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SCIENTIFIC EDITORIAL

Treatment of mitral regurgitation: From sternotomy to percutaneous approach — A paradigm shift?

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Mitral valve repair (MVR) remains the gold standard [1] treatment for mitral valve regurgitation, with excellent results for dystrophic disease. Nevertheless, the most recent adaptations concern the treatment of ischaemic or functional mitral regurgitation and the development of less invasive approaches. The availability of video-assisted surgeries or percutaneous approaches is therefore the subject of growing interest [2].

Less invasive resection

One of the most frequently used procedures for MVR has been the more or less extended tissue resection (in particular, P2 quadrangular resection). Today, the trend is to resect less tissue, perform triangular resection, repair without any resection [3], or use Goretex neochordae [4]. One original yet unorthodox technique — the Alfieri stitch creating a double orifice mitral valve — gave surprising and long-lasting results [5]. This technique even had specific value in functional mitral regurgitation, where the recurrence of regurgitation was less frequent when an Alfieri stitch was added compared with single annuloplasty [6].

Less invasive surgical approach

All surgical specialities have developed minimally invasive techniques using videoscopy (e.g. cholecystectomy, menisectomy, surgery for pneumothorax, thoracic sympathectomy). In cardiac surgery, one meta-analysis reported results from more than 14,000 patients [7]. The conclusion was that minimally invasive surgery may be an alternative to conventional mitral valve surgery, with similar rates of mortality and morbidity (renal, pulmonary, cardiac complications, pain perception, and readmissions), reduced sternal complications, transfusions, postoperative atrial fibrillation, duration of ventilation, and intensive care unit and hospital length of stay. However, this should be balanced against the increased risk of stroke, aortic dissection, phrenic nerve palsy and groin infections or complications. These complications (mainly in the endoclamp group) could be avoided.

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As a consequence, the minimally invasive approach with a transthoracic aortic clamp can maintain the benefit with a lower risk of complications. This surgery has become routine in reference centres; moreover, it is a stepping-stone to future beating heart valve repairs. Beating heart valve surgery merges the advantages of open heart surgery with the transesophageal echocardiogram (TEE)-guided approach used during endovascular procedures: image guidance allows monitoring during the procedures to guide the intervention according to the dysfunction rather than to the anatomical lesion, taking advantage of the physiological conditions; this is in contrast to the conventional surgical approach, which is performed under cardioplegic arrest. A good example of the advantage of beating heart approach is neochordal implant:

- transapical implantation of neochordae has been described with different technologies (left mini-thoracotomy): NeoChord Inc. (Minnetonka, USA) is developing a transapical device that allows the correction of a prolapsed leaflet. Animal studies and even a 'first in man' trial have been published [8], with encouraging results;
- trans left atrial approach (right mini-thoracotomy): Valtech Cardio (Or Yehuda, Israel) is developing an adjustable length neochordae device, which is implanted with a sutureless approach into the tip of the papillary muscle and then attached to the free edge of the leaflet. Afterwards, the length is adjusted under TEE on a beating heart.

Less invasive percutaneous approach

To be effective percutaneous techniques have to respect the rules of surgical repair. The success of percutaneous mitral commissurotomy was mainly due to the fact that balloon inflation faithfully reproduced the original surgical commissurotomy. Mitral valve repair is much more complex and therefore not so easy to reproduce. Percutaneous mitral valve repair includes three main technological categories: coronary sinus indirect annuloplasty, direct annuloplasty and direct leaflets correction.

Coronary sinus indirect annuloplasty

Coronary sinus indirect annuloplasty consists of inserting a device into the coronary sinus to modify the mitral annulus. Although it is intrinsically easy to perform, this approach has several limitations. The annuloplasty is only partial, with a risk of compressing the circumflex artery in up to 6% of cases and a risk of tamponade in 3–6%. To date, three devices have been tested in humans:

- MONARCTM device (Edwards Lifesciences Inc.): 72 patients treated [9];
- CARILLONTM Mitral Contour System (Cardiac Dimensions Inc.): 48 patients treated [10];
- Viacor PTMA© (PTMA Viacor Inc.): 27 patients treated [11].

Thirty-day death rates are low, between 0% and 2%, but efficacy has been evaluated in only small non-randomized series using surrogate endpoints. Within the first year, the effective regurgitant orifice area decreased by approximately 30% and the regurgitant volume by 20–25%. The response was heterogeneous and certain patients experienced more marked reduction of mitral regurgitation. The future of coronary sinus annuloplasty is compromised, although efficacy has been demonstrated in selected patients.

Direct annuloplasty

Direct annuloplasty more closely resembles surgical annuloplasty. These technologies are at an early phase of development. The Mitralign Percutaneous Annuloplasty System (Mitralign, Tewksbury, MA, USA) is a device used to perform selective plications of the annulus with a retrograde approach (from the left ventricle) via a transfemoral arterial access site. A couple of plications are obtained to reduce annular dimensions, by means of pledgetted anchors penetrating the base of the leaflets. Guided Delivery Systems (Santa Clara, CA, USA) is developing a cinching device (Accucinch) consisting of multiple anchors implanted subannularly below the leaflets, from commissure to commissure, and joined by a contracting wire. A flexible ring 'Cardioband' introduced through a right mini-thoracotomy and through the left atrium can be screwed into the mitral annulus under TEE. Preclinical development has been completed and early human experience is ongoing.

Direct leaflets correction

Present techniques are far from meeting the complexity and variability of diverse anatomical situations of mitral valve disease and the corresponding spectrum of surgical techniques of valve repair. The only current solid project (MitraClip Inc., Abbott Vascular; CE mark in 2008) reproduces the 'Alfieri stitch' by fixing the two leaflets with a clip introduced through a venous transfemoral and transseptal approach. However, this percutaneous approach does not exactly reproduce Alfieri's rules, since Alfieri himself highlighted the necessity to add an annuloplasty to obtain durable results.

The Endovascular Valve Edge-to-Edge Repair Study (EVEREST II) [12] randomized 279 patients with severe mitral regurgitation in 37 centres to MitraClip ($n = 184$) or surgical valve repair or replacement ($n = 95$). Mitral regurgitation was of organic origin in 73% of the cases. At 12 months, the rates of the primary outcome for efficacy were 55% in the percutaneous-repair group and 73% in the surgery group ($p = 0.007$). The respective rates of the components of the primary outcome were as follows: death, 6% in each group; surgery for mitral valve dysfunction, 20% vs 2%, respectively. Major adverse events (mainly blood transfusions) occurred in 15% of patients in the percutaneous-repair group and in 48% of patients in the surgery group at 30 days ($p < 0.001$). At 12 months, both groups had improved left ventricular size, New York Heart Association (NYHA) functional class, and quality-of-life measures, compared with baseline. In summary, percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, but the procedure was associated with superior safety (mainly fewer blood transfusions) and similar improvements in clinical outcomes at 1 year.

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In a study related to EVEREST II (High-Risk Registry) in individuals ineligible for randomization, 78 patients were treated with a Mitraclip, and their results were compared with those of a control group of 38 patients treated with optimal medical medication. This observational study showed a higher survival rate in the Mitraclip group (76% vs 55% at 1 year).

Today, ACCESS-EU – a European multicentre, post-approval registry – reported on 566 patients with mean age of 74 ± 10 years, procedure time of 117 minutes, and length of hospital stay of 7.7 days. The rate of hospital death was 2% and 6-month survival 89%, with no embolizations; the rate of mitral regurgitation was less than 2 at 6 months was 80%, and patients showed improved NYHA functional class, quality of life and 6-minute walk distance [13].

In the MitraClip experience (> 5000 patients implanted worldwide, particularly in northern Europe and Italy), procedural success rates are high and severe procedure-related complications rare. Feasibility does not, however, imply efficacy, and it is too early to ascertain the clinical utility of these techniques. The effect on NYHA class is a relevant outcome but its assessment may be subjective.

Given the low operative risk and the excellent immediate- and long-term results of valve repair for valve prolapse, it is unlikely that the MitraClip will replace surgery in the near future. Nevertheless, percutaneous techniques could be an option in patients with degenerative mitral regurgitation who are at high surgical risk because of advanced age and presence of comorbid conditions [14]. With regard to functional or ischaemic mitral regurgitation, the situation is more difficult, since, unlike in organic mitral regurgitation, surgery is not a reference treatment [15]. Consequently, in Europe today, functional mitral regurgitation comprises close to 80% of the indications, highlighting the need for specific randomized trials assessing the clinical benefit of the MitraClip in functional or ischaemic mitral regurgitation.

In conclusion, less invasive procedures are progressing in every medical domain, with new techniques that are in-between traditional surgery and percutaneous approaches. Minimally invasive mitral valve surgery is now validated, with improved results, provided it is performed in an experienced centre. Moreover, this procedure is a first step for future less invasive techniques such as transapical approaches.

In contrast to surgical mitral valve repair, which is a mature procedure, percutaneous procedure results (mainly with the MitraClip) should improve over time. Although some procedures (e.g. neochordae implantation, adjustable annuloplasty band) are in their infancy, it is likely that percutaneous treatments will play a part in the treatment of mitral regurgitation. Beyond early feasibility studies, randomized trials are now mandatory in order to confirm these promising results.

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