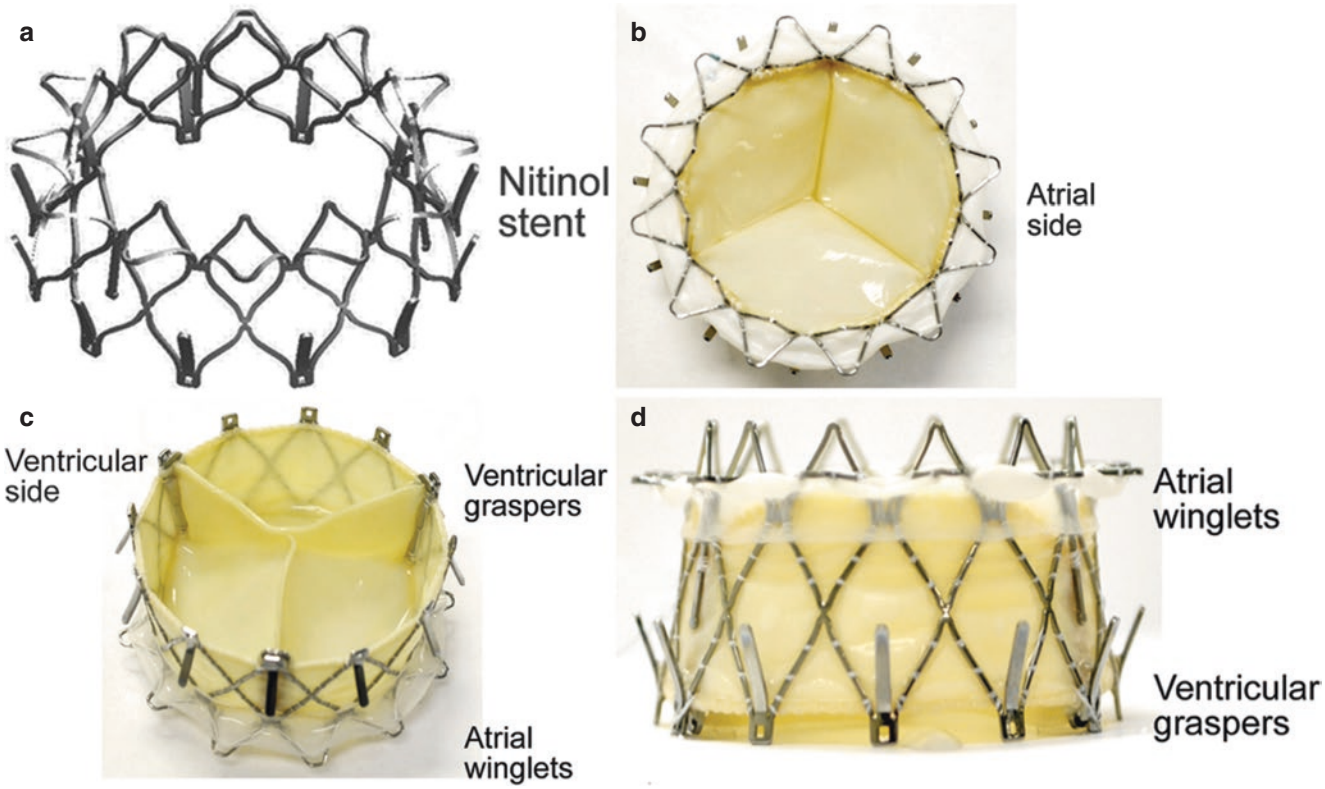

Fig. 8.22 NaviGate valved stent. (**a**) Nitinol stent frame. (**b**) Inflow (left atrial) view. (**c**) Outflow (left ventricular) view. (**d**) Side view. From Navia et al. [132]. Reprinted with permission from Europa Digital & Publishing

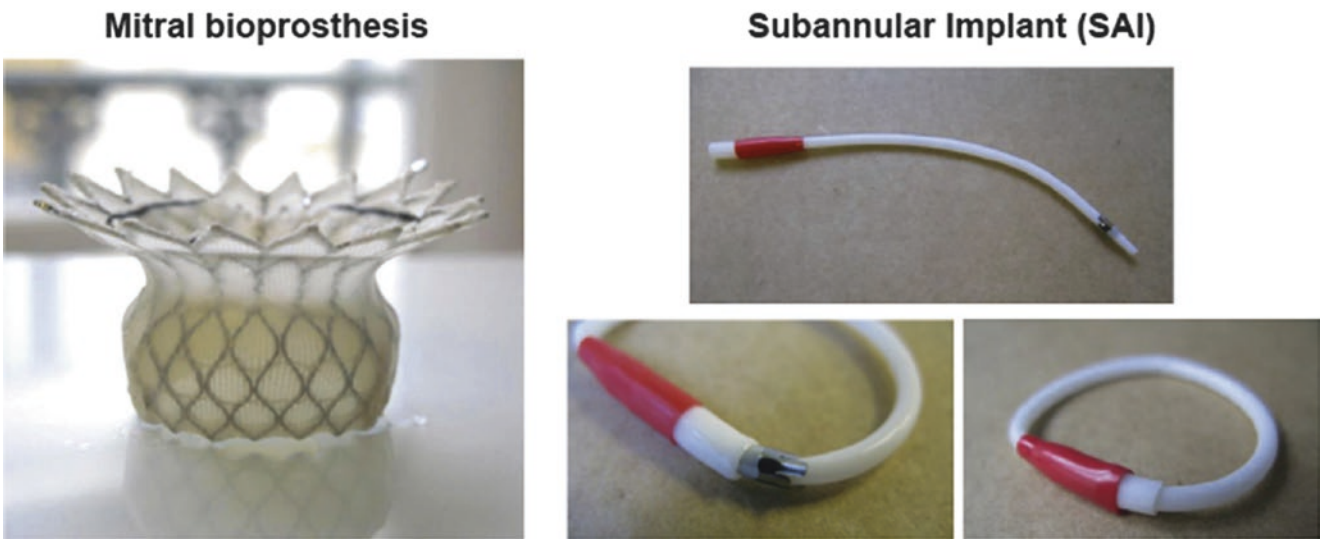

Fig. 8.23 HighLife device. Mitral bioprosthesis (*left*) and subannular implant (*right*). From Barbanti et al. [133]. Reprinted with permission from Elsevier

Table 8.14 HighLife TMVR system trial

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
HighLife TMVR System Study	Prospective, multicenter, single-arm, nonrandomized trial, 20 pts	1. Experimental: TMVR	1. Severe MR 2. High risk/ unsuitable for open-heart surgery or other percutaneous therapy 3. NYSHA II–IVa 4. Maximally tolerated GDMT for at least 3 months 5. Meets anatomical criteria for device	1. Unsuitable anatomy 2. MS or severe MAC, or rheumatic dx 3. Prior MV intervention 4. LVEF <30% 5. LVEDD >7 cm 6. HOCM 7. Significant CAD requiring revascularization 8. Any surgery or intervention within 30 days	1. Freedom from major adverse events (30 days) 2. Continued intended performance of the valve (30 days) 3. Technical success	1. Device success (up to 12 months) 2. Procedure success (up to 12 months) 3. Patient success (up to 12 months) 4. Hemodynamic performance (up to 5 years) 5. Functional improvement (12 months) 6. Quality of life improvement (12 months)	5 years	December 2023

CAD coronary artery disease, *dx* diagnosis, *GDMT* goal-directed medical therapy, *HOCM* hypertrophic obstructive cardiomyopathy, *LVEDD* left ventricular end-diastolic dimension, *LVEF* left ventricular ejection fraction, *MAC* mitral annular calcification, *MR* mitral regurgitation, *MS* mitral stenosis, *MV* mitral valve, *NYHA* New York Heart Association, *TMVR* transcatheter mitral valve replacement

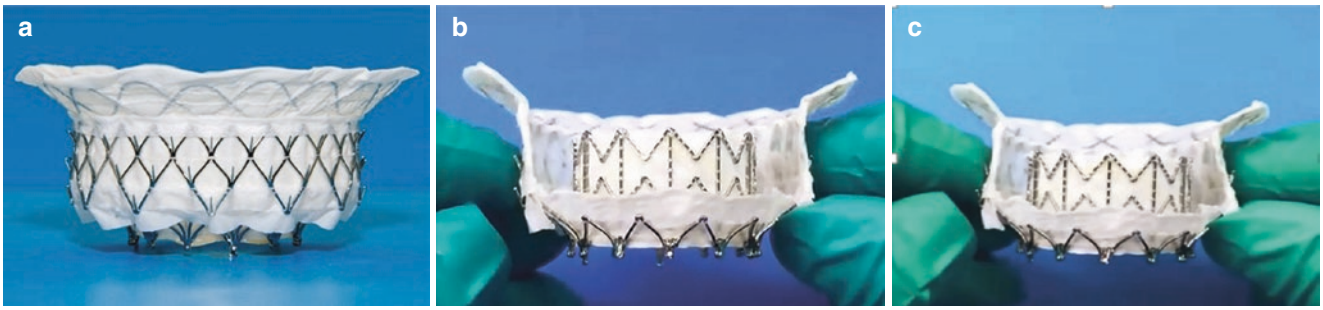

Fig. 8.24 Twelve/Intrepid valve. (**a**) The Intrepid TMVR prosthesis. Cut-outs show the device's dual-stent design (**b**) and overall flexibility (**c**), allowing the device to conform to the shape of native mitral annulus. From Meredith et al. [134]. Reprinted with permission from Europa Digital & Publishing

tric stent structures are required to make such a design work. The Medtronic/Twelve Intrepid valve is an example of such a device.

Medtronic/Twelve Intrepid Valve

The Medtronic/Twelve Intrepid system (Medtronic, Minneapolis, MN, USA) has a unique dual structure that consists of an inner self-expanding, nitinol-framed, trileaflet bovine pericardial valve that is housed concentrically within a larger, self-expanding nitinol outer fixation ring. The outer ring engages with the dynamic mitral annulus; this separates the fixation of the dynamic annulus, and movement thereof throughout the cardiac cycle, from the functioning of the inner valve. The inner stent valve has a 27-mm diameter and an effective orifice area of 2.4 cm^2, while the outer valve structure is currently available in 43-, 46-, and 50-mm outer diameter sizes. The outer ring is sized to be larger than the native MV annulus, has varying radial stiffness, and is covered by a polyester fabric skirt to prevent leaks and accommodate tissue ingrowth. The atrial portion is flexible and conforms to the native annulus, while the ventricular portion is stiffer and resists compression, thus producing a cork effect during systolic pressure to resist migration. The system need not be rotationally aligned and does not require any tethering mechanism or capture of native leaflets (Fig. 8.24) [134]. The device is housed in a transapical hydraulic delivery system that facilitates controlled expansion and deployment [134].

The intrepid valve is currently under investigation in the APOLLO trial, a multicenter, global, prospective, randomized trial comparing TMVR by the Intrepid system to conventional MV surgery. Currently active clinical trials of the Medtronic/Twelve Intrepid device are described in Table 8.15.

Table 8.15 Intrepid system trials

Device/trial name	Trial design	Arms	Inclusion criteria	Exclusion criteria	Primary outcome measures	Secondary outcome measures	Follow-up	Est. study completion date
Twelve Pilot Study	Prospective, multicenter, nonrandomized trial, 10 pts	1. Experimental: TMVR	1. Severe MR (3 to 4+) 2. Symptomatic MR (NYHA II–IV) 3. Transapical delivery feasible 4. Mitral anatomy compatible with Twelve TMVR	1. LVEF <20% 2. Intracardiac mass, thrombus, vegetation 3. Prior valve surgery or need for valve surgery 4. Prior stroke within 4 weeks 5. Need for coronary revascularization 6. hx of or active endocarditis 7. Renal insufficiency (Cr >2.5 mg/dL)	1. Adverse events (30 days)	1. Procedural success (5 years) 2. Reduction of MR (5 years)	5 years	July 2023
Intrepid/ APOLLO	Global, multicenter RCT, 1380 pts estimated	1. Experimental: Surgical candidate, TMVR 2. Comparator: Surgical candidate, SMVR 3. Experimental: Non-surgical candidate, TMVR	1. Severe, symptomatic MR 2. Candidate for MV replacement	1. Prior TMVR w/ device implant 2. Anatomic contraindications 3. Severe MAC 4. Need for emergent/urgent surgery 5. Hemodynamic instability	All-cause mortality, stroke, reoperation or reintervention, cardiovascular hospitalization (1 year)	1. All-cause mortality, stroke, AKI, prolonged ventilation, deep wound infection, reoperation/ reintervention, major bleeding (30 days or discharge) 2. Change in NYHA class (1 year) 3. Quality of life improvement per SF-12, KCCQ (30 days, 1 year) 4. Echo-degree of MR (1 year) 5. Days alive out of hospital (1 year) 6. Cardiovascular hospitalizations (1 year)	Pre- and post-procedure, discharge, 30 days, 6 months, annually through 5 years	October 2025

Cr creatinine, *hx* history, *KCCQ* Kansas City Cardiomyopathy Questionnaire, *LVEF* left ventricular ejection fraction, *MAC* mitral annular calcification, *MR* mitral regurgitation, *MV* mitral valve, *NYHA* New York Heart Association, *RCT* randomized, controlled trial, *SMVR* surgical mitral valve repair, *TMVR* transcatheter mitral valve replacement

Conclusions

One of greatest difficulties in comparing outcomes among different minimally invasive MV procedures lies in the varying techniques used. Little to no prospective data are available that compare minimally invasive MV surgery with sternotomy valve surgery, and no data are available about the relative effectiveness of the various minimally invasive methods except for retrospective reports from individual surgeons or institutions. Additionally, many of the published studies included data from institutions with a limited volume of these specialized and technically demanding procedures. Nonetheless, the data clearly demonstrate that minimally invasive valve surgery performed in the appropriate clinical setting by a high-volume institution, with a well-developed surgical method, leads to outcomes that are equivalent, if not superior, to those of valve surgery through a sternotomy.

A minimally invasive MV procedure performed via a mini-thoracotomy is a true sternal-sparing and less-invasive procedure. Benefits include shorter ventilator times and intensive care unit and hospital length of stay. In addition, patients return to their normal lifestyles sooner because of less surgical trauma and greater chest-wall stability, which allow them to regain function faster than standard sternotomy patients. Other benefits include lower transfusion and analgesic requirements and better cosmesis. A decrease has been documented in the composite complication rate in higher-risk patients (i.e., those more 75 years old, obese, COPD, and low LVEF), as has a trend toward lower surgical mortality.

Mitral valve procedures currently remain in the domain of the surgeon. Mitral valve repair techniques take time to learn and can be technically demanding. Nonetheless, surgical correction of essentially all MV abnormalities has produced excellent results and durability at experienced centers.

In addition, there exists a large, unmet clinical need for less-invasive therapies with a more favorable risk/benefit profile for the treatment of MR, and a correspondingly large potential patient population that would benefit from these therapies. The pioneering success of the MitraClip, especially in the treatment of high-risk patients, has proven the magnitude of this unmet need in clinical practice. Furthermore, the success of this device has led to a great deal of device development for transcatheter MV repair and replacement. Nonetheless, the results are still far from optimal, and for the time being, these technologies will be limited to patients not eligible for surgery.

References

1. Corbi P, Rahmati M, Donal E, et al. Prospective comparison of minimally invasive and standard techniques for aortic valve replacement: initial experience in the first hundred patients. J Card Surg. 2003;18:133–9.
2. Lamelas J, Sarria A, Santana O, Pineda AM, Lamas GA. Outcomes of minimally invasive valve surgery versus median sternotomy in patients age 75 years or greater. Ann Thorac Surg. 2011;91:79–84.
3. Santana O, Reyna J, Benjo AM, Lamas GA, Lamelas J. Outcomes of minimally invasive valve surgery in patients with chronic obstructive pulmonary disease. Eur J Cardiothorac Surg. 2012;42:648–52.
4. Santana O, Reyna J, Grana R, Buendia M, Lamas GA, Lamelas J. Outcomes of minimally invasive valve surgery versus standard sternotomy in obese patients undergoing isolated valve surgery. Ann Thorac Surg. 2011;91:406–10.
5. Cohn LH. Fifty years of open-heart surgery. Circulation. 2003;107:2168–70.
6. Cosgrove DM 3rd, Sabik JF, Navia JL. Minimally invasive valve operations. Ann Thorac Surg. 1998;65:1535–8; discussion 1538–9.
7. Chan EY, Lumbao DM, Iribarne A, et al. Evolution of cannulation techniques for minimally invasive cardiac surgery: a 10-year journey. Innovations (Phila). 2012;7:9–14.
8. Xu RB, Rahnavardi M, Nadal M, et al. Beating heart minimally invasive mitral valve surgery in patients with previous sternotomy: the operative technique and early outcomes. Open Heart. 2018;5:e000749.
9. Grossi EA, Loulmet DF, Schwartz CF, et al. Minimally invasive valve surgery with antegrade perfusion strategy is not associated with increased neurologic complications. Ann Thorac Surg. 2011;92:1346–9; discussion 1349–50.
10. Murzi M, Cerillo AG, Miceli A, et al. Antegrade and retrograde arterial perfusion strategy in minimally invasive mitral-valve surgery: a propensity score analysis on 1280 patients. Eur J Cardiothorac Surg. 2013;43:e167–72.
11. Murzi M, Glauber M. Central versus femoral cannulation during minimally invasive aortic valve replacement. Ann Cardiothorac Surg. 2015;4:59–61.
12. Lamelas J, Williams RF, Mawad M, LaPietra A. Complications associated with femoral cannulation during minimally invasive cardiac surgery. Ann Thorac Surg. 2017;103:1927–32.
13. LaPietra A, Santana O, Mihos CG, et al. Incidence of cerebrovascular accidents in patients undergoing minimally invasive valve surgery. J Thorac Cardiovasc Surg. 2014;148:156–60.
14. Iribarne A, Karpenko A, Russo MJ, et al. Eight-year experience with minimally invasive cardiothoracic surgery. World J Surg. 2010;34:611–5.
15. Navia JL, Cosgrove DM 3rd. Minimally invasive mitral valve operations. Ann Thorac Surg. 1996;62:1542–4.
16. Gillinov AM, Cosgrove DM. Minimally invasive mitral valve surgery: mini-sternotomy with extended transseptal approach. Semin Thorac Cardiovasc Surg. 1999;11:206–11.
17. Loulmet DF, Carpentier A, Cho PW, et al. Less invasive techniques for mitral valve surgery. J Thorac Cardiovasc Surg. 1998;115:772–9.
18. Wang D, Wang Q, Yang X, Wu Q, Li Q. Mitral valve replacement through a minimal right vertical infra-axillary thoracotomy versus standard median sternotomy. Ann Thorac Surg. 2009;87:704–8.

19. Cohn LH, Adams DH, Couper GS, et al. Minimally invasive cardiac valve surgery improves patient satisfaction while reducing costs of cardiac valve replacement and repair. Ann Surg. 1997;226:421–6; discussion 427–8.
20. Farhat F, Lu Z, Lefevre M, Montagna P, Mikaeloff P, Jegaden O. Prospective comparison between total sternotomy and ministernotomy for aortic valve replacement. J Card Surg. 2003;18:396–401; discussion 402–3.
21. Vanermen H, Vermeulen Y, Wellens F, De Geest R, Degrieck I, Van Praet F. Port-access mitral valve surgery. Perfusion. 1998;13:249–52.
22. Mohr FW, Falk V, Diegeler A, Walther T, van Son JA, Autschbach R. Minimally invasive port-access mitral valve surgery. J Thorac Cardiovasc Surg. 1998;115:567–74; discussion 574–6.
23. Carpentier A, Loulmet D, Carpentier A, et al. [Open heart operation under videosurgery and minithoracotomy. First case (mitral valvuloplasty) operated with success]. C R Acad Sci III. 1996;319:219–23.
24. Falk V, Walther T, Autschbach R, Diegeler A, Battellini R, Mohr FW. Robot-assisted minimally invasive solo mitral valve operation. J Thorac Cardiovasc Surg. 1998;115:470–1.
25. Carpentier A, Loulmet D, Aupecle B, et al. [Computer assisted open heart surgery. First case operated on with success]. C R Acad Sci III. 1998;321:437–42.
26. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 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. JACC. 2017;70:252–89.
27. Lehr EJ, Guy TS, Smith RL, et al. Minimally invasive mitral valve surgery III: training and robotic-assisted approaches. Innovations (Phila). 2016;11:260–7.
28. Wolfe JA, Malaisrie SC, Farivar RS, et al. Minimally invasive mitral valve surgery II: surgical technique and postoperative management. Innovations (Phila). 2016;11:251–9.
29. Irisawa Y, Hiraoka A, Totsugawa T, et al. Re-expansion pulmonary oedema after minimally invasive cardiac surgery with right minithoracotomy. Eur J Cardiothorac Surg. 2016;49:500–5.
30. Kitahara H, Okamoto K, Kudo M, et al. Successful management of severe unilateral re-expansion pulmonary edema after mitral valve repair with mini-thoracotomy using extracorporeal membrane oxygenation. Gen Thorac Cardiovasc Surg. 2017;65:164–6.
31. Wang Y, Gao CQ, Wang G, Wang JL. Transesophageal echocardiography guided cannulation for peripheral cardiopulmonary bypass during robotic cardiac surgery. Chin Med J. 2012;125:3236–9.
32. Carrier M, Cyr A, Voisine P, et al. Vacuum-assisted venous drainage does not increase the neurological risk. Heart Surg Forum. 2002;5:285–8.
33. Colangelo N, Torracca L, Lapenna E, Moriggia S, Crescenzi G, Alfieri O. Vacuum-assisted venous drainage in extrathoracic cardiopulmonary bypass management during minimally invasive cardiac surgery. Perfusion. 2006;21:361–5.
34. Mihos CG, Santana O, Lamas GA, Lamelas J. Outcomes of right minithoracotomy mitral valve surgery in patients with previous sternotomy. Ann Thorac Surg. 2011;91:1824–7.
35. Santana O, Funk M, Zamora C, Escolar E, Lamas GA, Lamelas J. Staged percutaneous coronary intervention and minimally invasive valve surgery: results of a hybrid approach to concomitant coronary and valvular disease. J Thorac Cardiovasc Surg. 2012;144:634–9.
36. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet. 2006;368:1005–11.
37. Doshi JV, Agrawal S, Garg J, et al. Percutaneous mitral heart valve repair—MitraClip. Cardiol Rev. 2014;22:289–96.
38. Gammie JS, Sheng S, Griffith BP, et al. Trends in mitral valve surgery in the United States: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Ann Thorac Surg. 2009;87:1431–7; discussion 1437–9.
39. Mirabel M, Iung B, Baron G, et al. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? Eur Heart J. 2007;28:1358–65.
40. Patel JB, Borgeson DD, Barnes ME, Rihal CS, Daly RC, Redfield MM. Mitral regurgitation in patients with advanced systolic heart failure. J Card Fail. 2004;10:285–91.
41. Carpentier A, Chauvaud S, Fabiani JN, et al. Reconstructive surgery of mitral valve incompetence: ten-year appraisal. J Thorac Cardiovasc Surg. 1980;79:338–48.
42. Fornes P, Heudes D, Fuzellier JF, Tixier D, Bruneval P, Carpentier A. Correlation between clinical and histologic patterns of degenerative mitral valve insufficiency: a histomorphometric study of 130 excised segments. Cardiovasc Pathol. 1999;8:81–92.
43. Lam JH, Ranganathan N, Wigle ED, Silver MD. Morphology of the human mitral valve. I. Chordae tendineae: a new classification. Circulation. 1970;41:449–58.
44. Ranganathan N, Lam JH, Wigle ED, Silver MD. Morphology of the human mitral valve. II. The value leaflets. Circulation. 1970;41:459–67.
45. Carpentier A. Cardiac valve surgery—the "French correction". J Thorac Cardiovasc Surg. 1983;86:323–37.
46. Pepi M, Tamborini G, Maltagliati A, et al. Head-to-head comparison of two- and three-dimensional transthoracic and transesophageal echocardiography in the localization of mitral valve prolapse. J Am Coll Cardiol. 2006;48:2524–30.
47. Schwammenthal E, Chen C, Benning F, Block M, Breithardt G, Levine RA. Dynamics of mitral regurgitant flow and orifice area. Physiologic application of the proximal flow convergence method: clinical data and experimental testing. Circulation. 1994;90:307–22.
48. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RW, Sonnenblick EH. Dynamic aspects of acute mitral regurgitation: effects of ventricular volume, pressure and contractility on the effective regurgitant orifice area. Circulation. 1979;60:170–6.
49. Braunwald E, Awe WC. The syndrome of severe mitral regurgitation with normal left atrial pressure. Circulation. 1963;27:29–35.
50. Carabello BA. The current therapy for mitral regurgitation. J Am Coll Cardiol. 2008;52:319–26.
51. Gaasch WH, Meyer TE. Left ventricular response to mitral regurgitation: implications for management. Circulation. 2008;118:2298–303.
52. Enriquez-Sarano M, Hannachi M, Jais JM, Acar J. [Hemodynamic and angiographic results following surgical correction of mitral insufficiency. Apropos of 51 repeated catheterizations]. Arch Mal Coeur Vaiss. 1983;76:1194–1203.
53. Starling MR, Kirsh MM, Montgomery DG, Gross MD. Impaired left ventricular contractile function in patients with long-term mitral regurgitation and normal ejection fraction. J Am Coll Cardiol. 1993;22:239–50.
54. Wisenbaugh T, Spann JF, Carabello BA. Differences in myocardial performance and load between patients with similar amounts of chronic aortic versus chronic mitral regurgitation. J Am Coll Cardiol. 1984;3:916–23.
55. Corin WJ, Murakami T, Monrad ES, Hess OM, Krayenbuehl HP. Left ventricular passive diastolic properties in chronic mitral regurgitation. Circulation. 1991;83:797–807.
56. Messika-Zeitoun D, Johnson BD, Nkomo V, et al. Cardiopulmonary exercise testing determination of functional capacity in mitral regurgitation: physiologic and outcome implications. J Am Coll Cardiol. 2006;47:2521–7.
57. Crawford MH, Souchek J, Oprian CA, et al. Determinants of survival and left ventricular performance after mitral valve replace-

ment. Department of Veterans Affairs Cooperative Study on Valvular Heart Disease. Circulation. 1990;81:1173–81.
58. Adams DH, Rosenhek R, Falk V. Degenerative mitral valve regurgitation: best practice revolution. Eur Heart J. 2010;31:1958–66.
59. El-Tallawi KC, Messika-Zeitoun D, Zoghbi WA. Assessment of the severity of native mitral valve regurgitation. Prog Cardiovasc Dis. 2017;60:322–33.
60. Chinitz JS, Chen D, Goyal P, et al. Mitral apparatus assessment by delayed enhancement CMR: relative impact of infarct distribution on mitral regurgitation. JACC Cardiovasc Imaging. 2013;6:220–34.
61. Cawley PJ, Hamilton-Craig C, Owens DS, et al. Prospective comparison of valve regurgitation quantitation by cardiac magnetic resonance imaging and transthoracic echocardiography. Circ Cardiovasc Imaging. 2013;6:48–57.
62. Lopez-Mattei JC, Ibrahim H, Shaikh KA, et al. Comparative assessment of mitral regurgitation severity by transthoracic echocardiography and cardiac magnetic resonance using an integrative and quantitative approach. Am J Cardiol. 2016;117:264–70.
63. Ngaage DL, Schaff HV. Mitral valve surgery in non-ischemic cardiomyopathy. J Cardiovasc Surg. 2004;45:477–86.
64. Dagum P, Timek TA, Green GR, et al. Coordinate-free analysis of mitral valve dynamics in normal and ischemic hearts. Circulation. 2000;102:III62–9.
65. Miller DC. Ischemic mitral regurgitation redux—to repair or to replace? J Thorac Cardiovasc Surg. 2001;122:1059–62.
66. Enriquez-Sarano M, Tajik AJ, Schaff HV, Orszulak TA, Bailey KR, Frye RL. Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. Circulation. 1994;90:830–7.
67. Ling LH, Enriquez-Sarano M, Seward JB, et al. Early surgery in patients with mitral regurgitation due to flail leaflets: a long-term outcome study. Circulation. 1997;96:1819–25.
68. Schaff HV. Asymptomatic severe mitral valve regurgitation: observation or operation? Circulation. 2009;119:768–9.
69. Magne J, Girerd N, Senechal M, et al. Mitral repair versus replacement for ischemic mitral regurgitation: comparison of short-term and long-term survival. Circulation. 2009;120:S104–11.
70. Jones EC, Devereux RB, Roman MJ, et al. Prevalence and correlates of mitral regurgitation in a population-based sample (the Strong Heart Study). Am J Cardiol. 2001;87:298–304.
71. Singh JP, Evans JC, Levy D, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). Am J Cardiol. 1999;83:897–902.
72. Rosen SE, Borer JS, Hochreiter C, et al. Natural history of the asymptomatic/minimally symptomatic patient with severe mitral regurgitation secondary to mitral valve prolapse and normal right and left ventricular performance. Am J Cardiol. 1994;74:374–80.
73. Grigioni F, Tribouilloy C, Avierinos JF, et al. Outcomes in mitral regurgitation due to flail leaflets a multicenter European study. JACC Cardiovasc Imaging. 2008;1:133–41.
74. Tribouilloy C, Grigioni F, Avierinos JF, et al. Survival implication of left ventricular end-systolic diameter in mitral regurgitation due to flail leaflets a long-term follow-up multicenter study. J Am Coll Cardiol. 2009;54:1961–8.
75. Javadikasgari H, Gillinov AM, Idrees JJ, et al. Valve repair is superior to replacement in most patients with coexisting degenerative mitral valve and coronary artery diseases. Ann Thorac Surg. 2017;103:1833–41.
76. Mick SL, Keshavamurthy S, Gillinov AM. Mitral valve repair versus replacement. Ann Cardiothorac Surg. 2015;4:230–7.
77. Mohty D, Orszulak TA, Schaff HV, Avierinos JF, Tajik JA, Enriquez-Sarano M. Very long-term survival and durability of mitral valve repair for mitral valve prolapse. Circulation. 2001;104:I1–7.
78. Bolling SF, Li S, O'Brien SM, Brennan JM, Prager RL, Gammie JS. Predictors of mitral valve repair: clinical and surgeon factors. Ann Thorac Surg. 2010;90:1904–11; discussion 1912.
79. Bonow RO, Adams DH. The time has come to define centers of excellence in mitral valve repair. J Am Coll Cardiol. 2016;67:499–501.
80. Gammie JS, Zhao Y, Peterson ED, O'Brien SM, Rankin JS, Griffith BP. J. Maxwell Chamberlain Memorial Paper for adult cardiac surgery. Less-invasive mitral valve operations: trends and outcomes from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Ann Thorac Surg. 2010;90:1401–8, 1410.e1; discussion 1408–10.
81. Dillon J, Yakub MA, Nordin MN, Pau KK, Krishna Moorthy PS. Leaflet extension in rheumatic mitral valve reconstruction. Eur J Cardiothorac Surg. 2013;44:682–9.
82. Maisano F, Torracca L, Oppizzi M, et al. The edge-to-edge technique: a simplified method to correct mitral insufficiency. Eur J Cardiothorac Surg. 1998;13:240–5; discussion 245–6.
83. Maisano F, Schreuder JJ, Oppizzi M, Fiorani B, Fino C, Alfieri O. The double-orifice technique as a standardized approach to treat mitral regurgitation due to severe myxomatous disease: surgical technique. Eur J Cardiothorac Surg. 2000;17:201–5.
84. Milano CA, Daneshmand MA, Rankin JS, et al. Survival prognosis and surgical management of ischemic mitral regurgitation. Ann Thorac Surg. 2008;86:735–44.
85. Micovic S, Milacic P, Otasevic P, et al. Comparison of valve annuloplasty and replacement for ischemic mitral valve incompetence. Heart Surg Forum. 2008;11:E340–5.
86. Silberman S, Oren A, Klutstein MW, et al. Does mitral valve intervention have an impact on late survival in ischemic cardiomyopathy? Isr Med Assoc J. 2006;8:17–20.
87. Thourani VH, Weintraub WS, Guyton RA, et al. Outcomes and long-term survival for patients undergoing mitral valve repair versus replacement: effect of age and concomitant coronary artery bypass grafting. Circulation. 2003;108:298–304.
88. Vassileva CM, Boley T, Markwell S, Hazelrigg S. Meta-analysis of short-term and long-term survival following repair versus replacement for ischemic mitral regurgitation. Eur J Cardiothorac Surg. 2011;39:295–303.
89. Gillinov AM, Wierup PN, Blackstone EH, et al. Is repair preferable to replacement for ischemic mitral regurgitation? J Thorac Cardiovasc Surg. 2001;122:1125–41.
90. Reece TB, Tribble CG, Ellman PI, et al. Mitral repair is superior to replacement when associated with coronary artery disease. Ann Surg. 2004;239:671–5; discussion 675–7.
91. Al-Radi OO, Austin PC, Tu JV, David TE, Yau TM. Mitral repair versus replacement for ischemic mitral regurgitation. Ann Thorac Surg. 2005;79:1260–7; discussion 1260–7.
92. Acker MA, Parides MK, Perrault LP, et al. Mitral-valve repair versus replacement for severe ischemic mitral regurgitation. N Engl J Med. 2014;370:23–32.
93. Kron IL, Hung J, Overbey JR, et al. Predicting recurrent mitral regurgitation after mitral valve repair for severe ischemic mitral regurgitation. J Thorac Cardiovasc Surg. 2015;149:752–761 e751.
94. Gelsomino S, Lorusso R, De Cicco G, et al. Five-year echocardiographic results of combined undersized mitral ring annuloplasty and coronary artery bypass grafting for chronic ischaemic mitral regurgitation. Eur Heart J. 2008;29:231–40.
95. Ciarka A, Braun J, Delgado V, et al. Predictors of mitral regurgitation recurrence in patients with heart failure undergoing mitral valve annuloplasty. Am J Cardiol. 2010;106:395–401.
96. Magne J, Pibarot P, Dagenais F, Hachicha Z, Dumesnil JG, Senechal M. Preoperative posterior leaflet angle accurately predicts outcome after restrictive mitral valve annuloplasty for ischemic mitral regurgitation. Circulation. 2007;115:782–91.

97. Kongsaerepong V, Shiota M, Gillinov AM, et al. Echocardiographic predictors of successful versus unsuccessful mitral valve repair in ischemic mitral regurgitation. Am J Cardiol. 2006;98:504–8.
98. Roshanali F, Mandegar MH, Yousefnia MA, Rayatzadeh H, Alaeddini F. A prospective study of predicting factors in ischemic mitral regurgitation recurrence after ring annuloplasty. Ann Thorac Surg. 2007;84:745–9.
99. Magne J, Senechal M, Dumesnil JG, Pibarot P. Ischemic mitral regurgitation: a complex multifaceted disease. Cardiology. 2009;112:244–59.
100. De Bonis M, Lapenna E, Verzini A, et al. Recurrence of mitral regurgitation parallels the absence of left ventricular reverse remodeling after mitral repair in advanced dilated cardiomyopathy. Ann Thorac Surg. 2008;85:932–9.
101. Wijdh-den Hamer IJ, Bouma W, Lai EK, et al. The value of preoperative 3-dimensional over 2-dimensional valve analysis in predicting recurrent ischemic mitral regurgitation after mitral annuloplasty. J Thorac Cardiovasc Surg. 2016;152:847–59.
102. Bouma W, Lai EK, Levack MM, et al. Preoperative three-dimensional valve analysis predicts recurrent ischemic mitral regurgitation after mitral annuloplasty. Ann Thorac Surg. 2016;101:567–75; discussion 575.
103. Levine RA, Schwammenthal E. Ischemic mitral regurgitation on the threshold of a solution: from paradoxes to unifying concepts. Circulation. 2005;112:745–58.
104. Borger MA, Murphy PM, Alam A, et al. Initial results of the chordal-cutting operation for ischemic mitral regurgitation. J Thorac Cardiovasc Surg. 2007;133:1483–92.
105. Kron IL, Green GR, Cope JT. Surgical relocation of the posterior papillary muscle in chronic ischemic mitral regurgitation. Ann Thorac Surg. 2002;74:600–1.
106. Langer F, Rodriguez F, Ortiz S, et al. Subvalvular repair: the key to repairing ischemic mitral regurgitation? Circulation. 2005;112:I383–9.
107. Langer F, Schafers HJ. RING plus STRING: papillary muscle repositioning as an adjunctive repair technique for ischemic mitral regurgitation. J Thorac Cardiovasc Surg. 2007;133:247–9.
108. Langer F, Groesdonk HV, Kunihara T, Schafers HJ. Dynamic RING + STRING for ischemic mitral regurgitation: papillary muscle repositioning and modification of the septal-lateral diameter in the loaded beating heart under echocardiographic guidance. J Thorac Cardiovasc Surg. 2011;141:1315–6.
109. Fattouch K, Castrovinci S, Murana G, et al. Papillary muscle relocation and mitral annuloplasty in ischemic mitral valve regurgitation: midterm results. J Thorac Cardiovasc Surg. 2014;148:1947–50.
110. Hvass U, Tapia M, Baron F, Pouzet B, Shafy A. Papillary muscle sling: a new functional approach to mitral repair in patients with ischemic left ventricular dysfunction and functional mitral regurgitation. Ann Thorac Surg. 2003;75:809–11.
111. Benjo AM, Macedo FY, Santana O, Lamelas J. Papillary muscle sling placement for functional mitral regurgitation during minimally invasive valve surgery. Innovations (Phila). 2012;7:448–51.
112. Santana O, Solenkova NV, Pineda AM, Mihos CG, Lamelas J. Minimally invasive papillary muscle sling placement during mitral valve repair in patients with functional mitral regurgitation. J Thorac Cardiovasc Surg. 2014;147:496–9.
113. Nappi F, Lusini M, Spadaccio C, et al. Papillary muscle approximation versus restrictive annuloplasty alone for severe ischemic mitral regurgitation. J Am Coll Cardiol. 2016;67:2334–46.
114. Mandegar MH, Saidi B, Yousefnia MA, Alaeddini F, Roshanali F. Long-term effect of papillary muscle approximation combined with ventriculoplasty on left ventricle function in patients with ischemic cardiomyopathy and functional mitral regurgitation. Eur J Cardiothorac Surg. 2011;40:756–60.
115. Athanasuleas CL, Buckberg GD, Stanley AW, et al. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. J Am Coll Cardiol. 2004;44:1439–45.
116. Athanasuleas CL, Stanley AW Jr, Buckberg GD. Restoration of contractile function in the enlarged left ventricle by exclusion of remodeled akinetic anterior segment: surgical strategy, myocardial protection, and angiographic results. J Card Surg. 1998;13:418–28.
117. Jones RH, Velazquez EJ, Michler RE, et al. Coronary bypass surgery with or without surgical ventricular reconstruction. N Engl J Med. 2009;360:1705–17.
118. Wakasa S, Shingu Y, Ooka T, Katoh H, Tachibana T, Matsui Y. Surgical strategy for ischemic mitral regurgitation adopting subvalvular and ventricular procedures. Ann Thorac Cardiovasc Surg. 2015;21:370–7.
119. Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL. Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. Circulation. 1995;91:1022–8.
120. Gammie JS, O'Brien SM, Griffith BP, Ferguson TB, Peterson ED. Influence of hospital procedural volume on care process and mortality for patients undergoing elective surgery for mitral regurgitation. Circulation. 2007;115:881–7.
121. Bonow RO, Carabello BA, Chatterjee K, et al. 2008 focused update incorporated into the 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). J Am Coll Cardiol. 2008;52:e1–142.
122. Maisano F, Taramasso M, Nickenig G, et al. Cardioband, a transcatheter surgical-like direct mitral valve annuloplasty system: early results of the feasibility trial. Eur Heart J. 2016;37:817–25.
123. Sharma R, Gafoor S. Percutaneous mitral valve repair: the next wave. Card Interv Today. 2017;11:65–70.
124. Goldberg SL, Lipiecki J, Sievert H. The CARILLON Mitral Contour transcatheter indirect mitral valve annuloplasty system. EuroIntervention. 2015;11(Suppl W):W64–6.
125. Erglis A, Thomas M, Morice MC, et al. The Arto transcatheter mitral valve repair system. EuroIntervention. 2015;11(Suppl W):W47–8.
126. Bapat V, Buellesfeld L, Peterson MD, et al. Transcatheter mitral valve implantation (TMVI) using the Edwards FORTIS device. EuroIntervention. 2014;10(Suppl U):U120–8.
127. Bapat V, Lim ZY, Boix R, Pirone F. The Edwards Fortis transcatheter mitral valve implantation system. EuroIntervention. 2015;11(Suppl W):W73–5.
128. Verheye S, Cheung A, Leon M, Banai S. The Tiara transcatheter mitral valve implantation system. EuroIntervention. 2015;11(Suppl W):W71–2.
129. Regueiro A, Granada JF, Dagenais F, Rodes-Cabau J. Transcatheter mitral valve replacement: insights from early clinical experience and future challenges. J Am Coll Cardiol. 2017;69:2175–92.
130. Sondergaard L, Ussia GP, Dumonteil N, Quadri A. The CardiAQ transcatheter mitral valve implantation system. EuroIntervention. 2015;11(Suppl W):W76–7.
131. Perpetua EM, Reisman M. The Tendyne transcatheter mitral valve implantation system. EuroIntervention. 2015;11(Suppl W):W78–9.
132. Navia JL, Baeza C, Maluenda G, et al. Transcatheter mitral valve replacement with the NaviGate stent in a preclinical model. EuroIntervention. 2017;13:e1401–9.
133. Barbanti M, Piazza N, Mangiafico S, et al. Transcatheter mitral valve implantation using the HighLife system. JACC Cardiovasc Interv. 2017;10:1662–70.
134. Meredith I, Bapat V, Morriss J, McLean M, Prendergast B. Intrepid transcatheter mitral valve replacement system: technical and product description. EuroIntervention. 2016;12:Y78–80.