The management of patients with extensive mitral annular calcification undergoing valve replacement using an algorithm based on MAC morphology

Patients with extensive mitral annular calcification (MAC) + underwent surgical valve replacement
January 1, 2013 – September 31, 2022
N = 72

MAC Morphology

- Partial (<270°)
  - C-MVR (N = 56)

- Horsehoe or Greater (≥270°)
  - H-TMVR (N = 16)

1 Year Survival: 82.8%
1 Year Survival: 54.7%

Conventional valve replacement techniques can be utilized with good perioperative outcomes when the MAC morphology is favorable. In instances where MAC morphology is unfavorable a hybrid approach can be implemented as a bailout.

MAC = mitral annular calcification; C-MVR = conventional mitral valve replacement; H-TMVR = hybrid transcatheter mitral valve replacement
Contemporary Surgical Techniques for Mitral Valve Replacement in Extensive Mitral Annular Calcification

Ahmed El-Eshmawi MD, Gilbert H. L. Tang MD, MSc, MBA, Erick Sun MD, Sophia L. Alexis MD, Busra Cangut MD, Dimosthenis Pandis MD, MSc, Percy Boateng MD, David H. Adams MD

Department of Cardiovascular Surgery, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Disclosure Statement

Dr. David H. Adams is the National Co-Lead Investigator of the TRILUMINATE U.S. Pivotal Trial (Abbott), the ReChord FDA Pivotal Trial (NeoChord), the APOLLO FDA Pivotal Trial (Medtronic), and the CoreValve U.S. Pivotal Trial (Medtronic). The Icahn School of Medicine at Mount Sinai receives royalty payments from Edwards Lifesciences and Medtronic for intellectual property related to Dr Adams's involvement in the development of two mitral valve repair rings and 1 tricuspid valve repair ring.

Dr. Gilbert H. L. Tang is a consultant and physician advisory board member for Medtronic and Abbott Structural Heart, a physician advisory board member for Boston Scientific and JenaValve, and a consultant for NeoChord, and has received speaker’s honoraria from Siemens Healthineers and East End Medical.

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Corresponding Author

Ahmed El-Eshmawi, MD
Department of Cardiovascular Surgery
Icahn School of Medicine at Mount Sinai
1190 Fifth Ave, GP2W, Box 1028
New York, NY 10029
USA
Tel: (212) 659-6820
Fax: (212) 659-6818
E-mail: ahmed.el-eshmawi@mountsinai.org

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IRB Approval
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Informed Consent Statement
The study protocol was approved by our local institutional review board (STUDY-22-00800, 08/29/2022) and was compliant with the Health Insurance Portability and Accountability Act regulations and the ethical guidelines of the 1975 Declaration of Helsinki. The approval included a waiver of informed consent.
Glossary of Abbreviations

H-TMVR = hybrid transcatheter mitral valve replacement
C-MVR = conventional mitral valve replacement
MAC = mitral annular calcification
TEE = transesophageal echocardiography
3D/TEE = three dimensional transesophageal echocardiography
AV = atrioventricular
MR = mitral regurgitation
MAP = mean arterial pressure
HR = heart rate
HOCM = hypertrophic obstructive cardiomyopathy
PFO = patent foramen ovale
CPB = cardiopulmonary bypass
iNO = inhaled nitric oxide
IABP = intra-aortic balloon pump
ICU = intensive care unit
SAM = systolic anterior motion
IQR = interquartile range
LOS = length of stay
CI = confidence interval
NHYA = New York Heart Association
LA = left atrial
LVEDD = left ventricular end diastolic diameter
LVESD = left ventricular end systolic diameter
RV = right ventricular
LV = left ventricular
PL = posterior leaflet
AL = anterior leaflet
TV = tricuspid valve
LA = left atrium
MDCT = multi-detector-computed tomography
LVOT = left ventricular outflow tract
TAVR = Transcatheter aortic valve replacement
TEER = Transcatheter edge to edge repair
RRT = Renal replacement therapy
DSWI = Deep sternal wound infection
PVL = Paravalvular regurgitation

Central Picture
Central Picture Legend
Algorithm for surgical management of patients with extensive mitral annular calcification.

Central Message
Contemporary techniques for surgical mitral valve replacement in extensive MAC are safe and feasible. Hybrid approaches should remain a bailout in select patients due to its higher risk.

Perspective Statement
Conventional mitral valve replacement using respect strategies without en-bloc annular decalcification is safe and feasible in most patients with extensive annular calcification. Hybrid
approaches using balloon expandable devices under direct vision should be reserved as a bailout to standard surgery in highly selected patients due to the increased perioperative risks.

**Structured Abstract**

Objectives: Mitral annular calcification remains a formidable lesion in cardiac surgery with significant perioperative morbidity and mortality particularly when en-bloc annular decalcification is implemented. Respect strategies as well as hybrid approaches have provided safe alternatives. We report the short-term results of our institution’s experience with mitral valve replacement in patients with extensive annular calcification.

Methods: This is a retrospective review of 72 consecutive patients with extensive annular calcification who underwent open surgical mitral valve replacement from January 1, 2013 to September 31, 2022. Degree of annular calcification was graded as partial, horseshoe, or circumferential. We excluded patients with calcification involving less than one third of the annulus and patients with rheumatic heart disease.

Results: Mean patient age was 71.6 ± 10.9 years old and 50 (69.4%) were female. There were 51 (70.8%) patients in NYHA class ≥3, 47 (65.3%) with pulmonary hypertension. There were 41 (56.9%) patients with partial, 12 (16.7%) with horseshoe, and 19 (26.4%) with circumferential calcification. Fifty-six (77.8%) patients underwent conventional valve replacement. Sixteen patients underwent a hybrid procedure using balloon expandable devices. Concomitant procedures were performed in 61 (84.7%) patients. In-hospital mortality and one-year survival were 3.57% and 82.8% in the standard valve replacement cohort and 25.0% and 54.7% in the hybrid cohort, respectively.
Conclusion: Conventional mitral valve replacement using respect strategies is safe and associated with good outcomes in patients with extensive annular calcification. Hybrid approaches using novel devices should remain as a bailout in select patients due to higher perioperative risks and poor short-term outcomes.

Keywords
Mitral Valve
Annular Calcification
Hybrid Valve Replacement

Graphical Abstract
**Introduction**

Despite the recent advances in the field of cardiovascular surgery and interventions, mitral annular calcification (MAC) remains a challenging anatomic and physiologic entity in...
cardiovascular surgery with high perioperative and periprocedural morbidity and mortality as well as poor long-term outcomes.

Although the risk factors associated with MAC are becoming better defined, its cause remains unclear. In today’s population, MAC has a higher prevalence among elderly patients, women, and in the presence of comorbidities such as hypertension, diabetes, end-stage renal disease, aortic stenosis, hypertrophic obstructive cardiomyopathy, and advanced degenerative mitral disease. Mediastinal radiation is also an increasingly recognized cause of a more extensive form of MAC as part of radiation heart disease, commonly seen in survivors of mantle field radiation for Hodgkin’s lymphoma.

There has also been a recent increase in patients presenting with symptomatic severe MAC due to an aging population in addition to the increase in the referral for surgery in high-risk patients with MAC who failed screening for transcatheter therapy. For many decades, MAC has carried a formidable reputation in cardiac surgery with several historical reports of high-risk for perioperative complications particularly when en-bloc annular decalcification/annular reconstruction techniques were implemented, including risk of atrioventricular (AV) groove disruption, prosthetic paravalvular leak (PVL), stroke, and myocardial ischemia. However, with the evolution of cardiac imaging, transcatheter therapies, and balloon expandable devices, novel techniques were explored in patients with extensive MAC not amenable for standard valve replacement techniques. Hybrid procedures using transcatheter valves (H-TMVR) via direct access implantation of balloon expandable devices in MAC during open surgery have recently gained interest in select MAC patients.
In this manuscript, we will discuss our decision algorithm, operative strategies, and short-term outcomes for patients with severe MAC using conventional as well as hybrid surgical approaches.

Methods

Study Population

This is a retrospective review of 72 consecutive patients with symptomatic severe mitral valve disease due to extensive MAC and underwent open surgical mitral valve replacement from January 1, 2013 to September 31, 2022. We defined extensive MAC as MAC involving more than one third of the annulus on CT scanning. We excluded patients with MAC involving less than one third of the annulus and patients with MAC in the context of rheumatic heart disease.

Preoperative Screening, Planning, and Optimization

All patients were admitted to the hospital for preoperative evaluation and planning. A detailed cardiac imaging evaluation of MAC including transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), and multidetector computed tomography (CT), as well as right and left heart catheterization was done for all patients. A comprehensive multidisciplinary team evaluation, including consultation by nephrology, pulmonology, neurology, endocrinology, electrophysiology, and heart failure when appropriate, was performed. Medical optimization was initiated and maintained by the Heart Team for decompensated patients, with a focus on optimizing heart rhythm and rate, volume status, pulmonary artery pressure and cardiac output, nutritional status, and physical therapy.

We categorized the extension of MAC based on a specific CT guided anatomic classification as partial (involving at least 1/3 of the annular circumference and less than 270
degree), horseshoe (commissure-to-comissure, 270–300 degree) and circumferential (more than 300 degree). In addition, annular dimensions and eccentricity, maximal thickness and height of the calcium in MAC bar, extension of MAC into left atrium and ventricle, aortomitral angle, valve sizing and neo-left ventricular outflow tract (LVOT) anatomy, were determined (Figure 1). Three-dimensional TEE provided a detailed anatomic assessment of MAC and associated mitral disease, annular dimensions, leaflet anatomy, and risk of LVOT obstruction because of the anterior leaflet and or basal septal hypertrophy.

Surgical Technique

In our mitral reference center, all extensive MAC operations were evaluated and performed by a single group of surgeons (DA, AE, PB, GT). All cases were performed through a median sternotomy. Standard cardiopulmonary bypass techniques with central aortic and bicaval cannulation with aortic cross clamping were used. Myocardial protection was achieved via cold blood cardioplegia given in an antegrade as well as retrograde fashion. The mitral valve was accessed via Sondergaard’s groove or occasionally through a transseptal approach in patients with a small left atrium, complex reoperations, and patients with an in-situ aortic prosthesis. In patients with a porcelain aorta, peripheral cannulation was used with hypothermic fibrillatory arrest to avoid aortic manipulation. Intraoperative surgical analysis was done in all patients to confirm the extension of MAC. Valve replacement then proceeded as described in the algorithm outlined in Figure 2.

C-MVR: This technique was preferred for patients with primarily partial MAC. In these patients the anterior leaflet with its subvalvular apparatus was resected and the posterior leaflet was preserved. The mitral valve was replaced with standard prostheses using a non-everting suture technique with pledgeted sutures placed on the ventricular side. We implemented 3 main suture
techniques for C-MVR: peri-annular sutures using large needles around the calcium bar, intra-leaflet implantation where sutures are passed through the posterior leaflet, and a modified anterior leaflet flip technique where the anterior leaflet is detached and flipped toward the posterior leaflet so that both leaflets create a neo-annulus buttress to reinforce the suture line and provide protection against ventricular disruption (Videos 1 and 2) (Figure 3). Partial decalcification was performed selectively to even the landing surface and allow for suture placement as well as to debride friable parts of the MAC bar. We preferably used a combination of sharp and rongeur dissection when decalcification was implemented. En-bloc decalcification/annular reconstruction was not used in any patient.

H-TMVR: A transatrial approach was used in this patient subset. The anterior mitral leaflet was partially resected with its corresponding subvalvular apparatus to reduce the risk of LVOT obstruction. Commissural gaps were closed to circularize the annulus and reduce the risk of paravalvular regurgitation. The Sapien 3 valve (Edwards Lifesciences LLC, Irvine, CA) was modified by placing one or more rows of Teflon felt at the atrial side to improve sealing against the MAC and reduce the risk of PVL. Sutures placed at non-calcified sections of the annulus were tied to both the Teflon cuff and the valve stent after valve deployment to provide additional reinforcement of the transcatheter prosthesis to reduce the risk of device migration and embolization. This approach was done under direct visualization without the need for guidewires or fluoroscopy and with assistance from an interventional surgeon (GT). Balloon sizing was used for confirmation. The valve was then crimped on the balloon delivery system and deployed into the mitral orifice with proper orientation of the commissures to match the intertrigonal distance while keeping the Teflon cuff more atrial and the open cells toward the LVOT. Sutures were then passed through the Teflon felt ring and stent frame and tied (Video 3) (Figure 4).
Early in the series, we used the Melody valve (Medtronic Inc, Minneapolis, MN), which was the only available device, consisting of balloon expandable stented bovine jugular vein graft primarily designed for the pulmonary position. The insertion technique was similar to the Sapien 3 valve except that we did not use Teflon felt wrapping or sutures and the valve was deployed more towards the atrium after folding both valve ends due to its higher profile.

Postoperative Care

Similar to standard bioprosthetic mitral valve replacement, all patients in the H-TMVR group received lifelong aspirin and a minimum of 3 months of Coumadin with a target international normalized ratio of 2.0-3.0. Patients with a contraindication to anticoagulation or who were high-risk for bleeding received only aspirin. Transthoracic echocardiography was performed in all patients prior to discharge.

Data Collection

Clinical variables were identified through retrospective review of the electronic medical record. Information regarding 1-year survival were obtained by reviewing retrospective electronic health records. The study protocol was approved by our local institutional review board (STUDY-22-00800, 08/29/2022) and was compliant with the Health Insurance Portability and Accountability Act regulations and the ethical guidelines of the 1975 Declaration of Helsinki. The approval included a waiver of informed consent. Morbidities were defined according to the 2018 Society for Thoracic Surgeons (STS) Adult Cardiac Surgery Risk Models. Censoring was done based on last patient encounter according to electronic health records.

Statistical Analysis

Normally distributed continuous variables were represented as mean + standard deviation. Nonparametric and categorical variables were represented as median and interquartile range or as
the number of patients as a percentage of the sample, respectively. Normality of variables was assessed using the Shapiro-Wilk test and with visual estimation against a normally distributed bell curve and a quantile-quantile plot. Midterm follow-up with done using standard Kaplan-Meier survival curves and modified Kaplan-Meier survival curves to account for the instability in the right-tail of small risk set data. The statistical analyses were performed with the use of SAS 9.4 statistical software (SAS Institute, Inc).

Results

Patient Characteristics

Mean patient age was 71.6 ± 10.9 years old and 50 (69.4%) were female. There were 51 (70.8%) patients in NYHA class ≥3, 47 (65.3%) with pulmonary hypertension, and 12 (16.7%) (16.7%) with mediastinal radiation. Median STS Score risk for mortality was 4.1% (IQR 2.4%-6.4%). Seven (9.7%) patients had structural valve procedures including TAVR and percutaneous edge-to-edge repair, all in the C-MVR group. Nineteen (26.4%) patients were reoperations. Mitral dysfunction was mixed in 21 (29.6%) patients, regurgitant in 31 (43.6%), and stenotic in 19 (26.8%). There were 41 (56.9%) patients with partial, 12 (16.7%) with horseshoe, and 19 (26.4%) with circumferential MAC. Patient demographics, comorbidities, clinical characteristics, and preoperative echocardiographic parameters are summarized in Table 1.

Procedural Characteristics

Fifty-six (77.8%) patients underwent C-MVR using standard bioprosthetic valves: 32 (57.1%) utilizing peri-annular suture placement, 12 (21.4%) with intra-leaflet implantation, 15 (26.8%) using an anterior leaflet flip technique, and 10 (17.9%) using partial annular
decalcification (Table 2). We did not encounter any cases of AV groove disruption, mid-ventricular tears, or coronary ischemia in this patient group.

The remaining 16 patients were deemed not to be candidates for C-MVR after valve exploration and surgical analysis, and underwent H-TMVR using a balloon-expandable valve as per our protocol. The device was successfully deployed in all patients. Ten patients had a Sapien 3 valve placed, while 6 patients had a Melody valve inserted early in the series. Two patients required insertion of more than one valve. One of them had a Sapien 3 valve that embolized into the left atrium so a new Sapien 3 valve had to be crimped and deployed after adding more annular sutures that were then passed into the Teflon skirt. The other patient had a Melody valve that embolized into the left atrium. The same Melody valve was retrieved, however due to balloon over-dilation for stabilization severe transvalvular regurgitation occurred, necessitating a second Melody valve-in-valve.

Concomitant procedures were done in 61 (84.7%) patients. The most common procedure was tricuspid intervention in 52 (72.2%) and Cryo-Maze ablation in 21 (29.1%). Median cardiopulmonary bypass time was 147 (115-178) minutes and cross clamp time was 118.5 (87-138) minutes.

Perioperative Outcomes

All valve-related complications were seen in the H-TMVR group. They included severe LVOT obstruction in 3 (4.2%) patients, valve embolization in 2 (2.8%), AV groove disruption in 1 (1.4%) requiring conversion to conventional valve replacement, and ventricular perforation (primarily repaired) in 1 (1.3%) patient.

On pre-discharge TTE, there were 2 (2.8%) patients with PVL of moderate or greater degree, one in each group. Both were successfully closed percutaneously due to symptomatic
mitral regurgitation. There were 2 (3.6%) in-hospital mortalities in the C-MVR cohort, one due to aspiration pneumonia, and the other due to multiorgan failure. In the H-TMVR cohort there were 4 (25.0%) patients who died in-hospital mostly due to intraoperative complications (2 had severe LVOTO and 1 had AV groove disruption).

1-year survival was 82.8% in the C-MVR cohort and 54.7% in the H-TMVR cohort. Tables 2 and 3 summarize the operative findings and outcomes for both patient subgroups.

Discussion

For decades, mitral valve replacement in the setting of severe annular calcification has been associated with high perioperative morbidity and mortality. This has been paralleled with an increasing MAC patient population referred for surgery due to the increased screening for transcatheter valve therapies. Hence, there has been an increasing demand for safe and novel surgical strategies to deal with extensive MAC in mitral valve surgery particularly given that the current MAC population are older and have more extensive form of the disease with multiple comorbidities while significant anatomic limitations remains a major barrier against widespread application of transcatheter technologies in patients with extensive MAC.

Key Findings

For MAC interventions, a dedicated multidisciplinary team approach is a prerequisite to success

All patients in the current study followed a strict protocol in evaluation based on advanced cardiac imaging and multidisciplinary team assessment to evaluate surgical candidacy, surgical approach, perioperative risk, and medical optimization prior to surgery. The MAC classification and management algorithm should be used by the cardiac surgeon and the structural heart interventionist to guide management (Graphical Abstract).
Conventional mitral valve replacement is safe in MAC

In our valve reference center, our default strategy for severe MAC remains valve replacement with standard surgical prostheses using “Respect” surgical techniques for most patients with non-circumferential or partial MAC. Three main techniques for valve implantation were adopted: a modified anterior leaflet flip technique, intraleaflet implantation, and periannular suture placement to avoid en-bloc annular decalcification and reconstruction. En-bloc annular decalcification/reconstruction of the AV groove was avoided in all patients, given that the current MAC population is high-risk due to advanced age, more extensive forms of MAC, and prevalence of extra cardiac comorbidities. In fact, several patients in this study were already rejected from other transcatheter valve therapies or had already received transcatheter therapy with TAVR and transcatheter mitral edge-to-edge repair. Given the lack of consensus regarding the safest strategy to replace the mitral valve in patients with extensive MAC we adopted a more conservative approach using “Respect strategies” with chordal preservation while avoiding en-bloc annular decalcification which likely contributed to our 0% incidence of atrioventricular groove disruption in the conventional valve replacement group. However, this strategy did result in using a smaller mitral prosthesis implantation which will require longer term follow-up to determine if this would have any potential clinical consequences.

We did not encounter any cases of AV groove disruption, ventricular rupture, LVOT obstruction or perioperative ischemia in the C-MVR cohort, which had an in-hospital mortality of 3.6%. One patient was discharged with moderate paravalvular regurgitation that was amenable to percutaneous closure. Comparing outcomes on C-MVR literature is difficult, as most studies come from case series, with no details on the extent of MAC or the patients’ risk profile. A study by Kaneko et al provided extensive data from 9551 patients undergoing C-MVR, with estimated
higher inpatient mortality of 5.8% among patients with MAC compared with patients without MAC (4.4%). However, this analysis was based on the Society of Thoracic Surgeons Adult Cardiac Surgery Database, which lacks information on the severity of MAC. Our study is unique in that we have a detailed description of MAC severity based on a specific classification in all patients and we excluded rheumatic disease related MAC which is considered a less severe form of calcification and usually occurs in a younger patient population.

*Hybrid transatrial approaches are feasible in select MAC patients*

H-TMVR via transatrial implantation of a balloon-expandable transcatheter valve after resection of the anterior leaflet can be performed safely in horseshoe or circumferential MAC. We have adopted several techniques that help minimize the risk of operative complications to ensure a more durable valve replacement. The anterior leaflet of the mitral valve can be resected to reduce the risk of LVOT obstruction. Commissural gaps can also be closed to better circularize the annulus and reduce paravalvular leak. The Sapien 3 valve can be modified by placing one or more rows of Teflon felt at the atrial side to improve sealing against the MAC and reduce the risk of paravalvular leak (Figure 4). Sutures can be placed at non-calcified sections of the annulus and tied to the Teflon cuff after valve deployment to provide additional reinforcement of the transcatheter prosthesis to reduce the risk of device migration and/or embolization. This H-TMVR approach can also offer a unique advantage of allowing the surgeon to perform concomitant procedures.

Prior to standardization of the H-TMVR technique, we had a challenging learning curve related to patient selection and how to minimize the risks of LVOT obstruction and other intraoperative complications. This learning curve has been made more challenging by the
relatively low volume of patients suitable for H-TMVR, given that our default approach is conventional valve replacement.

The Sapien valve provided several advantages since it is a low profile valve with an open distal stent to minimize the risk of LVOT obstruction, with pericardial leaflets that can sustain the ventricular pressure, as well as a skirt to limit the risk of PVL. However, it remains off-label for use in the mitral position. Future prostheses dedicated for the mitral position might help minimize some of those hurdles encountered in the H-TMVR group.

Almost all valve-related complications occurred in the H-TMVR group of patients, particularly early in our experience prior to standardization of technique and understanding the LVOT obstruction risk. At this early stage, we had incidences of significant LVOT obstruction (3 patients), valve embolization (2 patients), left ventricular tear that was repaired primarily in one patient, and AV groove disruption requiring conversion to C-MVR. Our overall in hospital mortality was 25%, and all of those deaths happened in patients with intraoperative complications (Supplemental Figure 2). Despite the high mortality, these results remain comparable to other studies showing high 30-day mortality in H-TMVR of 25.0% and 34.5%.

One-year outcomes are poor in patients with extensive MAC requiring H-TMVR

One-year survival was 82.8% in the C-MVR (7 mortalities before 1 year) versus 54.7% in the H-TMVR group (7 mortalities before 1 year) (Supplemental Figure 1). Patients with MAC associated with mitral valve disease experienced higher one-year mortality after H-TMVR. Those findings were confirmed by other clinical studies following MAC patients treated with H-TMVR. Guerrero et al and Yoon et al had one-year survivals of 53.7% and 62.8%, respectively. Hence, in patients with extensive MAC, appropriate patient selection is essential to avoid futile procedures. This could also be explained in part by better prosthesis performance in C-MVR.
patients, with less residual MR and less risk for LVOT obstruction, as well as the higher overall cardiovascular mortality in patients with more MAC burden\textsuperscript{10}.

**Implications for Practice**

In a mitral reference center, surgery for extensive mitral annular calcification is safe and feasible using a dedicated multidisciplinary team, CT based MAC management algorithms, versatile surgical techniques and novel hybrid approaches. Please see Figure 5 for a Graphical Abstract of this study.

Futile interventions and surgery should be avoided in patients with more severe forms of MAC due to predictable poor one-year survival.

**Limitations**

This study has several limitations which may influence the interpretation and generalizability of the results. Our study is a retrospective review and is therefore subject to all the inherent limitations related to this model of analysis. Follow-up was based on our own institutional chart review and therefore lacks complete death data which may impact true post-discharge mortalities for patients who left our health system. Our sample size particularly in the H-TMVR group limited the analysis giving that our default therapy for extensive MAC is C-MVR in most patients. There was a lack of longer term follow-up for echo and valve data limiting the ability to determine durability of these surgical techniques. Finally, implementation of the protocol and interpretations of those outcomes has been achieved within a single comprehensive valve center of excellence (level I center of excellence) with a very experienced team and our results may not be generalizable to no reference centers.
Conclusion

Conventional mitral valve replacement using respect techniques without en-bloc annular
decalcification remains safe and feasible in most patients with extensive mitral annular
calcification. Hybrid procedures using off-label balloon expandable devices, should be reserved
as a bailout in highly select patients due to the increased perioperative risk, non-forgiving learning
curve, and poor one-year survival.

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Table 1. Baseline characteristics

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<th>All (N = 72)</th>
<th>C-MVR (N = 56)</th>
<th>H-TMVR (N = 16)</th>
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<td>Age, mean (std)</td>
<td>71.6 (10.9)</td>
<td>70.9 (10.7)</td>
<td>73.9 (11.3)</td>
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<td>Female, n (%)</td>
<td>50 (69.44%)</td>
<td>37 (66.07%)</td>
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<tr>
<td>HTN, n (%)</td>
<td>55 (76.39%)</td>
<td>41 (73.21%)</td>
<td>14 (87.50%)</td>
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<td>Pulmonary HTN, n (%)</td>
<td>47 (65.28%)</td>
<td>37 (66.07%)</td>
<td>10 (62.50%)</td>
<td>0.79</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>19 (26.39%)</td>
<td>14 (25.00%)</td>
<td>5 (31.25%)</td>
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<tr>
<td>HLD, n (%)</td>
<td>52 (72.22%)</td>
<td>40 (71.43%)</td>
<td>12 (75.00%)</td>
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<td>CAD, n (%)</td>
<td>43 (59.72%)</td>
<td>31 (55.36%)</td>
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<td>CHF, n (%)</td>
<td>27 (37.50%)</td>
<td>22 (39.29%)</td>
<td>5 (31.25%)</td>
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<td>CKD, n (%)</td>
<td>16 (22.22%)</td>
<td>13 (23.21%)</td>
<td>3 (18.75%)</td>
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<td>Chronic Lung Disease, n (%)</td>
<td>8 (11.11%)</td>
<td>6 (10.71%)</td>
<td>2 (12.50%)</td>
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<td>Rheumatic Disease, n (%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>-</td>
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<td>Endocarditis, n (%)</td>
<td>2 (2.78%)</td>
<td>2 (3.57%)</td>
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<td>Mediastinal Radiation, n (%)</td>
<td>12 (16.67%)</td>
<td>9 (16.07%)</td>
<td>3 (18.75%)</td>
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<td>MI, n (%)</td>
<td>9 (12.50%)</td>
<td>6 (10.71%)</td>
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<td>Previous Intervention, n (%)</td>
<td>26 (36.11%)</td>
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<td>5 (31.25%)</td>
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<td>Median Sternotomy</td>
<td>19 (73.08%)</td>
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<td>TAVR</td>
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<td>MitraClip</td>
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<td>3 (14.29%)</td>
<td>0 (0.00%)</td>
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<td>51 (70.83%)</td>
<td>39 (69.64%)</td>
<td>12 (75.00%)</td>
<td>0.67</td>
</tr>
<tr>
<td>MAC Class, n (%)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
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<tr>
<td>Circumferential</td>
<td>19 (26.39%)</td>
<td>10 (17.86%)</td>
<td>9 (56.25%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Horseshoe</td>
<td>Partial</td>
<td>MV disease, n (%)</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>---------</td>
<td>-------------------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td>12 (16.67%)</td>
<td>8 (14.29%)</td>
<td>4 (25.00%)</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>41 (56.94%)</td>
<td>38 (67.86%)</td>
<td>3 (18.75%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Mixed</td>
<td>21 (29.58%)</td>
<td>14 (25.45%)</td>
<td>7 (43.75%)</td>
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</tr>
<tr>
<td>Pure Regurgitation</td>
<td>31 (43.66%)</td>
<td>30 (54.55%)</td>
<td>1 (6.25%)</td>
<td></td>
</tr>
<tr>
<td>Pure Stenosis</td>
<td>19 (26.76%)</td>
<td>11 (20.00%)</td>
<td>8 (50.00%)</td>
<td></td>
</tr>
<tr>
<td>EF, mean (std)</td>
<td>62.2% (7.5%)</td>
<td>61.2% (6.9%)</td>
<td>65.7% (8.9%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Pure Stenosis</td>
<td>19 (26.76%)</td>
<td>11 (20.00%)</td>
<td>8 (50.00%)</td>
<td>0.03</td>
</tr>
<tr>
<td>STS Score, median (IQR)</td>
<td>4.1% (2.4%-6.4%)</td>
<td>4.1% (2.0%-6.0%)</td>
<td>4.7% (3.3%-8.2%)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

C-MVR = conventional mitral valve replacement, H-TMVR = hybrid transcatheter mitral valve replacement, HTN = hypertension, DM = diabetes, HLD = hyperlipidemia, CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, MI = myocardial infarction, TAVR = transcatheter aortic valve replacement, NYHA = New York Heart Association, MAC = mitral annular calcification, MV = mitral valve, EF = ejection fraction, STS = Society of Thoracic Surgeons
Table 2. Operative details

<table>
<thead>
<tr>
<th>MVR Technique, n (%)</th>
<th>All (N = 72)</th>
<th>C-MVR (N = 56)</th>
<th>H-TMVR (N = 16)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL Flip</td>
<td>15 (26.79%)</td>
<td>15 (26.79%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Periannular Sutures</td>
<td>32 (57.14%)</td>
<td>32 (57.14%)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Intraleaflet Implant</td>
<td>12 (21.43%)</td>
<td>12 (21.43%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Decalcification</td>
<td>10 (17.86%)</td>
<td>10 (17.86%)</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>MV Prosthesis, n (%)</th>
<th>Valve Type</th>
<th>Bovine 12 (21.43%)</th>
<th>Porcine 44 (78.57%)</th>
<th>Sapien 3 -</th>
<th>Melody 10 (62.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Valve Size</td>
<td>C-MVR 25 32 (57.14%)</td>
<td>C-MVR 27 11 (19.64%)</td>
<td>C-MVR 29 9 (16.07%)</td>
<td>C-MVR 31 4 (7.14%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H-TMVR 23 -</td>
<td>H-TMVR 26 5 (31.25%)</td>
<td>H-TMVR 29 2 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>Concomitant Procedures, n (%)</td>
<td>TV Surgery 52 (72.22%)</td>
<td>C-MVR 25 32 (57.14%)</td>
<td>H-TMVR 23 3 (18.75%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maze 21 (29.17%)</td>
<td>C-MVR 27 11 (19.64%)</td>
<td>H-TMVR 26 5 (31.25%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CABG 11 (15.28%)</td>
<td>C-MVR 29 9 (16.07%)</td>
<td>H-TMVR 29 2 (12.5%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AVR 8 (11.11%)</td>
<td>C-MVR 31 4 (7.14%)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAVR Explant 1 (1.39%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intraop Amplatz Plug 1 (1.39%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CPB time, median (IQR) 147 (115-178)</td>
<td>146 (114.5-173)</td>
<td>151 (132-184)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>XC time, median (IQR) 118.5 (87-138)</td>
<td>118.5 (87-143)</td>
<td>118.5 (84.5-127.0)</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

MVR = mitral valve replacement, AL = anterior leaflet, MV = mitral valve, C-MVR = conventional mitral valve replacement, H-TMVR = hybrid transcatheter mitral valve replacement, TV = tricuspid valve, CABG = coronary artery bypass grafting, AVR = aortic valve replacement.
TAVR = transcatheter aortic valve replacement, CPB = cardiopulmonary bypass, XC = cross clamp
<table>
<thead>
<tr>
<th>Event</th>
<th>All (N = 72)</th>
<th>MVR (N = 56)</th>
<th>H-TMVR (N = 16)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve Embolization, n (%)</td>
<td>2 (2.78%)</td>
<td>0 (0%)</td>
<td>2 (12.50%)</td>
<td>0.00</td>
</tr>
<tr>
<td>AV Groove Disruption, n (%)</td>
<td>1 (1.39%)</td>
<td>0 (0%)</td>
<td>1 (6.25%)</td>
<td>0.05</td>
</tr>
<tr>
<td>LCX Injury, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>LVOTO, n (%)</td>
<td>3 (4.17%)</td>
<td>0 (0%)</td>
<td>3 (18.75%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Second Valve Placement, n (%)</td>
<td>2 (2.78%)</td>
<td>0 (0%)</td>
<td>2 (13%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Procedure Conversion, n (%)</td>
<td>1 (1.39%)</td>
<td>0 (0%)</td>
<td>1 (6.25%)</td>
<td>0.05</td>
</tr>
<tr>
<td>IABP, n (%)</td>
<td>2 (2.78%)</td>
<td>0 (0%)</td>
<td>2 (12.50%)</td>
<td>0.00</td>
</tr>
<tr>
<td>PVL Mod+, n (%)</td>
<td>2 (2.78%)</td>
<td>1 (1.79%)</td>
<td>1 (6.25%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Valve Reintervention, n (%)</td>
<td>0 (0.00%)</td>
<td>0 (0%)</td>
<td>0 (0.00%)</td>
<td>-</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>3 (4.17%)</td>
<td>3 (5.36%)</td>
<td>0 (0.00%)</td>
<td>0.34</td>
</tr>
<tr>
<td>New RRT, n (%)</td>
<td>5 (6.94%)</td>
<td>3 (5.36%)</td>
<td>2 (12.50%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Reop for Bleed, n (%)</td>
<td>2 (2.78%)</td>
<td>1 (1.79%)</td>
<td>1 (6.25%)</td>
<td>0.33</td>
</tr>
<tr>
<td>DSWI, n (%)</td>
<td>2 (2.78%)</td>
<td>0 (0%)</td>
<td>2 (13%)</td>
<td>0.00</td>
</tr>
<tr>
<td>In-Hospital Mortality, n (%)</td>
<td>6 (8.33%)</td>
<td>2 (3.57%)</td>
<td>4 (25.00%)</td>
<td>0.00</td>
</tr>
<tr>
<td>1 Year Survival, % (95% CI)</td>
<td>76% (87.63-64.63%)</td>
<td>82.82% (94.96-70.68%)</td>
<td>54.69% (80.43-28.95%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Hospital LOS, median (IQR)</td>
<td>10.5 (9-15.5)</td>
<td>10.5 (9-15)</td>
<td>10.5 (7.5-24.5)</td>
<td>0.46</td>
</tr>
<tr>
<td>ICU LOS, median (IQR)</td>
<td>2.0 (4-7)</td>
<td>2.0 (4-6)</td>
<td>3.0 (7-10.25)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

AV = atrioventricular, LCX = left circumflex, LVOTO = left ventricular outflow tract obstruction, IABP = intra-aortic balloon pump, PVL = paravalvular leak, RRT = renal replacement therapy, DSWI = deep sternal wound infection, ICU = intensive care unit, LOS = length of stay
Figure 1.
Figure 2.
Figure 3.
Figure 5.

The management of patients with extensive mitral annular calcification undergoing valve replacement using an algorithm based on MAC morphology

Patients with extensive mitral annular calcification (MAC) + underwent surgical valve replacement
January 1, 2013 – September 31, 2022
N = 72

MAC Morphology

Partial (<270°)
C-MVR (N = 56)

Horsehoe or Greater (≥270°)
H-TMVR (N = 16)

1 Year Survival: 82.8%
1 Year Survival: 54.7%

Conventional valve replacement techniques can be utilized with good perioperative outcomes when the MAC morphology is favorable. In instances where MAC morphology is unfavorable a hybrid approach can be implemented as a bailout.

MAC = mitral annular calcification; C-MVR = conventional mitral valve replacement; H-TMVR = hybrid transcatheter mitral valve replacement
Supplemental Figure 1.

![Survival Probability](image-url)
Supplemental Figure 2.
Graphical Abstract

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Figure and Video Legends

Figure 1. Anatomic analysis of mitral annular calcification (MAC) and feasibility of transcatheter valves using multidetector computed tomography. Clockwise from top left: (A) intercommissural and anterior-posterior dimensions are determined. (B) Aortomitral angle and a virtual transcatheter valve (Sapien 3) are placed to assess the fitting inside the MAC and left ventricular outflow tract (LVOT) obstruction risk. (C) Severity of MAC, using a clockface orientation, is determined, with 270-300 degree deemed horseshoe and more than 300 degree circumferential. (D, E) Maximum calcium thickness and height with the MAC are calculated to determine the extent of anchoring with the transcatheter valve.

Figure 2. Mount Sinai algorithm for management of MAC, where C-MVR is done for partial (< 270) MAC and H-TMVR was done for horseshoe and circumferential MAC (>270).

Figure 3. Modified anterior leaflet flip technique for C-MVR. Anterior leaflet disinserted (A), anterior leaflet flipped toward posterior leaflet creating neo-annulus (B).

Figure 4. H-TMVR stepwise technique: Valve analysis showing horse-shoe MAC (A), anterior leaflet resection (B), Sapien 3 valve wrapped in felt strips (C), valve balloon deployment (D), fully deployed valve (E), 2D and 3D TEE reconstruction demonstrating well seated valve (F-H).

Figure 5. Graphical Abstract.
Supplemental Figure 1. Standard Kaplan-Meier curve comparing C-MVR and H-TMVR 1 year survival.

Supplemental Figure 2. Learning curve for H-TMVR implantation.

Video 1. Periannular suture technique, where non everted sutures are passed behind the calcium bar, and the valve is implanted in a supra-annular position.

Video 2. Anterior leaflet flip technique, the anterior leaflet is disinserted and flipped over toward the posterior leaflet preserving the whole subvalvular apparatus creating a “neo-annulus” in front of the MAC bar.

Video 3. Direct access trans-atrial implantation of a Sapien 3 valve into MAC.
A
Anterior-Posterior
26.4 mm
17.5 mm
Intercomissural
B
\( \alpha \approx 121^\circ \)
Aortomitral Angle
Sapien 3 Virtual Valve
Posterior Calcium Ridge
C
D
13.7 mm
Maximum Calcium Width
E
20.0 mm
Maximum Calcium Height
The management of patients with extensive mitral annular calcification undergoing valve replacement using an algorithm based on MAC morphology

Patients with extensive mitral annular calcification (MAC) + underwent surgical valve replacement
January 1, 2013 – September 31, 2022
N = 72

MAC Morphology

Partial (<270°)  Horsehoe or Greater (≥270°)

C-MVR (N = 56)  H-TMVR (N = 16)

1 Year Survival: 82.8%  1 Year Survival: 54.7%

Conventional valve replacement techniques can be utilized with good perioperative outcomes when the MAC morphology is favorable. In instances where MAC morphology is unfavorable a hybrid approach can be implemented as a bailout.

MAC = mitral annular calcification; C-MVR = conventional mitral valve replacement; H-TMVR = hybrid transcatheter mitral valve replacement.
Mitral Valve Replacement for Extensive Mitral Annular Calcification; Surgical Strategies and Outcomes

Ahmed El-Eshmawi, Gilbert Tang, Erick Sun, Sophia Alexis, Dimosthenis Pandis, Percy Boateng, and David H. Adams

Department of Cardiovascular Surgery
Icahn School of Medicine at Mount Sinai
New York, NY