Coronary Sinus in the Management of Functional Mitral Regurgitation
The Mother Lode or Fool’s Gold?

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The past 5 years have seen the introduction into the preclinical arena of myriad devices for the potential treatment of functional and ischemic mitral regurgitation by a percutaneous approach.1 A number of the device concepts have taken advantage of the relatively easy access to the posterior annulus of the mitral valve provided by the coronary sinus. Although attractive on initial consideration as a delivery route for devices that remodel the posterior mitral annulus, a number of potential shortcomings to this approach may ultimately limit its clinical success.

Annular remodeling of the mitral valve for functional mitral regurgitation (FMR) has been demonstrated to have short-term and some intermediate-term efficacy in the clinical surgical setting.2 The pathophysiology of FMR in patients with dilated cardiomyopathy is central regurgitation caused by failure of mitral leaflet coaptation. The causes of this malcoaptation are multifactorial and include annular dilatation and ventricular dilation, which cause apical distraction of the papillary muscles, producing tethering of the mitral leaflets. Although the whole annulus has been demonstrated to dilate in FMR, there is a disproportionate increase in the anterior-posterior or septal-lateral diameter.3, 4 The basic premise behind the surgical approach is that through the use of an undersized ring to overcorrect the dilation of the mitral annulus, both the annular dilatation and the tethering of the leaflets from apical papillary muscle displacement can be treated. The tenets for optimal surgical correction include performing the annuloplasty with a complete rather than a partial ring and firmly anchoring the ring in the fibrous trigones and the anatomic skeleton of the mitral annulus. Despite some success with the surgical approach, long-term efficacy has been a concern because of recurrence of mitral regurgitation in the first 6 months.5 This recurrence is due largely to further remodeling of the left ventricle with progressive dilatation and mitral leaflet tethering despite the initial overcorrection of the mitral annulus by the downsized ring.

A number of coronary sinus–delivered devices have undergone successful demonstration of proof of concept in the preclinical model.6–9 Correction of mitral regurgitation induced by acute ischemia has been demonstrated in the short term in canine and ovine animal models. This has led to clinical feasibility studies with at least 2 of the devices. A number of hurdles, however, make success in the preclinical experience not translate completely to the clinical setting. Among the issues are the inability to accurately replicate changes that occur in the human disease in the animal model and the anatomic variations that exist between the animal heart and the human heart.

This latter concern is raised in an elegant and detailed study of anatomic dissection of the coronary sinus in autopsy specimens by Maselli et al10 in this issue. The main conclusion of this study mirrors the clinical experience of cardiac surgeons who have performed “cut and sew Maze” procedures for atrial fibrillation, namely, that the coronary sinus is not immediately subjacent to the mitral annulus but rather to the free wall of the left atrium. The authors dissected 61 hearts from autopsy specimens without known heart disease and found that the mean distance from the coronary sinus to the mitral annulus was 9.7±3.2 mm, with a maximal distance of up to 19 mm. This confirmed earlier anatomic studies that showed a mean distance between the mitral annulus and coronary sinus of 10 to 14 mm, depending on the distance from the coronary os.11 The potential clinical implications of this anatomic relationship are significant. As opposed to surgical annuloplasty in which the ring is firmly anchored in the fibrous skeleton of the mitral annulus to achieve optimal correction, clinical efficacy of percutaneous devices will instead need to rely on traction of the left atrial wall to decrease the septal-lateral diameter of the mitral orifice. If the short- and intermediate-term results of an optimally placed surgical device are found wanting, one has to have real concerns regarding the potential clinical durability of devices delivered through the coronary sinus with the less than optimal placement afforded by this approach. Although a decrease in the septal-lateral diameter with correction of FMR has been demonstrated acutely in both animals and humans, relying on left atrial wall traction to maintain this correction over time seems somewhat optimistic.

The second concern raised in the study by Maselli et al10 and others is the distance of the coronary sinus from the fibrous trigones. We have learned from surgical experience that firm anchoring of the annuloplasty device to both fibrous trigones is necessary to achieve optimal results. The inability to anchor devices in both fibrous trigones by the coronary
sinus approach also raises concerns of potential clinical efficacy. The third issue clearly delineated in the study is the interrelationship between the coronary sinus, the mitral annulus, and coronary arteries. The authors report that the main circumflex coronary artery or its branches were located between the coronary sinus and mitral annulus in 64% and a diagonal or ramus branch in 16% of cases. This raises the obvious potential concern of coronary ischemia induced by device placement. A shortcoming of this study, however, is the fact that the anatomic analysis was performed in normal rather than diseased hearts and that the change in these relationships in hearts with dilated left atria and left ventricles present in dilated cardiomyopathies remains to be defined.

The study by Maselli et al highlights one of the hurdles of translational research, ie, extrapolating bench and preclinical experience to the clinical setting. Clinical trials now in progress and soon to be initiated need to closely monitor for the potential clinical issues raised by this study. Early and long-term clinical efficacy outcomes and the potential for adverse events from coronary ischemia need to be carefully captured in trial end points. An additional concern is the placement of another piece of hardware in the coronary sinus in heart failure patients. Will the placement of an annular remodeling device in the coronary sinus possibly preclude lead placement for resynchronization therapy or, vice versa, will previous resynchronization therapy preclude annular device placement? Is coronary sinus thrombosis going to become an issue at some point? With all percutaneous valve studies, the ultimate determination of success will be the tradeoff in decreased efficacy that is acceptable for an increase in safety in these patients. Other therapeutic device possibilities may ultimately be necessary to obtain sufficient clinical efficacy. The combination of a coronary sinus annuloplasty device with an edge-to-edge device may prove more effective than either alone. Alternatively, mitral valve replacement by a percutaneous or transapical approach may ultimately be more effective than either type of repair device by minimizing the potential for recurrent mitral regurgitation resulting from progressive ventricular remodeling. This is an expanding group of sick patients in dire need of further therapeutic options. The clinical and anatomic barriers raised in this study notwithstanding, aggressive pursuit of effective device therapy should continue.

Disclosures
None.

References

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