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Percutaneous Treatment of Mitral Valve Regurgitation: An Evolving Field

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In the past two decades great interest has developed for less-invasive, percutaneous mitral valve (MV) repair strategies [1]. This is mainly due to the increasing number of elderly patients with comorbidities and/or patients with left ventricular (LV) dysfunction, that are associated with a high surgical risk [2].

Whereas surgery still remains the gold-standard treatment for primary/degenerative mitral regurgitation (MR) [3,4], the optimal treatment for secondary mitral regurgitation remains controversial [5,6]. This leaves an important window for transcatheter treatments.

Transcatheter mitral valve repair is, in fact, one of the greatest evolving fields in valvular heart interventions, with a continuous growing number of devices [7,8]. As previously underlined, the mitral valve apparatus is a complex anatomical and functional structure. Therefore, different devices have been developed capable of targeting the various components of the mitral valve: MV annulus, MV leaflets, and the subvalvular apparatus. This tries to mimic surgical mitral valve repair, either as single or combined procedures. The availability of such a wide-spectrum of devices allows to achieve a tailored approach for treating each patient: the right device according to the specific lesion [9].

Device Innovations

Leaflet repair

Percutaneous edge-to-edge repair remains the most common percutaneous treatment used to address MR (>100,000 patients), and it is the only guideline-recommended transcatheter procedure in selected patients [10-12]. In the past couple of years extensive debate has risen regarding the role of MitraClip treatment in secondary mitral regurgitation and heart failure, in patients that remained symptomatic despite optimal medical therapy [13] (Figure 1A). Following what initially appeared like contradictory results of two important randomized clinical trials, MITRA-FR [14] and COAPT [15], it became even more obvious that the percutaneous edge-to-edge technology is beneficial in a specific subset of patients, namely those with disproportionately severe MR with respect to LV size and function [16], even though specific echocardiographic parameters have not been identified as independent prognostic values [17,18].

However, the use of the MitraClip device is not only limited by clinical features, but also by anatomical criteria, known as EVEREST Criteria. Recently, newer generations of MitraClip devices have been created, with wider arms, improved grasping and continuous left atrial pressure monitoring. Such innovations allow treatment of a wider range of challenging anatomies. Newer devices have also recently received CE mark approval (2019), such as the PASCAL system [19] (Figure 1B), which was designed in order to overcome some limitations of the MitraClip device, trying to expand patient eligibility for the edge-to-edge percutaneous repair [20]. The device features larger paddles with a central spacer to maximize leaflet coaptation and the clasps allow for independent leaflet capture, together with smooth maneuvering of the whole system. Additional data on durability and the interplay with the MitraClip device need to be further investigated [21].

Another option in patients affected by leaflet prolapse is artificial chordal implantation, which can be performed transapically, off-pump, on a beating heart [22,23] (Figure 1C). Various devices have been created and prospective clinical trials are ongoing. Results show these procedures are safe, with minimal morbidity and mortality, an

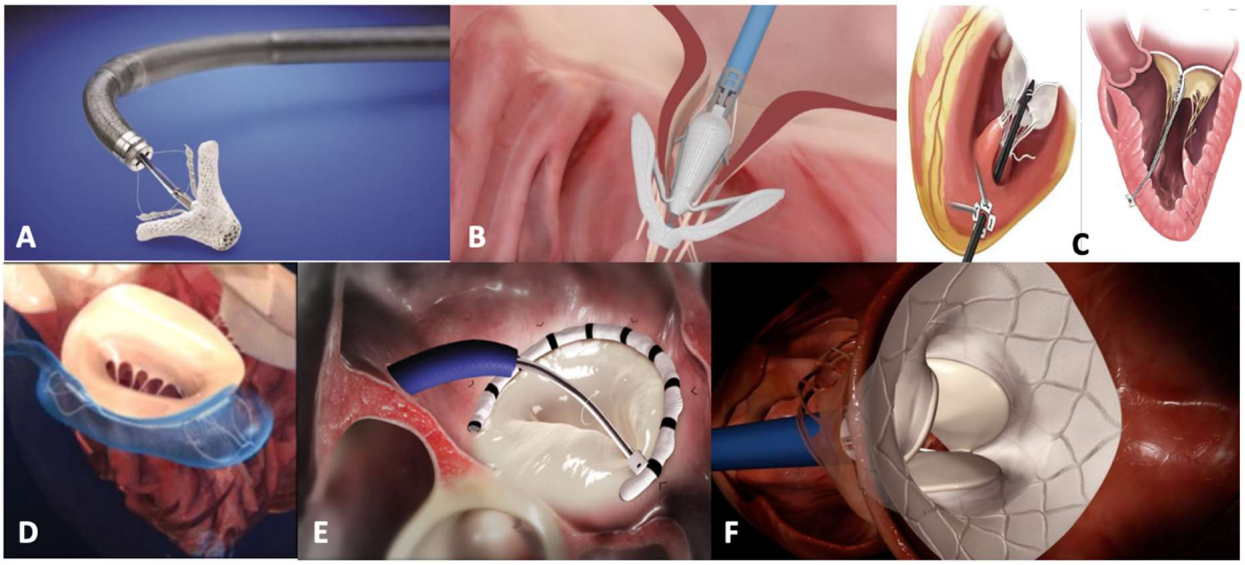

Figure 1: Transcatheter mitral valve repair and replacement devices. **(A)** MitraClip system; **(B)** PASCAL device; **(C)** Artificial chordal implantation; **(D)** Indirect annuloplasty system; **(E)** Direct annuloplasty device; **(F)** Transcatheter mitral valve replacement.

important reduction in MR and left ventricular reverse remodelling is obtained [24,25]. However, patient selection, once more, seems the critical issue: such devices provide focal support where the loop is implanted, resulting in un-even coaptation along the prolapsing segment. Therefore, the optimal candidate for this type of approach is a patient with posterior leaflet prolapse, without marked MV annulus dilation [24].

Annuloplasty devices

Up to one third of patients screened for a percutaneous leaflet repair technique are excluded due to unfavourable anatomy, including marked annular dilation. These devices further expand the transcatheter toolbox for MV treatment and are expected to improve overall results, either as single or combined procedures. They can be divided within two large categories: direct and indirect annuloplasty systems (Figure 1D and 1E). The former more closely reproduce surgical annuloplasty techniques, with more promising reported results [26]. The latter instead take advantage of the favourable position of the coronary sinus with respect to the MV annulus [27]. Such devices have been on the market for quite a long time, and despite the reproducible and not technically demanding delivery of the majority of them, effectiveness and applicability of such devices remains limited [28]. However, interestingly enough, pivotal and randomized trials are being recently performed to assess outcomes of patients with secondary MR undergoing percutaneous annuloplasty procedures (REDUCE FMR Trial and ACTIVE Trial). Among many, the Cardioband device has been associated to leaflet repair or chordal replacement procedures to maximise MR reduction [29]. The potential future of such combined treatments still needs to be extensively studied.

Mitral valve replacement

Among the available percutaneous mitral valve treatment devices, MV replacement remains the least evolved. Both anatomical aspect and technical challenges strongly limit the wide-spread diffusion of such technologies. Proper anchoring and sealing of the prostheses to obtain stability remain important issues, together with the limited space the mitral valve and the left ventricular outflow tract with the high risk of protrusion and obstruction [30]. Furthermore, the great majority of devices require a transapical access, and only very few are designed for a transvenous trans-septal delivery [31] (Figure 1F).

Future Perspectives

Treatment of MV regurgitation has generated great interest in the past decades, with an extremely broad range of treatment options. With this constantly growing toolbox, going from surgical interventions to percutaneous repair/replacement procedures or solely medical therapy, it is of utmost importance that patients affected by mitral regurgitation are evaluated and treated in dedicated heart-valve centres. The right choice of treatment for each individual patient is crucial, and is based on etiology, valve anatomy, valvular lesion, general conditions of the patient and patient's will. All these aspects need to be evaluated by the Heart Team in order to offer the best possible

treatment to every individual, gaining a patient-tailored approach [32]. Therefore, "which treatment option to which patient".

In the future, percutaneous procedures will aim at combining various repair techniques in order to more strongly reproduce surgical techniques and try and obtain more effective and durable results. Regarding transcatheter MV replacement, technology will evolve and the number of transvenous trans-septal delivery systems will hopefully increase, further expanding treatment options.

Several trials regarding transcatheter devices for MV repair/replacement are still ongoing and will possibly shed some light on the best therapeutic option for each clinical scenario.

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