Current Techniques for Severe Mitral Annular Calcification

Jessica K. Millar, MD,1,2 Gorav Ailawadi, MD, MBA2

1 Department of Surgery, University of Michigan, Ann Arbor, Michigan
2 Department of Cardiac Surgery, University of Michigan, Ann Arbor, Michigan

Disclosures: The authors have no relevant or material financial interests that relate to the research described in this paper.

Acknowledgements:
We would like to thank Paul Sorajja, MD for providing the Tendyne case example and images referenced.

Funding:
This project was supported by grant number T32-HL007853 from the National Heart, Lung, and Blood Institute (NHLBI) (J. Millar, PI: David J. Pinksy, MD). The content is solely the responsibility of the authors and does not necessarily represent the views of the NHLBI.

Corresponding Author:
Gorav Ailawadi, MD, MBA
Department of Cardiac Surgery
University of Michigan
Email: ailawadi@med.umich.edu
Phone: 734-764-9588

Article Word Count: 1,525/2,500 (excludes references, tables, and legends)
Glossary of Abbreviations

AVR = Aortic valve replacement

BEV = Balloon expandable valves

CABG = Coronary artery bypass grafting

EF = Ejection Fraction

LVOT = Left ventricular outflow tract

MAC = Mitral annular calcification

MR = Mitral valve regurgitation

MS = Mitral valve stenosis

MVR = Mitral valve replacement

PA = Pulmonary artery

TEER = Transcatheter edge-to-edge repair

TMVR = Transcatheter mitral valve replacement
Central Picture Legend (88 / 90 characters)
New techniques and technology for the treatment of severe mitral annular calcification.

Central Message (169 / 200 characters)
Ongoing development of surgical and transcatheter approaches have helped advance treatment of mitral valve disease in the setting of mitral annular calcification (MAC).

Perspective Statement (396 / 405 characters)
Mitral annular calcification (MAC) remains a technically challenging disease with increased morbidity and mortality in the setting of mitral valve surgery. Due to the variable nature, there is no universally accepted approach to surgically address MAC. However, growing experience with surgical and transcatheter devices has helped expand the toolbox of tailored treatment strategies for this challenging disease.

Key Words: Mitral annular calcification, transcatheter mitral valve replacement, transcatheter edge-to-edge repair

Mitral annular calcification (MAC) remains a technically challenging disease process with increased morbidity and mortality in the setting of mitral valve replacement (MVR) compared to mitral valve surgery without MAC.\textsuperscript{1,2} MAC can vary significantly in pattern and severity creating diagnostic and technical challenges. It may be classified based on segment extension, with single segment extension affecting P2 being the most prevalent.\textsuperscript{3} Alternatively, it may be classified by circumferential spread, comprising Type 1 (partial MAC; <270\degree annular calcium), Type 2A (≥270\degree annular calcium with absence of predicted LVOT), and Type 2B...
However, there is no universally accepted approach to surgically address MAC. As such, various approaches have been employed to address MAC including complete resection of all calcifications with annular reconstruction, partial resection with removal of enough calcium to adequately seat a bioprosthesis valve, and transcatheter valve-in-MAC approaches. However, as recognition and referral for MAC disease continues to grow, re-evaluation and incorporation of new techniques and technology to address MAC is necessary. Here, we present current strategies to address severe MAC through several case examples. Images were obtained following signed informed consent from each patient. All non-contributory personal health information and patient identifiers were removed.

**Case Presentations and Surgical Techniques:**

**Ultrasonic Emulsification**

A 71-year-old female with a history of rheumatic mitral regurgitation (MR) and mitral stenosis (MS), focal MAC (Figure 1A), and NYHA Class 3 heart failure underwent a minimally invasive MVR. During the procedure, debridement of focal calcium was performed utilizing ultrasonic emulsification via a Sonopet ultrasonic aspirator (Stryker, Kalamazoo, MI) prior to placement of a 29mm Epic valve (Abbot Laboratories, Chicago, IL) (Figure 1B and 1C). She recovered well without heart failure for several years postoperatively.

Ultrasonic emulsification/aspiration provides a method of controlled, purposeful debridement and allows for “remodeling” of the annulus to an extent sufficient enough to seat an adequately sized prosthesis. With such technique, complete resection and excessive manipulation of MAC is
not necessary. Additionally, it allows for the avoidance of excessive torque on the annulus thus minimizing the risk of AV groove disruption. Placement of sutures with the severely calcified annulus can be challenging. Removal or softening of the calcium can permit easier suture placement and unconventional suture placement (such as placement in the left atrial wall) may be necessary to ensure equal distribution of forces along sutures. In our previously reported experience, ultrasonic emulsification/aspiration allows for safe treatment of patients with severe MAC using conventional, suture-based mitral valve prosthesis.6

Transcatheter Edge-to-Edge Repair

An 82-year-old frail female with a history of sarcoidosis presented with severe MR. On pre-operative evaluation she was found to have an ejection fraction (EF) of 70%, an elevated pulmonary artery (PA) pressures of 96 mmHg, and a flail P3 segment resulting in her severe MR (4+). Additionally, she was found to have a focal area of moderate MAC and a valve area of 4.5cm² (Figure 2A). Given her overall health status, she underwent transcatheter edge-to-edge repair (TEER) with placement of 2 MitraClip devices (Abbot Laboratories, Chicago, IL) in the commissure with trace residual MR (Figure 2B and 2C).

Due to the high surgical morbidity and mortality associated with MAC, less invasive yet efficient alternatives to surgery are needed. TEER with MitraClip placement in select patients has been demonstrated to be a safe and feasible alternative to achieve significant reduction of MR and substantial clinical improvement in high-risk surgical patients.7 Recent retrospective studies demonstrated similar procedural success (91.8% in MAC vs 95.1% in non-MAC) and incidence of procedural complications, no difference in 1-year cardiovascular mortality (15.3% in MAC vs
9.2% in non-MAC), and ability to achieve an MR grade ≤2 at 1-year follow-up (90.6% in MAC vs 79.5% in non-MAC) following TEER.7

Challenges to TEER in the setting of MAC include retraction of the posterior leaflet, extension of calcium onto the leaflets, or small native valve area. MAC may cause such significant posterior leaflet retraction that less than 5mm of tissue is available to grasp and secure attachment may not be possible.8 Similarly, extension of calcium onto the leaflet may increase the risk of leaflet tear.8 In the case presented, that patient’s MAC was focal with an adequate leaflet grasping zone free of calcium. In such cases with acceptable anatomy, TEER may be considered as a valid alternative to surgery in select, high-risk patients with severe MR and MAC.

Surgical Implantation of Transcatheter Aortic Valve

An 81-year-old female with a history of previous 4-vessel coronary artery bypass grafting (CABG) and aortic valve replacement (2011) presented years later with severe MS (mean gradient 14 mmHg) in the setting of severe MAC (Figure 3A) and elevated PA pressures (68 mmHg). She underwent a minimally invasive MVR with placement of a Sapien 3 valve (Edwards Lifesciences, Irvine, CA) (Supplemental Video). During this procedure, the A2 segment and papillary muscle were resected and a septal resection was performed to minimize left ventricular outflow tract (LVOT) obstruction (Figure 3B).9 Pledged annular sutures were placed through the MAC with two redundant felt strips anchored circumferentially in the landing zone to help minimize paravalvular leak (Figure 3B). The valve was placed 60-70% within the
left atrium to avoid LOVT obstruction and the annular sutures were secured to the frame of the valve (Figure 3C). The patient recovered well and remained without hospitalization for 4 years.

Transcatheter MVR (TMVR) with balloon expandable valves can be a suitable approach for select patients with severe MAC. Previous multicenter global registry studies evaluating outcomes following TMVR with balloon-expandable valve (BEV) in patients with severe MAC demonstrated a high rate of technical success (72%) but a concurrent high rate of adverse events (29.7%).\textsuperscript{10} The use of balloon expandable aortic valves in MAC has the advantage of minimizing suture placement and complications of debridement, but can result in significant paravalvular leak and LVOT obstruction and, therefore, remains an alternative for selected high-risk patients with limited treatment options.\textsuperscript{10} These risks are highest when performed via a transeptal percutaneous approach, however, surgical transatrial TMVR can minimize LVOT obstruction and paravalvular leak using the techniques described here. Early results have demonstrated a technical success rate of 94.4% with paravalvular leak and LVOT obstruction (especially in cases without septal myomectomy) comprising the greatest risks.\textsuperscript{11} Importantly, these results also demonstrated a greater risk of mortality in patients with significant MR vs isolated MS (Hazard ratio: 2.32).\textsuperscript{11} As such, those patients with MR associated with MAC may benefit less from TMVR than patients with isolated MS.

The Surgical Implantation of Transcatheter Valve in Native Mitral Annular Calcification (SITRAL) study (ClinicalTrials.gov Identifier: NCT02830204) is an ongoing study to evaluate the safety and feasibility of surgical implantation of balloon expandable valves (BEV) in patients with MAC who are at high-risk for mitral valve surgery or deemed inoperable due to the extent
of calcification. This hybrid approach offers a unique treatment option for those patients with mitral valve disease complicated by severe MAC who may be at increased risk for other conventional approaches or at risk for LVOT obstruction with transcatheter MVR (TMVR). This open surgical implantation approach has been demonstrated to have a 30-day mortality rate of 13.7% and a technical success rate of 94.1%. However, there remains anatomical limitations to this approach as patients with large native annulus are at increased risk for paravalvular leak.

Tendyne TMVR

A 75-year-old female with no past medical history presented for acute congestive heart failure secondary to MR in the setting of severe MAC (Figure 4A). Given the degree of MAC, she was not a candidate for any option described thus far. She underwent transapical placement of a 34Fr Tendyne valve (Figure 4B and 4C). This approach utilizes an investigational device contoured to fit the mitral valve annulus. The valve is composed of an outer and inner frame as well as an anchoring tether/hemostatic pad allowing it to be placed transapically. Uniquely, the valve is both retrievable and repositionable. This device is currently limited to investigational use only as part of the Clinical Trial to Evaluate the Safety and Effectiveness of Using the Tendyne Transcatheter Mitral Valve System for the Treatment of Symptomatic Mitral Regurgitation (SUMMIT; ClinicalTrials.gov Identifier: NCT03433274). Patients with moderate-severe mitral regurgitation as well as those with symptomatic mitral valve disease due to severe MAC who would otherwise be deemed unfit for mitral valve surgery are eligible and may offer to new insight to emerging TMVR devices.

Conclusion:
Several current and emerging strategies exist for patients requiring mitral valve intervention with MAC. While these patients present with unique technical challenges and carry with them elevated operative risks, meaningful clinical improvements are possible and appropriate intervention should still be pursued. Ultrasonic emulsification/aspiration can be used to focally debride calcium and can make conventional repair/replacement feasible. In high-risk patients with a valve area >4cm$^2$, TEER may still be feasible with focal MAC and adequate amount of unaffected leaflet tissue. In patients with MS and MAC, surgical BEV may the optimal approach. In patients with MR and MAC, ongoing TMVR trials with mitral specific devices may provide novel treatment options. Institutional capabilities and anatomic exclusions may limit these options for some patients, and some may still require traditional surgical approaches. However, the ongoing development of surgical and transcatheter approaches has increased the toolbox for tailored treatment strategies and improved patient care.

References

3. Loulmet DF, Ranganath NK, Neragi-Miandoab S, Koeckert MS, Galloway AC, Grossi EA. Advanced experience allows robotic mitral valve repair in the presence of extensive...


14. *Clinical Trial to Evaluate the Safety and Effectiveness of Using the Tendyne Transcatheter Mitral Valve System for the Treatment of Symptomatic Mitral Regurgitation (SUMMIT) Study*. https://clinicaltrials.gov/ct2/show/study/NCT03433274
Figure Legends

Figure 1: Utilization of Ultrasonic Emulsification A. Pre-operative CT and 2D echocardiogram demonstrating focal MAC (right and middle panel) with MR (left panel). B. Intraoperative images demonstrating initial MAC (right panel), followed by placement of a 29mm Epic valve via a minimally invasive approach (middle and left panel). C. Post-operative 2D echocardiogram demonstrating resolution of MR.

Figure 2: Transcatheter Edge-to-Edge repair with Native MAC A. Pre-operative echocardiogram demonstrating severe MR, flail P3 segment, and moderate focal posterior MAC. B. 3D (right panel) and 2D echocardiogram (left panel) demonstrating placement of first MitraClip. C. 3D (right panel) and 2D echocardiogram (left panel) demonstrating placement of second MitraClip.

Figure 3: Surgical Implantation of Transcatheter Valve A. Pre-operative CT and 3D echocardiogram demonstrating severe MAC. B. Intraoperative images demonstrating removal of A2 segment (right panel), septal resection (middle panel), and placement of felt strip (left panel). C. Final implantation of Sapien 3 valve (bottom panel).

Figure 4: Tendyne MVR A. Pre-operative CT demonstrating severe MAC. B. Intra-operative fluoroscopy demonstrating placement of Tendyne valve. C. Post-operative 3D echocardiogram and CT demonstrating placement of Tendyne valve.

C
Supplemental Video 1: Surgical Implantation of Transcatheter Valve. Discussion of the technique details, tips, and troubleshoot strategies during surgical implantation of a transcatheter valve in native MAC.
Central Picture
Figure 1:
Figure 2:
Figure 3:
Figure 4: