Editorial

Percutaneous mitral valve repair: an attractive perspective and an opportunity for teamwork

Ottavio Alfieri, Francesco Maisano, Antonio Colombo*, Carlo Pappone**, Giovanni La Canna§, Alberto Zangrillo§§

*Cardiac Surgery, *Interventional Cardiology, **Electrophysiology, §Non-Invasive Diagnostic Cardiology, §§Anesthesiology, San Raffaele Institute University Hospital, Milan, Italy*

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Address:

Prof. Ottavio Alfieri

Divisione di Cardiochirurgia IRCCS H San Raffaele Via Olgettina, 60 20132 Milano E-mail: ottavio.alfieri@hsr.it

Mitral valve repair is one of the most gratifying surgical operations. A wide spectrum of techniques may be used with versatility by surgeons to correct a large variety of lesions responsible for mitral regurgitation (MR). The operative risk is very low and the long-term results (up to 30 years) are excellent, the postoperative survival being similar to that of the general population matched for age and sex. Furthermore, when surgery is carried out before the occurrence of left ventricular dysfunction, the quality of life is superimposable to that of healthy individuals, with no restriction in activity and no anticoagulation[1,2].

Surgical repair of the mitral valve is feasible either through midline sternotomy or using a minimally invasive approach with or without robotic technology[3].

Percutaneous mitral valve repair is now emerging as an alternative modality for the treatment of MR. The percutaneous method constitutes an attractive therapeutic evolution, since it may provide restoration of normal mitral valve function without surgical incisions and extracorporeal circulation, in a closed and beating heart.

In contrast to the minimally invasive approach, therefore, the percutaneous technique is expected to offer not only a cosmetic advantage, but also a real and substantial reduction in the overall trauma, leading to immediate recovery after the procedure and to ultra-fast hospitalization.

An overview of the current technology for transcatheter mitral valve repair will be herein provided. In addition, the expectations for the future and the drivers for change in the modality of treatment of MR will be discussed. Finally, an opinion on the possible actors in this new field of cardiovascular medicine will be given.

Techniques and technologies

Two techniques of mitral valve reconstruction have been transferred from surgery to the percutaneous approach: edge-to-edge repair and annuloplasty.

The edge-to-edge repair, introduced by us in the surgical arena several years ago, has been effective in correcting organic as well as functional MR, particularly when combined with annuloplasty[4,5]. When the edge-to-edge repair and the annuloplasty are applied in association, therefore, a perfect mitral valve function may be restored in the great majority of patients presenting with MR. The edge-to-edge technique may be performed percutaneously using either a clip device[6] or a catheter-based suction-and-suture system, derived from a surgical instrument for beating-heart mitral leaflet approximation[7].

The clip device consists of a surgical alloy and covered by a biocompatible polyester. Under echocardiographic guidance, the clip is delivered to the heart through the femoral vein, fed through the atrial septum via a transseptal puncture, and then positioned in the left ventricle just below the mitral valve. The physician opens the prongs of the clip and, at end systole, closes them, grasping the free edge of the leaflets at the site of regurgitation. A competent double orifice mitral valve is thus

created. The current delivery catheter size is 22F. The system is illustrated in figure 1.

The suction-and-suture device, developed a few years ago, is currently being refined further. The leaflets are attracted by suction utilizing vacuum aspiration and subsequently approximated with sutures delivered and fastened with a 16F catheter. The distal end of the catheter, with the suction ports and the apparatus to punch the suture through the leaflets is shown in figure 2.

Percutaneous annuloplasty is feasible introducing a variety of *ad hoc* devices into the coronary sinus. Several companies are developing transcatheter mitral valve repair products with different designs. Taking advantage of the close anatomical relationship between the posterior mitral annulus and the coronary sinus, the dimensions of the posterior mitral annulus are reduced by these devices, and consequently the area of the mitral orifice is decreased.

In figure 3, one of these devices, made of nitinol and fixed with stents placed into the coronary sinus, is illustrated.

More recently, a transventricular percutaneous approach has been developed, based on the placement of several anchors around the mitral annulus to reduce the diameter of the orifice. The current methods of percutaneous mitral valve repair and the companies which have been developing the related technology are listed in table I.

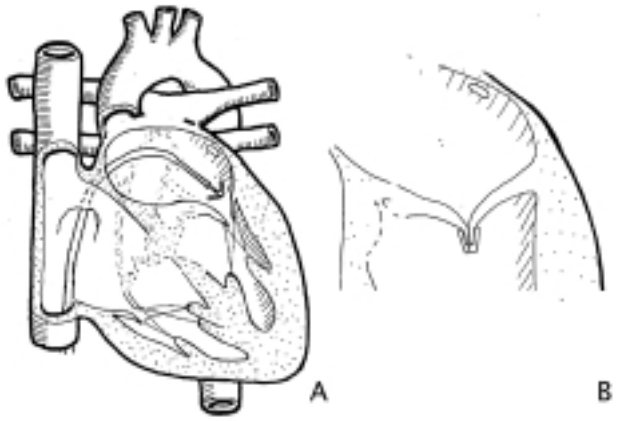

Figure 1. A: *the E-valve clip device is inserted into the left atrium through a transseptal approach, and is positioned face to face with the mitral valve. The catheter is steerable to facilitate positioning. The prongs of the clip are open, and ready to grasp the leaflets.* B: *the clip has been detached from the delivery catheter and is in place, grasping both leaflets on the ventricular surface and creating a double orifice mitral valve.*

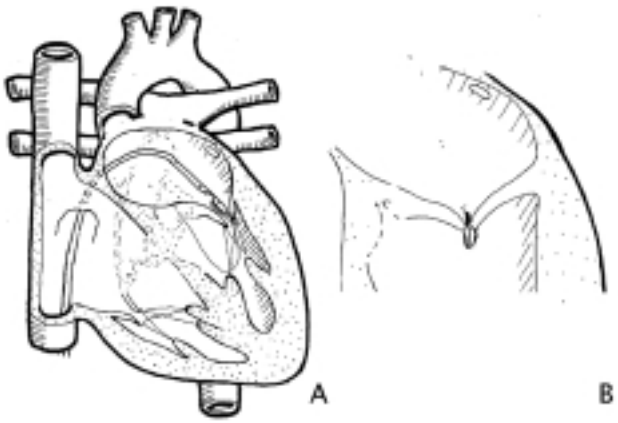

Figure 2. A: *the suction-and-suture over-the-wire device is inserted into the left atrium through a transseptal approach, and is positioned face to face with the mitral valve. One leaflet has been previously sutured. Once the second leaflet will be sutured, the catheter will be withdrawn, and the suture pulled and exteriorized.* B: *by means of a fastening catheter, a small nitinol clip is used to fasten the suture on the leaflets and complete the procedure.*

Clinical experience

Although animal experiments have been carried out extensively and mostly with promising results, clinical experience is extremely limited. All the percutaneous

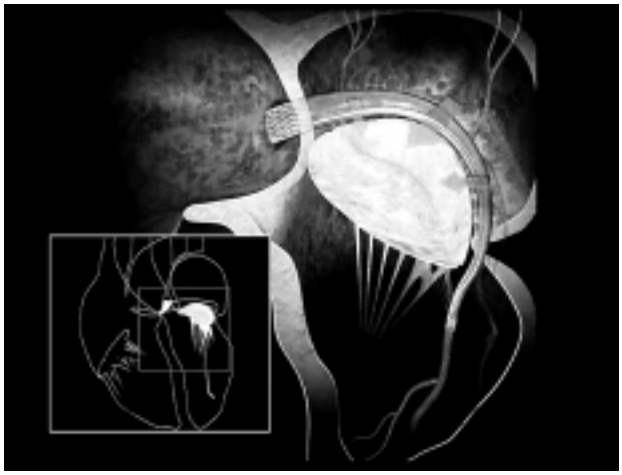

Figure 3. *The annuloplasty device has been inserted into the coronary sinus. The distal and the proximal ends are equipped with a self-expandable stent, to stabilize the device. Once the device is in place, the wire connecting the two stents will shorten within a few weeks because of progressive loss of absorbable material. The shortening of the device will induce a progressive reduction in the size of the coronary sinus, and push the posterior leaflet toward the anterior, thus reshaping the annulus and improving coaptation.*

Table I. Companies involved in the field.

Technique	Company
Edge-to-edge	Edwards Lifesciences E-valve
Coronary sinus annuloplasty	Edwards (Iomed) Cardiac Dimensions Mitralife (ev3) Viacor QuantumCor
Transventricular annuloplasty	Mitralign

mitral valve repair development programs are essentially still in their preclinical phase, with the exception of the E-valve clip device which has been already utilized in humans to create a double orifice mitral valve. Up to September 2004, 17 patients had been enrolled in a feasibility and safety study called EVEREST I (Endovascular Valve Edge-to-edge REpair STudy): 12 patients have been treated by centrally applying one clip and 3 patients by applying two clips to correct MR according to the edge-to-edge concept (Ted Feldman, personal communication). The eligible patients for the EVEREST I trial are those with moderate to severe or severe MR who could well be candidates for mitral valve surgery. The regurgitant jet should originate from the central part of the mitral valve. Excluded are those patients with an ejection fraction < 30%, with a left ventricular end-systolic diameter > 55 mm, with renal insufficiency, endocarditis and rheumatic heart disease. The primary endpoint of the study is freedom from adverse events (death, myocardial infarction, cardiac tamponade, cardiac surgery for failed clip, clip detachment, permanent stroke and septicemia) at 30 days. The secondary endpoint is the efficacy of the procedure in decreasing the severity of MR, as assessed by echocardiography at 30 days and 6 months. The patients enrolled in the trial had MR due to prolapse of one or two leaflets or functional MR. The *interim* EVEREST I results have been presented at the American College of Cardiology meeting in mid-March 2004 by Ted Feldman. The only reported adverse event was clip detachment from one leaflet in a patient who subsequently underwent uneventful mitral repair surgery. An improvement in MR was acutely achieved in 90% of the patients, and these results appear to be sustained over time. The mean duration of the procedure was 3.2 hours (ranging from 1.5 to 6.2 hours and being significantly shorter after the learning phase), and the mean hospital stay was 1.8 days (range 1 to 3 days).

In summary, therefore, a double orifice mitral valve may be safely constructed using a percutaneous approach. The procedure is effective in consistently reducing MR in the great majority of patients. The duration of the procedure in the last cases was < 2 hours.

Expectations for the future

Although these procedures are quite promising, we are unlikely to see a significant reduction in surgical volumes anytime this decade, mainly because it will be presumably difficult for the evolving percutaneous techniques to match surgical results and to gain acceptance. Furthermore, several factors will probably drive a more gradual development and adoption rather than rapid uptake.

First of all, the present technology is still in the evolving phase and therefore suboptimal. The production of easily and effectively usable catheter-based systems is expected to require considerable investments and efforts and therefore to be rather slow. Secondly, due to the complexity of the procedures, experience would be concentrated in a few centers, and training of a large number of physicians will remain a major issue. In addition, the regulatory path to approval and commercialization is expected to be long, since randomized clinical trials with a reasonably extended follow-up are likely to be required. Finally, the process leading to reimbursement tends to take years, and lack of profitability for physicians and hospitals will probably delay widespread adoption.

On the other hand, other considerations could favor a different evolution for the present-day scenario. In contrast with percutaneous aortic valve replacement, which, at least initially, will be limited to non-surgical or high-risk candidates, percutaneous mitral valve repair could be targeting current surgical candidates, and patient preference for transcatheter approach could be relatively high. Rapid advancements in mitral valve repair products in combination with improvements in imaging modalities could accelerate the adoption of the percutaneous techniques. A much less invasive procedure, as provided by catheter-based methods, might produce a radical change in indications and lead to correction of MR in a very early stage of the disease. Finally, reduction rather than abolishment of MR can be considered an acceptable therapeutic goal in many patients, and this attitude will favor the percutaneous approach to mitral repair.

The actors in the field

The complexity of percutaneous mitral valve repair is such that new knowledge and specific expertise have to be acquired by those physicians who will be involved in catheter-based heart valve procedures. Certainly, specific training for the creation of specialists prepared to run clinical percutaneous valve repair/replacement programs should be envisioned.

From the initial experience, it seems to be clear that these emerging areas of cardiovascular medicine will require "teamwork", with close cooperation of different specialists (cardiac surgeon, interventional cardiologist, echocardiographist and anesthesiologist). The essential role of the interventional cardiologist with specific expertise in transseptal puncture and catheter manipulation within the heart under fluoroscopic- and other imaging modality-guidance is out of question. On the other hand, a full involvement of cardiac surgeons in developing and practicing the percutaneous approach is highly desirable, since the complex morphology of the mitral valve and the great variety of lesions responsible for MR are well known to them. In addition, the rate of complications requiring immediate surgical intervention (for cardiac tamponade or valve-related problems) is expected not to be negligible. Im-

portantly, only a cooperative program between cardiac surgeons and cardiologists is able to offer the truly best solution for the individual patient, taking into due account the specific anatomic lesion, the mechanism of MR and the clinical profile.

Other actors are also relevant for the success of percutaneous valve treatment programs. The crucial role of the echocardiographist in guiding the procedure, assessing the outcome and identifying complications is quite obvious. The cooperation of the anesthesiologist throughout the procedure is also essential to provide stability of the circulation and to control all the vital functions.

The companies which are involved in the pioneering phase of percutaneous valve repair/replacement technology should be aware that successful clinical programs will depend on optimal cooperation among different specialists.

An extraordinary opportunity for teamwork is foreseeable.

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