Editorial

The PASCAL transcatheter mitral valve repair system for the treatment of mitral regurgitation: another piece to the puzzle of edge-to-edge technique

Carmelo Grasso, Antonio Popolo Rubbio

Cardiac-Thoracic-Vascular Department, Ferrarotto Hospital, University of Catania, Catania, Italy

Correspondence to: Carmelo Grasso, MD. Via Palazzotto, 8-95128 Catania, Italy. Email: melfat75@gmail.com.

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Moderate-to-severe mitral regurgitation, aside its etiology, represents a really common valvular heart disease that is associated with a significant increase in overall morbidity and mortality if left untreated (1).

Nowadays, the possibilities of intervention on mitral valve are extremely varied and, besides medical therapy and the classic surgical valve replacement or repair approaches, in the last ten years less invasive therapies have been established for the treatment of recipients who cannot be subjected to conventional surgical therapy because of substantial high-risk (2). Considering the increased lifespan of patients with chronic valvular disease, it is not surprising the heavily interest and long-term investment in the development of different percutaneous devices for the treatment of mitral valve regurgitation, which expanded the actual therapeutic offer.

The different technologies designed for the transcatheter mitral valve repair (TMVR) challenge the inherent anatomical complexity of this valve as the mechanism, heterogeneity or location of regurgitation (3). All current techniques available or under development reflect the need to target the various components of the mitral valve, thus permitting a tailored treatment able to mimic the traditional surgical intervention (leaflet repair, annuloplasty, chordal replacement) as single or combined approach (4). In light of this, it is clear to understand that the decision making process is rather complex and must take into account both the choice of the most suitable therapeutic strategy and the more appropriate timing of intervention.

Among these techniques, the edge-to-edge technique is a well-established surgical technique for mitral valve repair, which consists in restoring valvular competence anchoring the free edge of the middle scallop of the anterior leaflet to the corresponding free edge of the posterior one, with the creation of a double-orifice valve (5). Since his origin in 1991, although it has been employed mainly for the correction of mitral valve prolapse, this technique has been suitably extended to correction of functional mitral regurgitation. In this regard, following the successfully experience of this technique, the TMVR with the MitraClip system (Abbott, Abbott Park, IL, USA) saw recently its birth.

The MitraClip system represents the most widely used technology to address edge-to-edge TMVR of degenerative or functional mitral regurgitation, in patients with increased risk for surgery. To date, over 50,000 patients have been treated worldwide. Its safety, efficacy and results on quality of life have been partly verified by real-world observational, single-arm prospective registries (6-8) and one randomized trial (9), with encouraging results in term of device success, reduction of NYHA class and re-hospitalization rate and improvement in functional capacity. Further information will be derived from the results of currently ongoing trials with the objective of comparing the MitraClip with medical therapy alone.

This device presents some inherent issues, which may

contraindicate this approach in some challenging anatomical cases, confirming that the clinical and echocardiographic selection of the patients candidate for this intervention represents a crucial moment (10). A technical improvement of the device with the arrival of the new MitraClip NT (Abbott Vascular) allowed better responsive and consistent steering of the system in left atrium, more efficient leaflet capture with consequent improved grasping and deeper leaflet insertion and an easier clip retraction in case of non-satisfactory result.

The invention of a new device for edge-to-edge TMVR, which can overstep the anatomical limitations of the MitraClip procedure and optimize the results of this mini-invasive technique, represents an important contribution for the interventional cardiology, but like any novelty in this field it deserves both interest and caution.

In this issue of *The Lancet* (11), Fabien Praz *et al.* describe their multi-center, prospective, observational experience in using the novel PASCAL TMVR system (Edwards Lifesciences, Irvine, CA, USA). This is the first-in-man study applying the PASCAL system for the treatment of degenerative, functional or mixed mitral regurgitation, for which the authors merit congratulations. In their series (n=23), the authors assert the feasibility of this intervention, with respect to procedural, discharge and 30-day outcome, in accordance to the endpoints defined by the Mitral Valve Academy Research Consortium. In the study, intraprocedural deaths did not occur, although one patient with technical failure died during the hospital stay. The technical success was substantially high (n=22; 96%), confirmed by device success at 30-day (n=18; 78%) and reduction in NYHA functional class ≤II grade in 95% of the cases.

There are several learning points from this first experience in the use of the PASCAL system for mitral regurgitation reduction. First, the implantation of at least one device was successful in all patients. Moreover, according to authors, the PASCAL system overcomes some pitfalls of the MitraClip system by simplifying navigation in the left atrium and achieving reduction of mitral regurgitation with larger size of the implant, wide paddles and optional independent leaflet grasping in challenging anatomies, with no determinant impact on post-procedural mitral valve gradient. High quality transesophageal echocardiographic imaging is of critical importance for the right deployment of the implant.

As every first experience, we should consider some limitations in this work. The patient population presents a high risk according to STS score, with consequent relatively high rate of mortality within 30-day follow-up (3 patients; 13%), namely conditioning the future "long-term" outcome. In this case, studies involving larger population with lower surgical risk will better enlighten this aspect, as well as longer follow-up of this recipient. However, it is important to underline that the risk for patients candidate to MitraClip procedure in registries such as GRASP, ACCESS-EU, TRAMI (6-8) it's not so different as the one presented for this first experience with the PASCAL system, although it's recognized that several clinical factors may have an impact on mortality outcome despite the prediction of current score like STS, which revealed limited adaptability in patients treated with percutaneous therapies (12).

Another point, which merit discussion, is the consideration that patients who did not fulfill the EVEREST anatomical criteria are less likely to have device success after MitraClip. As it's well known, the EVEREST trial is the pivotal study that assessed the results of MitraClip therapy compared with surgical repair, especially in patients with degenerative disease (9). This study has the credit of having defined the principal anatomical inclusion and exclusion criteria for the MitraClip procedure, but from the real-word experience it has been reported that a considerable proportion of patients with mitral regurgitation does not correspond to the strict EVEREST criteria for eligibility.

Previously, Attizzani *et al.* (10) demonstrated high rates of device success and favorable outcome after MitraClip regardless of the exclusion EVEREST criteria, as larger left ventricle dimension, severe impaired left ventricle function e valve geometry characteristics concerning coaptation depth or length and flail gap. This analysis showed that significant improvement in mitral regurgitation after MitraClip remained sustained at 30-day and 1-year follow-up, both in patients who strictly followed the EVEREST criteria and in patients who underwent the procedure beyond the EVEREST criteria. In particular, with respect for patients with complex anatomy, specific advanced techniques and special maneuvers can be used for grasping. On the other hand, an additional study recently published (13) showed lower durability of edge-to-edge TMVR with the MitraClip up to 3.5 years of follow-up in patients who do not fulfill the EVEREST criteria, with higher tendency of re-intervention with the same technique. In conclusion we can admit that complex mitral valve anatomy remains still a concern in this field, although good results

may be also influenced by both proper selections of the patient and volume of patients treated per center (14). In this regard, in an adaptation of the classification proposed by Boekstegers *et al.*, we can consider optimal anatomy for "start-up centers", limited suitability (i.e., valve area >3 cm^2, coaptation depth >11 mm, Carpentier IIIB) for "intermediate centers" and inappropriate anatomy (i.e., leaflet perforation or cleft, length of posterior leaflet <7 mm, Barlow's disease) only for "high-volume centers". This classification is hereby reported to show that the experience of operators in managing devices as the MitraClip in difficult anatomies is essential.

Based on these observations widely presented in the current literature, Praz and collaborators, in their appendix, provided the specific challenging anatomies of their cohort (mainly including short posterior leaflet, large malcoaptation area, severe annular dilatation >61 mm) for which other transcatheter therapies were judged inappropriate and for which compassionate use of PASCAL system was employed. The study showed that, thanks to his design, this device facilitates the capture of the mitral tissue especially in case of short posterior leaflets or in case of flail or prolapse gaps larger than 10 mm. This result is very attractive, especially in the prospective to reduce the difficulty for the operators in these difficult anatomies. Anyhow, like above mentioned, it will be interesting to understand if the device will maintain good results over the time, in term of durability of regurgitation reduction in complex mitral valve pathologies rather than the MitraClip or other percutaneous treatments already in the market. Remarkably, a specific challenge will be the result of PASCAL system in mitral valve with severe annular dilatation, for which MitraClip alone without annuloplasty did not showed satisfactory long-term results (15) and for which a combined therapy with multiple devices could be warranted (16). Addressing the theme of failure after TMVR, another point to determine will be the possibility to perform a repeat PASCAL procedure with respect to the mitral valve gradient in case of mitral regurgitation recurrence (17).

Even though we are aware that this is just the first step toward a deeper understanding of this new device, clinical evidences that answer to all these questions will define if the PASCAL system is going to live up to the expectations and if this procedure is going to have a complementary role to other edge-to-edge techniques or a competitive one.

Of course, results of Praz and collaborators need to be confirmed by larger studies with longer follow-up and in presence of a comparator arm. What is certain is that the new development of devices targeted for TMVR is the right path to follow, with the intention of expanding the population suitable for such kind of interventions. In this scenario, the PASCAL system is supposed to have the right credential to find its space in the complex and evolving puzzle of the edge-to-edge technique.

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Footnote

Conflicts of Interest: Dr. Carmelo Grasso is a proctor physician for Abbott S.r.l.

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