Secondary mitral regurgitation repair techniques and outcomes: Initial clinical experience with mitral valve translocation

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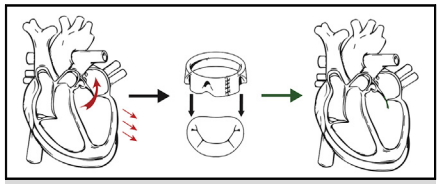
Video clip is available online.



Mitral valve translocation addresses valvular abnormalities in secondary mitral regurgitation.

CENTRAL MESSAGE

Mitral valve translocation using a circumferential pericardial patch placed between annulus and native valve is a novel and potentially durable treatment of secondary mitral regurgitation.

Most often the entire valve appears normal…there is little to fix, yet the valve leaks…the valve is structurally normal; it need not be replaced, but currently we do not know how to fix it." L. Henry Edmunds, Jr.[1]

SECONDARY MITRAL REGURGITATION

Mitral regurgitation (MR) is the most common valvular heart disease, with 2.3 million adults in the United States expected to be diagnosed with MR by 2030.[2] Secondary (functional) MR (SMR) is characterized primarily by underlying anatomic abnormalities, including annular dilation, altered left ventricular geometry, leaflet tethering, and insufficient leaflet coaptation,[3-5] but also can be associated with isolated atrial enlargement due to atrial fibrillation in the presence of heart failure with preserved ejection fraction.[6] The presence of SMR is an independent predictor of death,[2,7] and patients with SMR are at high risk of heart failure, which is present in more than 80% of patients with SMR and in almost 60% of patients with atrial mechanism SMR.[6,8] Few patients with SMR undergo surgical treatment, with studies reporting operative rates of only 4%-7%,[7,8] substantially lower than the reported rates for patients with degenerative MR.[9]

For the treatment of degenerative MR, surgical mitral valve (MV) repair is superior to prosthetic valve replacement, providing the benefits of lower operative mortality, improved ventricular function, and freedom from bioprosthetic valve degeneration, chronic anticoagulation, prosthetic valve endocarditis, and thromboembolism.[10-12] Such benefits also are likely applicable to patients with SMR. However, currently there are no MV repair strategies that offer long-term, durable results, primarily because existing techniques do not result in sufficient coaptation that can withstand progressive adverse ventricular remodeling and continued leaflet restriction.

The primary repair strategy for the treatment of SMR is restrictive mitral annuloplasty (RMA), in which an undersized, rigid, annuloplasty ring is implanted at the mitral annulus with the goal of downsizing the annulus and forcing an increase in leaflet coaptation, thereby eliminating MR. RMA has been the method of choice for MV repair in SMR owing to its low perioperative morbidity and mortality, simplicity, and maintenance of an intact subvalvular apparatus[13,14]; however, RMA has not been shown to provide durable correction of MR. The pivotal National Heart, Lung, and Blood Institute–sponsored Cardiothoracic Trials Network study found a nearly 60% rate of recurrence of moderate or greater MR at 2 years in patients undergoing RMA, compared with 4% in those undergoing MV replacement.[15] In another study, the rate of recurrent MR after RMA was found to increase progressively with the duration

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Supported by grateful patient funding to the Division of Cardiac Surgery, University of Maryland School of Medicine.

Received for publication July 30, 2021; accepted for publication Jan 12, 2022; available ahead of print Feb 20, 2022.

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JTCVS Techniques 2022;13:53-7

2666-2507

https://doi.org/10.1016/j.xjtc.2022.01.025

Abbreviations and Acronyms
MR = mitral regurgitation
MV = mitral valve
RMA = restrictive mitral annuloplasty
SMR = secondary mitral regurgitation
TEER = transcatheter edge-to-edge repair

of follow-up, with a rate of 15% to 25% at 6 months and approximately 70% by 5 years.[16]

Although RMA addresses abnormal annular dilation and increases leaflet coaptation,[17] it does not change the underlying aberrant geometry of the ventricle and subvalvular apparatus. Thus, RMA does not abrogate leaflet tethering or improve papillary muscle displacement, nor does the modest increase in coaptation following RMA protect against recurrent MR in the face of worsening left ventricular function.[18-21] Additionally, aggressive downsizing of the mitral annulus is associated with increased transmitral gradients and a higher risk of functional mitral stenosis.[22]

None of the available adjunctive therapies to RMA for treating SMR, including chordal cutting,[23] papillary muscle approximation,[24] and isolated anterior[25] or posterior[26,27] leaflet augmentation, achieves the goal of durable MV repair for SMR. Although papillary muscle approximation was found to be associated with a lower incidence of recurrent MR compared to RMA, more than a one-quarter of patients had recurrent moderate or greater MR at 5 years.[24]

Focal augmentation of the MV leaflets to treat SMR has been attempted using isolated anterior or posterior leaflet extension via implantation of autologous pericardial patches, usually in conjunction with a true-sized annuloplasty ring.[26,27] Although this can produce a modest increase in leaflet coaptation length,[27] it does not resolve leaflet tethering,[26] because the anatomy of the leaflet free edge remains unchanged. It also can create ballooning of the patch during both systole and diastole, as well as obstruct ventricular filling and mitral stenosis.

Transcatheter edge-to-edge repair (TEER) has been shown in the COAPT randomized trial to result in a substantial increase in survival and decrease in hospital admissions for heart failure in selected patients with SMR on guideline-directed medical treatment. COAPT has provided strong clinical evidence for the biologic benefit of MR reduction in this patient population.[28] However, TEER is limited by its variable efficacy in MR reduction, with rates of recurrent moderate MR between 26% and 47% and those of MR between 5% and 22% within 5 years.[28-30] Additionally, TEER can cause significant mitral stenosis in as many as one-quarter of patients and does not address tricuspid regurgitation, atrial fibrillation, or coronary artery disease.

MV TRANSLOCATION: LEARNING FROM NATURE

In patients with chronic aortic insufficiency, the left ventricle is often dilated; however, concomitant MR is infrequent.[31] Studies in this patient population have shown that MV leaflet area increases by >30% on average as a compensatory mechanism, preventing the onset of MR.[31] We have observed that the supranormal coaptation created during nonresectional repair of degenerative MR provides durable relief from MR.[32] Considering the observation of leaflet enlargement in patients with aortic insufficiency, we hypothesized that the optimal treatment of SMR might involve augmentation of leaflet surface area to create a supranormal coaptation surface.

We have developed a novel operative approach to address all of the pathophysiologic mechanisms of FMR, termed MV translocation (Figure 1; Video 1).[33] In MV translocation, the native MV is excised circumferentially within 1-2 mm of the annulus, leaving the commissures and subvalvular apparatus intact, and the insertion of a 1 cm frustum-shaped patch translocates the intact native valve into the ventricle, thereby improving coaptation. MV translocation creates circumferential augmentation of the MV leaflet, which creates a generous and supranormal surface of coaptation. The effective increase in leaflet area relieves leaflet tethering, while leaving the native mitral valve intact. Translocation protects against recurrence, should ongoing adverse remodeling occur. MV translocation differs from combined anterior and posterior leaflet augmentation in that instead of two separate patches of pericardium being implanted into the anterior and posterior leaflets, one continuous piece of pericardium is utilized. Since the translocation patch spans the commissures, the entire native valve is moved *en bloc* into the ventricle, thereby preserving the MV geometry.

The translocation patch is created from autologous pericardium, which is treated with 0.625% glutaraldehyde for three minutes. Autologous pericardium is the substrate of choice for this procedure due to its long-term durability and low thrombogenicity,[34,35] as well as easy accessibility and excellent handling characteristics.[36] The translocation patch is a frustum, a geometric form defined as the portion of a cone which remains following removal of the upper part by a plane parallel to the base of the cone. Once created, the 'top' of the frustum, having the smaller diameter, is sutured to the native annulus (atrial suture line), and the 'base' of the frustum, having the larger diameter, is sutured to the native MV leaflets (ventricular suture line). Optimal dimensions of the frustum were determined following both ex vivo modeling using a static air-filled model[37] and both acute and chronic animal studies. In an isolated swine heart model, data from our laboratory recently accepted for publication showed that a patch depth of 1.0 or 1.5 cm was

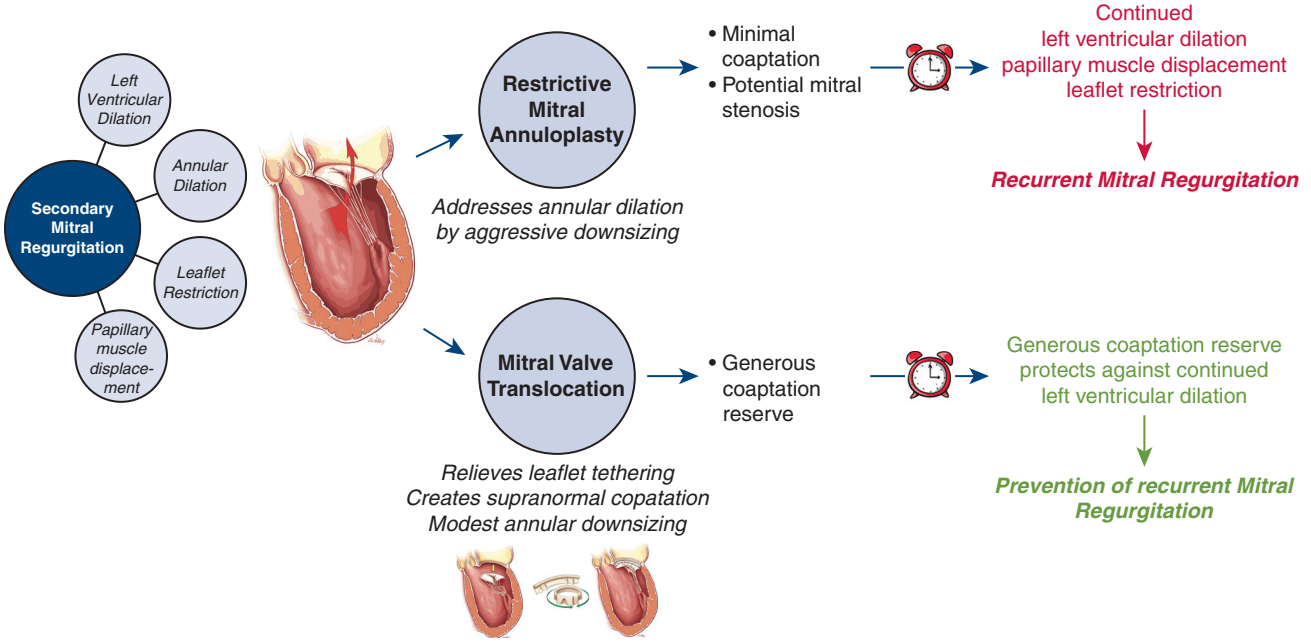
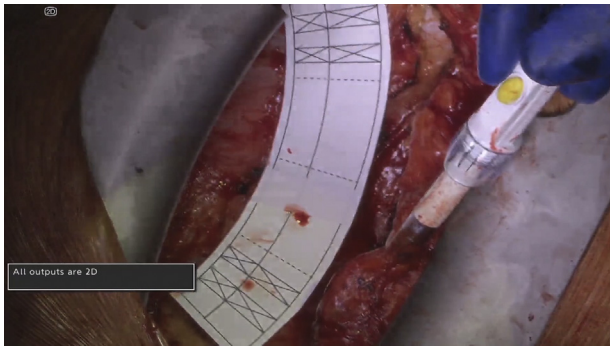


FIGURE 1. Secondary mitral regurgitation (MR), characterized by left ventricular and annular dilation, papillary muscle displacement, and leaflet tethering, is traditionally addressed by annuloplasty, which aggressively downsizes the mitral annulus to minimally increase coaptation and eliminate MR. However, over time, disease progression leads to recurrent MR. Translocation of the mitral valve (MV), in which a circumferential pericardial patch is interposed between the annulus and native MV, creates a supranormal leaflet coaptation, which may protect against continued left ventricular dilation and prevent recurrent MR.

associated with enhanced coaptation without alteration of native leaflet geometry. In an acute animal study, we found that translocation dramatically increased leaflet coaptation without impairing diastolic function in pigs with normal left ventricular function and did not pose an increased risk of systolic anterior motion. In a pivotal study utilizing a chronic animal model of ischemic MR, recently accepted for publication, translocation was associated with significantly greater coaptation length compared to RMA, with relief of leaflet tethering and preserved diastolic function. All animal studies were approved by the Institutional Animal Care and Use Committee at the University of Maryland Baltimore.

CLINICAL INTRODUCTION OF MV TRANSLOCATION

The first MV translocation was performed in 2018 (Institutional Review Board approval HP-00076929[33]). Early in the experience, the size of the patch was individualized based on intraoperative annular measurements, but eventually uniform dimensions were chosen so as to achieve a standard 100-mm atrial circumference and 110-mm ventricular circumference. This provides a modest annuloplasty effect for the majority of patients while ensuring a low post-operative mean gradient. Early in the experience, several small leaks were observed to originate in the outer suture line when a simple running suture technique was used (with 5-0 polypropylene suture). Therefore, the patch was modified to include an integrated sewing cuff consisting of extra pericardium that is rolled over to form a sturdy ring through which sutures can be placed. This also allowed for the use of interrupted pledgeted sutures (3-0 nonabsorbable polyester) for the atrial suture line, which has eliminated suture line leakage and improved the speed of the



VIDEO 1. During mitral valve (MV) translocation, the patch is fashioned from autologous pericardium harvested from the patient and briefly (3 minutes) treated with 0.625% glutaraldehyde. The native MV is excised at the annulus, leaving the subvalvular apparatus intact. Using pledgeted 3-0 nonabsorbable polyester sutures, the patch is implanted into the annulus, after which the native leaflets are sutured to the free edge of the patch using running 5-0 polypropylene sutures. Saline testing is used to determine valve competence following the completion of translocation. Video available at: https://www.jtcvs.org/article/S2666-2507(22)00108-0/fulltext.

operation. The design of the patch also incorporates 4 pleats placed on the portion of the patch that subtends the posterior leaflet. The purpose of the pleats is to reduce the circumference of the atrial suture line (the top of the patch that is sewn to the annulus), while the ventricular suture line (the bottom of the patch that is sewn to the mitral valve) retains a longer circumference, with the goal of maximizing diastolic valve opening.

Results from the initial human experience show that MV translocation is safe and repeatable, with no operative mortality, stroke, or renal failure. No patient required conversion to MV replacement. Initial follow-up of 15 patients with functional MR who underwent MV translocation between 2018 and 2020 showed that translocation successfully eliminated MR, with intraoperative transesophageal echocardiography showing none/trace MR in all patients and a median mean gradient of 3 mm Hg (interquartile range, 2-4 mm Hg). Translocation resulted in a mean coaptation length of 14 mm, significantly longer than the 2 mm normally observed in human MVs.[38]

In the second part of the experience (patients 11-15), in which patients underwent translocation with pleats that increased the ventricular circumference to exceed the atrial circumference, the tenting area was reduced following translocation, as were the anterior and posterior leaflet angles, indicating relief from leaflet tethering with the current patch iteration. The initial follow-up (median, 133 days; range, 0-284 days) demonstrated no/trace MR in 12 patients and mild MR in 3 patients. Three 3 deaths occurred within 1 year of the operation, 1 each related to progressive biventricular failure (at 7 months), ischemic cardiomyopathy and stomach ischemia (at 9 months), and progressive heart failure and refusal of follow-up (at 1 year). At the time of this report, 7 patients have reached the 8- to 12-month follow-up, and MR status is none/trace in 5 and mild in 2. One patient experienced a mild suture line leak that has remained stable. The median coaptation length has remained stable at 13.6 mm (interquartile range, 12.8-15.5 mm).

Limitations to the widespread adoption of MV translocation include the complexity of the technique with resulting increased cross-clamp and cardiopulmonary bypass times. As familiarity with the translocation technique has increased, and as we have introduced modifications to simplify implantation (eg, the use of pledgeted sutures), implantation time has decreased, with total patch implantation time for the most recent 11 patients averaging 77 minutes.

FUTURE DIRECTIONS

Follow-up of the first cohort of patients is ongoing, and careful clinical and echocardiographic evaluation will be critical to validate the mid-term safety and efficacy of translocation. Once this is established, it will be crucial to demonstrate that this approach is adoptable. Ongoing areas of research include simplification and improved efficiency of the surgical procedure, determination of optimal patch material, refinement of patient selection, and geometric optimization of the patch. Because of the widespread undertreatment of patients with SMR, there is a pressing need for multicenter randomized clinical trials to compare the worth of alternative treatments such as MV translocation with guideline-directed medical therapy in this large patient population. MV translocation is a promising technique for predictable, durable, and lasting repair of SMR. Surgical SMR repair with translocation allows comprehensive repair for patients with SMR, who frequently require concomitant surgical atrial fibrillation ablation, tricuspid valve repair, and revascularization.

Conflict of Interest Statement

J.G. serves as a consultant for Edwards Lifesciences and is a founder of Protaryx Medical and Marlin Medical. J.G., R.W.Q., and C.P. are inventors of the method described in this article and have submitted disclosures through the University of Maryland.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: mitral valve, functional mitral regurgitation, mitral repair, translocation