Chronic Ischemic Mitral Regurgitation:
Insights into Pandora’s Box

Running title: Borger; Ischemic MR: Pandora's box

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Chronic ischemic mitral regurgitation (cIMR) remains a vexing problem for a large number of patients and their respective clinicians. It is estimated that approximately 2 million Americans suffer from cIMR, and this number is likely to increase with an aging general population and improved survival rates for myocardial infarction. Despite the large number of patients with this disease, relatively few patients are referred for surgical therapy. This is reflected in the fact that the largest surgical series to date consist of only a few hundred patients operated on over a several year interval.

One important reason for the small number of cIMR surgical referrals is the lack of evidence of a survival benefit associated with surgery, despite observed improvements in heart failure symptoms and left ventricular (LV) dimensions. Improvements in reverse LV remodeling and functional status have also been demonstrated in patients with idiopathic dilated cardiomyopathy who undergo a restrictive annuloplasty procedure. The reason why survival is not increased in the face of improved reverse remodeling is unknown, but is likely related to perioperative mortality and/or recurrent MR during follow up. The lack of evidence of improved survival and the near absence of randomized controlled data have undoubtedly contributed to cardiologists’ hesitation in referring cIMR patients for surgical therapy.

While surgeons are quick to tout the benefits of surgery for cIMR, the reality is that the use of alternative treatment strategies such as cardiac resynchronization therapy and percutaneous techniques has increased markedly over the last few years. The number of percutaneous “edge-to-edge” procedures, in particular, is rapidly increasing in Europe in patients with functional MR, and is likely to occur in the United States if regulatory approval is granted.

In addition to a lack of proven survival benefit, another likely reason for the small number of cIMR patients being referred for surgery is the occurrence of recurrent MR following...
the gold standard operation – the undersized annuloplasty procedure. Recurrent MR rates of up to 30% are frequently quoted in the literature. In fairness, however, only a minority of patients actually received a true undersized annuloplasty operation (i.e. insertion of a complete, rigid annuloplasty ring that is two sizes smaller than the measured mitral size) in the oft-maligned paper from whence this data comes². Other authors have reported much lower MR recurrence rates post-restrictive annuloplasty⁵,⁸, although no center has been able to completely eliminate recurrent MR with this operation. This is not surprising given that cIMR is primarily a ventricular problem, and treating the annulus alone is unlikely to reverse the pathologic process.

In addition to recurrent MR, there is an increasing amount of evidence that undersized annuloplasty may also lead to postoperative functional mitral stenosis with associated symptomatology⁹,¹⁰.

Despite the abovementioned shortcomings, patients continue to be referred for surgical care when they have cIMR in combination with other indications for cardiac surgery (most commonly triple vessel disease), or highly symptomatic cIMR that cannot be medically further managed. Surgeons have tried to address the known problems associated with the undersized annuloplasty operation by developing a multitude of alternative surgical procedures, most of which involve some sort of subvalvular intervention¹. Whenever there are a lot of solutions to a single problem, however, it is likely that none of them work well. It is obvious that we need to find effective and reproducible alternatives for the surgical “Pandora’s box” that is known as cIMR.

In the current issue of Circulation, Szymanski et al¹¹ have revisited a concept that has existed for several years: the chordal-cutting procedure for cIMR. The working group of Robert Levine originally suggested that dividing secondary chords was a simple method of increasing
mitral leaflet mobility, and thereby limiting the amount of apical displacement and leaflet tethering that is pathognomonic of cIMR\textsuperscript{12}. Increasing mitral leaflet mobility may lead to a decreased rate of recurrent MR post-surgical intervention, since excessive leaflet tethering is known to be the principle determinant of recurrent MR after the undersized annuloplasty operation\textsuperscript{13,14}. In addition, increased leaflet mobility may allow for implantation of a larger annuloplasty ring size, possibly leading to a lower risk of postoperative functional mitral stenosis\textsuperscript{9,10} or annuloplasty dehiscence, an uncommon but recognized complication of the restrictive annuloplasty procedure. Preserved leaflet mobility may also prove beneficial by preserving blood vortex formation during LV filling, leading to improved ventricular work efficiency (\textsuperscript{15} and Dr. Jagat Narula, personal communication, October 2012).

Szymanski et al used a validated chronic sheep model of cIMR to evaluate the effects of secondary chordal-cutting\textsuperscript{11}. Their model involves ligation of the second and third obtuse marginal arteries and consistently results in myocardial infarction and cIMR, but is labour intensive and associated with a high mortality. The authors are to be commended for accurately emulating the restrictive annuloplasty operation with implantation of a complete, rigid ring that is 2 sizes smaller than the measured annular size\textsuperscript{3-5}. The investigators found an increase in leaflet mobility post-chordal cutting in surviving sheep, and the least amount of residual MR and LV remodeling in the chordal-cutting + annuloplasty group. Importantly, they also demonstrated preservation of LV function in the chordal-cutting group, a concern of previous sheep model investigations from Craig Miller’s group\textsuperscript{16,17}.

The possible reasons for the discrepant findings between the current paper and those from Craig Miller’s group are extensively discussed by Szymanski et al\textsuperscript{11}. It is interesting to note, however, that the findings of Szymanski’s sheep model work closely reflect our clinical
observations from a non-randomized study\textsuperscript{18}. We observed preserved LV function, despite worse preoperative ejection fraction, in a group of 43 patients undergoing the chordal-cutting procedure for cIMR. Patients who received chordal-cutting + annuloplasty also had improved leaflet mobility and reduced recurrent MR when compared to those who received annuloplasty alone\textsuperscript{18}. The improved leaflet mobility can be quite striking post-chordal cutting, and can even be observed before the left atrium is closed (Movie 1). As opposed to the sheep study by Szymanski et al, we sever only those secondary chordae arising from the affected papillary muscle (most commonly the posteromedial papillary muscle) and not from both papillary muscles.

Padala et al have recently assessed the effects of secondary chordal-cutting on marginal (primary) chordae in a pulsatile leaft heart simulator\textsuperscript{19}. These investigators found an increase in marginal chordal force when apical tethering was induced, with no further adverse effect of secondary chordal-cutting. However, division of secondary chords led to an increased force on marginal chords when the leaflets were tethered in an apical-lateral direction, with an even more pronounced effect during apical-lateral-posterior tethering\textsuperscript{19}. What effect such increased forces on the marginal chords may have on ventricular function is currently unknown, but it is important to note that the marginal chord force levels did not reach those required to induce chordal rupture.

Szymanski et al should be congratulated for performing a rigorous investigation of a vexing clinical problem. Whether or not their results translate into a wider application of the chordal-cutting procedure for cIMR remains to be seen. In addition, we need to determine if there is an upper boundary by which a chordal-cutting procedure is no longer beneficial. For example, previous studies have suggested that a tenting height (coaptation depth) of more than
10 mm is associated with an increased risk of recurrent MR post-restrictive annuloplasty.\textsuperscript{30}

Whether annuloplasty with chordal-cutting would be beneficial in such patients, or whether a mitral valve replacement operation should be performed, is unknown. However, ongoing clinical trials (Comparing the Effectiveness of Repairing Versus Replacing the Heart’s Mitral Valve in People With Severe Chronic Ischemic Mitral Regurgitation, ClinicalTrials.gov identifier NCT 00807040) may shed more insight into this question. In the meantime, further high quality research is required in order to gain more insight into the Pandora’s box of cIMR.

\textbf{Conflict of Interest Disclosures:} None.

\textbf{References:}


SUPPLEMENTAL MATERIAL

Movie Legend

**Movie 1.** Intraoperative video showing severe restriction of the medial portion of the posterior mitral valve leaflet. The water test shows a leak occurring at the area of leaflet restriction. Secondary chordae arising from the posteromedial papillary muscle and attaching to the medial aspect of the anterior and posterior mitral valve leaflets are located and divided. Care is taken not to injure the primary chordae. The mobility of the posterior leaflet is immediately improved thereafter, and a repeat water test reveals a competent valve. Best viewed with Windows Media Player.