Percutaneous Mitral Valve Repair
Are They Changing the Guard?

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Treatment strategies for patients with mitral regurgitation (MR) are changing. Current guidelines suggest that patients with symptoms, atrial arrhythmias (especially atrial fibrillation), pulmonary hypertension, or left ventricular (LV) decompensation heralded by changes in LV ejection fraction should undergo mitral valve surgery. In addition, for patients in whom valvular repair is likely, the guidelines also suggest that an asymptomatic patient with severe MR and normal LV function might undergo mitral valve repair to prevent the sequelae of chronic MR. Earlier and earlier treatment and mitral valve repair are now the surgical norm. In one sense, the guard is already changing.

The concept has not proceeded without controversy. The utility of the edge-to-edge technique as a stand-alone procedure is debated in the surgical literature. There are favorable reports, but others have indicated suboptimal midterm results for the edge-to-edge technique, especially in patients with ischemic MR when performed without an annuloplasty. This surgical experience has important implications for all percutaneous technologies. Clearly, long-term follow-up in phase II trials of PMVR will be needed before any conclusions can be drawn with certainty. I would be surprised if these early PMVR technologies produce results completely equal to those provided by the more complex surgical approach, with its attendant mortality and morbidity. Thus, evaluation of the results of PMVR must be performed with attention to important questions: Is less efficacy of PMVR acceptable in return for avoidance of operation? If so, how much less efficacy than the results of surgery (the “delta”) should be accepted? Are there patients who cannot be treated surgically without high risk who might be treated with less successful PMVR? How much greater efficacy is needed, with only minimal compromise in safety (the risk:benefit of PMVR), to treat patients with mild to moderate MR so as to lessen the long-term deleterious effects of MR on LV function? The list goes on, and PMVR will be a topic for collegial debate among cardiac surgeons and interventional cardiologists for a long time.

The obvious strategy for PMVR would be to have the percutaneous tools to combine an edge-to-edge (or other direct valvular) procedure with a percutaneous annuloplasty technique. That would mimic what is done surgically and produce even more change in our options for PMVR. In theory, this might result in the kind of long-term results that we presently expect from surgery. Percutaneous approaches...
to posterior annuloplasty might be accomplished by device placement in the coronary sinus, left atrium (or both) or by device placement behind the posterolateral wall of the LV. All of these approaches are under evaluation, and surely there will be losers and winners. The concept of PMVR is to improve mitral valve coaptation by reducing the circumference of the posterior mitral annulus or by moving the posterior annulus toward the anterior leaflet. At first glance this may seem a somewhat superficial way to consider repair of MR because surgical experience has pointed out how complex the mechanism(s) of MR can be. For example, congestive cardiomyopathy produces annular dilation and LV enlargement with apical papillary muscle displacement and systolic restriction of the mitral leaflets so that the line of coaptation is lessened. In ischemic disease, fibrosis of the papillary muscles can restrict mitral leaflet systolic function, but in addition, LV remodeling resulting from infarction can cause variable displacement of the papillary muscles and tethering of the leaflets. Thus, consideration of the amount of annular dilation, leaflet pathology, and abnormalities of the mitral supporting apparatus must be taken into account when any type of repair is contemplated.

In this issue of *Circulation*, Daimon and colleagues describe a percutaneous device, placed via a catheter into the coronary sinus, that reduces MR in an ovine model of chronic ischemic MR. The report is important because it shows not only that MR can be reduced by a coronary sinus device but also that ischemic MR can be treated, at least in the ovine model. The authors point out that the amount of MR in their model was moderate and not severe, which might have made the outcome easier to achieve. Their ischemic model, however, did produce changes both in LV wall thickness and annular diameter, much as would be expected in humans with ischemic disease. Other reports of coronary sinus implants also have shown improvement in MR with models of ischemic disease and also heart failure. Will all of these devices work in humans? The answer must await further studies and longer-term outcomes in animal models as well as human clinical trials.

Certainly the concept faces multiple anatomic challenges. Despite the fact that the coronary sinus lies adjacent to the mitral annulus, anatomic variability is great. In some patients, the sinus lies below or above the posterior annular plane behind the left atrium. If it is located directly behind the annulus, then a device might constrict the posterior annulus or move it forward relative to the anterior leaflet of the mitral valve and improve leaflet coaptation. If atrial muscle alone transmits the force of the device, however, then muscle stretch may occur over time and the desired effect may be lost. There also is potential for compromise of the circumflex coronary artery as it passes beneath the coronary sinus. Lastly, the long-term effect of a foreign body device within the coronary sinus is not known, although experience with transvenous LV pacemakers placed in a similar position has not produced major problems.

Because of the potential problems of a coronary sinus device, other approaches are under investigation. Newer concepts include intra-atrial devices that mimic surgical annuloplasty devices more closely. Implants might be placed directly onto the anterior and posterior fibrous annulus via a transseptal approach; a percutaneous transmyocardial cinching device placed within the pericardium might be an alternative solution. All of these and more are under consideration and await further study. Finally, the long-term experience of surgical annuloplasty repair provides valuable lessons in applying percutaneous technology indiscriminately. Reports suggest that the mitral trigone-to-trigone area is not a rigid fixed structure and dilation after placement of an incomplete mitral ring can occur in this area. Mitral leaflet tethering caused by papillary muscle displacement may not be correctable by annuloplasty alone, and placement of a flexible, rather than a rigid, posterior annuloplasty device may result in early return of MR. All of these issues ultimately must be confronted and overcome if PMVR is to become an alternative to surgical intervention.

One obvious step that PMVR must embrace is coupling a percutaneous annular remodeling device with percutaneous edge-to-edge or other direct leaflet alteration. This may seem a complex intervention at present, but it will be part of the evolution of PMVR without doubt. New technology may address some of these concepts, although undoubtedly there will be some patients who can be treated with the production of a double-orifice valve or annuloplasty alone.

Finally, some comment must be made about the evaluation of any attempt to repair MR, either by surgery or PMVR. The actual degree of MR is dependent on a host of variables. Vascular afterload, volume status, heart rate, and myocardial inotropy all can change the amount of MR from moment to moment. LV angiography as a measure is subjective at best. More objective data gathering by echocardiography has become the standard, but it is fraught with pitfalls. Calculation of regurgitant volume and regurgitant fraction is dependent on the learning curve of the operator. Other factors may confound measurements: (1) underestimation of the velocity (optimal Doppler alignment is parallel to blood flow), (2) incorrect placement of sample volume, (3) incorrect tracing of the modal velocity of the time velocity integral, (4) too small a number of measurements, (5) incorrect measurement of annulus diameter (if the measurement is wrong, then the error is squared), and (6) presence of a shunt, other valvular regurgitation, or hypertrophic cardiomyopathy.

Objective measurements of effective regurgitant orifice and regurgitant volume also are dependent on the learning curve of the operator, correct timing of the proximal isovelocity surface area radius in systole, correct measurement of the proximal isovelocity surface area radius, and the ability to obtain the complete regurgitant jet by continuous wave Doppler. These are not academic issues because evaluation of any device designed to reduce MR will almost certainly be accomplished echocardiographically. Rigid adherence to careful measurement is perhaps assumed when we read reports of new devices for PMVR, but it needs to be stressed. Inaccurate measurement of MR might lead to the conclusion that a device is either more or less effective than it really is. That will only serve to delay proper trials and understanding of the usefulness of PMVR devices.

Some PMVR devices are already being evaluated in phase II trials, and the hope is that these trials will succeed so that
we can offer alternative therapeutic options to patients. A number of new devices are under active development that will add to our percutaneous transcatheter armamentarium. I also believe that it is important that the guard not change too fast. The mitral valve leaflets, their supporting structures, and the LV interact in a symphony of movement when things are right and can be complexly altered by disease. A "one-size-fits-all" approach has not worked surgically and will not work for PMVR. Surgeons and cardiologists must pool expertise and experience to make PMVR a competitive, safe alternative for patients with MR, and patient selection must be a collaborative process. Nevertheless, A.A. Milne was right—the guard is surely changing.

Disclosure
Dr Block served as an investigator in the EVEREST I trial and is a stockholder in Evalve, Inc.

References

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