Minimally invasive treatment of mitral valve disease with severe mitral annular calcification

Andrew D. Wisneski, Barbara Hamilton, Tom C. Nguyen

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Minimally Invasive Trans-Aortic Transcatheter Mitral Valve Replacement for MAC

A safe, effective approach to treatment of mitral valve disease in patients with severe MAC.
Title: Minimally invasive treatment of mitral valve disease with severe mitral annular calcification

Meeting paper for Mitral Conclave 2022

Authors: Andrew D. Wisneski, Barbara Hamilton, Tom C. Nguyen

1- Division of Cardiothoracic Surgery, Department of Surgery, University of California San Francisco, San Francisco, California, United States

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Corresponding Author

Tom C. Nguyen, MD, FACS, FACC
Chief of Cardiothoracic Surgery
Co-Director, Heart and Vascular Center
Helen and Charles Schwab Distinguished Professor of Surgery
500 Parnassus Avenue, MU-West 405 Box 0118
San Francisco, CA 94143
Tel: 415-353-8195
Fax: 415-353-1312
Email: Tom.C.Nguyen@ucsf.edu

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**Glossary of Abbreviations**

- CT – computed tomography
- LV – left ventricle
- LVOTO – left ventricle outflow tract obstruction
- MAC – Mitral annular calcification
- NYHA - New York Heart Association
- THV - transcatheter heart valve
- TMVR – transcatheter mitral valve replacement
Central Picture

Central picture legend (89 char; 90 char max)
A 25mm Sapien 3 deployed into the mitral annulus after leaflet resection.

Central Message (182 char; 200 char limit)
Strategic use of minimally invasive, trans-atrial, transcatheter mitral valve replacement offers an innovative approach to safe, effective treatment of mitral valve disease with MAC.

Perspective Statement (393 char; 405 char limit)
Mitral valve disease with MAC remains a challenge for surgeons, and conventional surgical approaches have potential for heightened morbidity. Use of transcatheter mitral valve replacement (TMVR) technology has demonstrated strong promise with excellent clinical outcomes. We advocate for a minimally invasive trans-atrial approach for TMVR when mitral valve disease with severe MAC is present.
Structured Abstract (139 words; 250 word limit)

Objective: Mitral valve disease in presence of severe mitral annular calcification (MAC) remains a challenge for surgeons to address. Conventional surgical techniques have potential for heightened morbidity and mortality. The advent of transcatheter heart valve technology and transcatheter mitral valve replacement (TMVR) holds promise to treat mitral valve disease with MAC with excellent clinical outcomes.

Methods: We review current treatment strategies for MAC and studies in which TMVR techniques were used.

Results: Several studies and a global registry describe outcomes of TMVR for mitral valve disease with MAC. We describe our specific technique on how to perform a minimally invasive trans-atrial approach for TMVR.

Conclusions: TMVR demonstrates strong promise as a safe and effective way to treat mitral valve disease with MAC. We advocate for a minimally invasive trans-atrial approach when performing TMVR for mitral valve disease with MAC.

Keywords: mitral annular calcification, mitral annulus, transcatheter heart valve, trans-atrial access, transcatheter mitral valve replacement, left ventricle outflow tract obstruction, paravalvular leak.

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Manuscript Body

Introduction

Mitral annular calcification (MAC) is a chronic, degenerative process which leads to progressive calcium deposition on the mitral valve (MV) annulus\textsuperscript{1-3}. Mitral valve replacement in the setting of severe MAC is associated with heightened cardiovascular morbidity and mortality. Acute perioperative mortality can range from 3-9%, and there is a 1-2% associated risk of the devastating complication of atrioventricular groove disruption or left ventricular perforation (each with an associated >80% mortality)\textsuperscript{1,2,4}. Treatment of MV disease with MAC remains a challenge for cardiac surgeons today. However, with an improved understanding of MAC pathophysiology, and the advent of transcatheter heart valve (THV) technology, new strategies can be applied enabling surgeons to more safely and effectively treat MV disease with MAC.

In this topic overview, we will delve into the pathophysiology of MAC and how it is distinct from rheumatic mitral stenosis, review the existing literature on the use of THV for transcatheter mitral valve replacement (TMVR) in MAC, and describe our approach for a minimally invasive trans-atrial approach for TMVR.

Defining the Disease and Pathophysiology

Although rheumatic heart disease is the most common cause of mitral stenosis (MS), it is important to understand that MV disease with MAC is a distinct entity from rheumatic MS\textsuperscript{3}. In contrast to rheumatic MS, MAC is a condition that often presents in older patients with multiple medical co-morbidities and involves the base of the leaflets, and annulus, with circular narrowing from outside inwards. Risk factors for MAC include advanced age, female gender, chronic kidney disease, conditions that are associated with increased stress on the MV
(hypertension, aortic stenosis, hypertrophic cardiomyopathy, mitral valve prolapse), osteoporosis, and metabolic disorders such as Marfan syndrome and Hurler syndrome\textsuperscript{1, 2}. In rheumatic MS, fusion of the leaflets at the commissures is present, and the greatest narrowing occurs at the leaflet tips. While balloon valvuloplasty is helpful in relieving rheumatic MS (leading to a marked decrease in left atrial pressure), it is less so for MAC given that the leaflet tips in MAC are often unrestricted and there is no leaflet commissural fusion\textsuperscript{3}.

The hemodynamics of trans-mitral valve pressures tracing for both conditions yields insight into their differing pathophysiology. In rheumatic MS, there is leaflet impedance to atrial emptying. The left atrial catheterization tracing \textit{sine qua non} for rheumatic MS is elevation of the left atrial pressure greater than LV pressure during diastole with persistent diastolic separation of the left atrial and left ventricular pressures\textsuperscript{3}. In MAC, there is a high left atrial v-wave with rapid y-descent and equilibration of the atrial-ventricular pressure gradient indicative of minimal valvular impedance to flow. Doppler echocardiography is often used to determine if MS is severe, but the contour of the trans-mitral flow velocity should be carefully examined and cardiac catheterization may help to determine relative contributions of left atrial pressure elevation from mitral valve resistance versus abnormal left ventricular filling\textsuperscript{3}.

\textit{Treatment Options for Mitral Annular Calcification}

Up to 20\% of patients who undergo MV surgery have some degree of MAC, and MAC has been associated with several-fold higher mortality in isolated MV surgery compared to patients without MAC\textsuperscript{2-4}. Aside from the more advanced age and accompanying co-morbidities that add perioperative risk, several technical challenges arise from the annular calcium deposits. The calcium can prevent adequate apposition of the replacement mitral valve to the annulus.
resulting in perivalvular leak (PVL). Placing stitches in the calcified annulus also risks injury to
the left circumflex coronary artery, which may require urgent bypass, thereby adding procedural
complexity. Annular decalcification to permit better replacement mitral valve seating is possible
but may weaken the annulus resulting in atrioventricular groove disruption, which can incur
exceedingly high mortality.

The alternative is to leave the calcified annulus in place and try to minimize manipulation
or debridement of the existing calcium. This is balanced against the risk of settling for a smaller
valve size which may leave patients with residual MS. Brescia and colleagues recently described
their experience using the Sonopet ultrasonic aspirator (Stryker, Kalamazoo, Michigan) to
remodel the calcifications in MAC. In a series of 15 patients, a median 27mm replacement
mitral valve was implanted, resulting in reduced mean MV gradient and 0% operative mortality.
No atrioventricular groove disruptions occurred. Technology such as this ultrasonic aspirator
may be helpful to perform calcification debridement more safely when called for.

The goals of treatment for MV disease with MAC include replacing the valve safely in a
patient population already at greater risk, using the largest valve prosthesis possible to produce
the greatest effective orifice area, and using techniques to minimize PVL, left ventricle outflow
tract obstruction (LVOTO), and device embolization. With its expandable frame, the THV can
tolerate expansion in a non-perfectly circular annulus while maximizing orifice area and
preserving valve function. Furthermore, expansion under direct vision allows the surgeon to
carefully control the ultimate size given a patient’s anatomy. The combined techniques of an
open or minimally invasive surgical approach with a THV is particularly well-suited to help
achieve these goals for the surgical treatment of MAC (Figure 1).
The initial data describing TMVR for treatment of MAC is encouraging. Guerrero et al. reported results from a global registry that includes 64 patients from 32 international sites who underwent TMVR for severe MAC with the Edwards Sapien, Sapien XT or S3 platform. The cohort had a mean Society of Thoracic Surgeons mortality score of 14.4%. TMVR was technically successful in 72% of all cases, and 30-day mortality was 30%. Among the three access options—trans-septal, trans-apical, and trans-atrial—trans-atrial had the highest technical success at 89%, and the lowest 30-day mortality rate at 20%. With follow-up out to a year post-TMVR, the surviving cohort demonstrated clinical improvement, with lower New York Heart Association (NYHA) functional class scores over time. This study also highlights the merits of the trans-atrial approach. LVOTO occurred in 9.3% of cases, but none were from the trans-atrial approach. THV embolization occurred in 6.25% of cases, of which only one case occurred with the trans-atrial approach, and left ventricle perforation occurred in 3.1% of cases, none of which were from the trans-atrial approach. A follow-up report on the global registry reinforced the superior safety of the trans-atrial approach, as mortality risk was nearly 2.5-fold greater when comparing the trans-septal and trans-apical approaches to the trans-atrial approach.

Apart from the global registry study, Praz et al. published the largest series to date describing 26 patients who underwent sternotomy for TMVR; 100% of these procedures were technically successful, and NYHA functional class improved significantly at 30-day follow up. However, data from case reports and case series can be pooled together for a total of 74 cases of TMVR. 41 cases were performed via the trans-atrial approach, which had a 93% technical success rate, 14.6% 30-day mortality, and 2.4% risk of LVOTO. The rate of any-degree
184 PVL was 3% for the 41 trans-atrial cases, compared to 20% any-degree PVL for the 30 trans-septal cases, and 0% for the three transapical cases.

186 New technology and TMVR devices continue to be developed and clinical studies are currently underway. Gossli and colleagues report favorable early feasibility results of the Tendyne TMVR platform (Abbott Laboratories – Structural Heart, Bastion, IN) in 20 patients with MAC-associated mitral regurgitation. No procedural mortality occurred, one patient died within 30-days of the procedure, and eight patients had died by one year. At the one-year follow up, mitral regurgitation remained absent and NYHA functional class had improved in 11 of 12 patients that were alive. The Apollo Trial for Medtronic’s (Minneapolis, MN) Intrepid TMVR system is currently enrolling patients, and will include a cohort of patients with MAC. There remain strong research and innovation opportunities for TMVR with the goal of engineering devices to treat MAC safely and effectively.

197 How We Do It – Minimally Invasive Trans-atrial TMVR

198 We advocate for a minimally invasive trans-atrial approach given the direct approach to the mitral valve offered for patients of all habitus, along with reduced risk of PVL and valve embolization. To date, we have treated approximately 20 patients with this method. A pre-procedural cardiac computed tomography scan is obtained for every patient to view the mitral valve position and geometry (Figure 2). While clinician judgement and experience leads to identification of severe MAC when seen on imaging, the scoring system devised by Guerrero et al. provides an organized manner to describe the nature and severity of MAC. We consider some patients with moderate MAC and all patients with severe MAC for minimally-invasive TMVR in our practice.
A right mini-thoracotomy is performed at the 3\textsuperscript{rd} or 4\textsuperscript{th} intercostal space. After dissection of pericardial fat and entry into the pericardium lateral to the phrenic nerve, several retraction sutures are placed. The left atrium is accessed via the interatrial groove, and the atriotomy extended with angled Potts scissors (Figure 3). A left atrial retractor is placed, stabilized by a retractor post inserted through a separate chest incision. Care is taken to avoid excessive retraction which could distort or dislodge any previously placed THV in the aortic position, if present.

The non-calcified portion of the anterior mitral leaflet and its cordal attachments are excised, leaving a 2-3mm rim of leaflet tissue in order to prevent left ventricular outflow tract obstruction (LVOTO) (Figure 4). To minimize risk of atrioventricular groove disruption, we do not routinely resect the posterior leaflet or associated MAC. If a septal myectomy is necessary, this should be done before THV placement.

Annular 2-0 pledgeted Ethibond sutures are placed in an everting manner around the mitral annulus with the pledgets on the atrial side. We use a SH-1 needle to enable us to take bites around denser annular calcifications. In regions with heavy calcifications, we err on taking more left atrial tissue to create a seal, while other sutures around less dense calcifications or normal tissue will help anchor the valve. (Figure 4). Areas of key annular suture placement include each commissure, the junction of P1-P2, P2-P3, and any areas of deep indentation along the annulus. If dense MAC prevents annular suture placement, the suture can be placed in the residual leaflet tissue or atrial tissue.
The annulus is then sized with the Sapien transcatheter delivery balloon (Figure 5). The balloon should be inflated until it fits snugly, but not over inflated. Intraoperative balloon sizing remains a crucial step, and we emphasize that it is important to not rely solely on computed tomography measurements because THV oversizing may lead to LVOTO. In our institutional experience, most patients undergoing TMVR receive a Sapien 26mm or 29mm S3 valve. Before the valve is crimped, a 1cm-wide felt strip is sewn to the S3 skirt with 5-0 polypropylene suture taking care to not incorporate any of the bioprosthetic leaflet tissue (Figure 6). The felt strip should not be taller than 1cm in order to eliminate this as a potential contributor to LVOTO.

The valve is partially crimped onto the balloon as it has only to fit through the atriotomy incision. Full crimping of the THV is not necessary. The commissures are marked and the trigones are aligned with the THV (Figure 6). The partially crimped THV is inserted into the left atrium, and positioned coaxially with the annular plane. In our early experience, we would implant the THV annulus flush with the MV annulus, as depicted in the figure, but with experience began positioning the THV such that it sat more atrially in order to reduce contribution to LVOTO. Our current recommendations are to implant the felt strip such that 50-70% of its height sits above the MV annulus in the atrial side (Figure 7). Surgeon experience and judgement with the regional anatomy may dictate the optimal position of the valve relative to the annulus. The surgical assistant then inflates the balloon slowly until it is snug. Avoid overinflation to prevent annular rupture.

After the THV is deployed, the previously placed annular sutures are passed through the valve skirt and felt strip, and tied with the knots ending up on the atrial side of the valve. The balloon can be inflated again for another 10-20 seconds to ensure full device expansion, followed
by testing for valve leak. If PVL is detected, additional sutures at areas of deep indentation can be placed. If the valve position is satisfactory and no leaks are apparent on testing, the left atriotomy can then be closed, the heart de-aired, and cross clamp removed. Completion trans-oesophageal echocardiography should be used to confirm adequate valve position and function without significant PVL and LVOTO.

Conclusions

In mitral valve disease with MAC, replacement of the mitral valve remains a challenge and is associated with increased morbidity and mortality. The pathophysiology of MAC is distinct from that of rheumatic MS. Innovative treatment approaches for mitral valve disease with MAC include use of ultrasonic aspirator to remodel calcifications and use of THV to perform TMVR. Initial data showing excellent clinical outcomes is promising for TMVR for MAC. At our institution, we use a minimally invasive trans-atrial approach to TMVR. Further innovation and research are needed to devise technology specifically suited to mitral valve disease with MAC, as well as optimal procedural techniques.
References


Figure Legends

**Figure 1:** We advocate for minimally invasive trans-atrial transcatheter mitral valve replacement for treatment of mitral valve disease with severe mitral annular calcification.

**Figure 2:** Computed tomography scan of a patient with severe mitral annular calcification.

**Figure 3:** Left atriotomy performed at Sondergaard’s groove, extended with Potts scissors.

**Figure 4:** Resection of the anterior mitral valve leaflet, leaving a rim of tissue 2-3mm at the annulus.

**Figure 5:** After placement of annular stitches, a sizing balloon is snugly inflated to determine the optimal THV size.

**Figure 6:** Preparing the transcatheter heart valve. Left: a 1cm felt strip is sewn to the skirt of the Sapien S3. Middle: The valve is partially crimped. Right: The trigones are marked so that proper orientation of the valve can be maintained during deployment.

**Figure 7:** Deployment of the THV. Left: The crimped Sapien 3 is positioned coaxially at the annular plane, where about 70% of the valve apparatus will sit supra-annularly. Middle: The balloon is inflated slowly and the valve is in good apposition with the annulus. Right: The annular stitches will then be sutured through the skirt to secure the valve in place.
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