

Percutaneous mitral valve prostheses: 2019 update

Barbara Bellini and Antonio Colombo*

Sezione di Cardiologia Interventistica, Istituto Scientifico San Raffaele, Milano, Italy

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During the last few years, there has been significant advances in the treatment of patients with severe mitral incompetence either too high risk for surgery or inoperable, this because of the improvements in percutaneous mitral valve prostheses, as alternative to the transcatheter mitral repair techniques. Percutaneous mitral valve replacement offers several advantages over the repair techniques, such as the opportunity to treat mitral valve with different anatomic characteristics, even the more complex ones, and the occasion to correct completely mitral regurgitation. The development of such prostheses has been a long process, still on the making. During the initial stages of the procedure, the transapical approach was preferred. On the other hand, the transseptal approach, which has already been used in some patients, is the proper development path for this transcatheter technique. Many valvular prostheses have been produced, each using a different mechanism for secure anchoring and elimination of regurgitation. Early mortality for this procedure, although decreasing since the preliminary studies, is still high, not only because the technology is still in its initial phase but also for the very high risk of the patients treated. It is foreseeable, though, that in the near future, as the technology and patients selection improves, better results will follow.

Introduction

Mitral valve insufficiency is the second most common valvular disease seen in the adult population. Traditional cardiac surgery still represents the ideal treatment for patients with severe mitral valve insufficiency. However, up to 50% of patients with severe mitral regurgitation are not operated on because they are considered to be at too high a surgical risk due to advanced age, left ventricular dysfunction, and comorbidity. A significant proportion of these patients is affected with severe functional mitral incompetence, a condition in which, unlike the primitive form, no surgical technique to date has had a positive impact on survival.²

In recent years, many tools have emerged for the treatment of percutaneous mitral insufficiency. These devices aim to repair the mitral valve by acting on the leaflets, the annulus, the cords (percutaneous implant of neo-cords), or on the ventricle (percutaneous remodelling systems of the

left ventricle). To date, the MitraClip system, based on the 'edge-to-edge' or Alfieri repair principle, represents the most widely used transcatheter mitral treatment in the world, with more than 55 000 patients treated.

Transcatheter mitral repair systems, however, have important limitations, including reduced efficacy in terms of long-term durability,³ and poor applicability in the case of unfavourable anatomical conditions,⁴ such as the presence of particularly complex lesions, advanced damage of valve leaflets, or excessive ventricular remodelling. Not to be neglected is the fact that these methods are not easy to perform with a modest reproducibility.

The implantation of valve prostheses by percutaneous route could allow these limits to be overcome. The first transcatheter mitral valve implantation was performed in 2012,⁵ and since then the number of cases has seen a slow but steady growth.

Patient selection

To date, the percutaneous implantation of mitral valve prostheses is reserved for patients with severe mitral valve

*Corresponding author. Email: colombo@emocolumbus.it

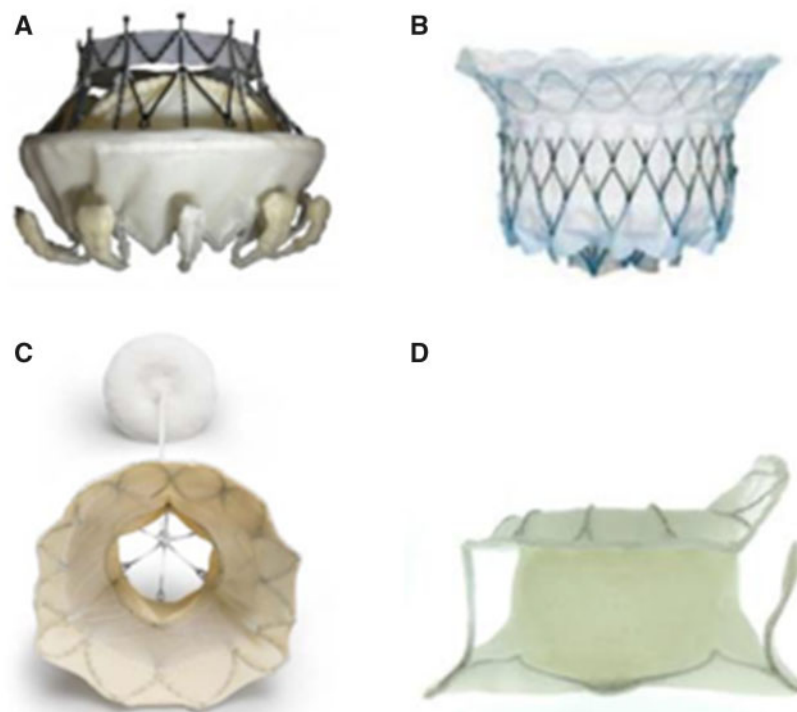


Figure 1 Main percutaneous mitral valves.

disease, symptomatic despite optimal medical therapy, in the absence of other therapeutic options and with specific anatomical characteristics.

From the clinical point of view, the selected patients are at very high operative risk or considered inoperable. Many of these valves were initially implanted in a ‘compassionate use’ regime.

From the anatomical point of view, patient selection requires meticulous computed tomography studies.⁶ The main characteristics that are evaluated are the morphology and size of the mitral annulus, the position and extent of calcifications in the mitral ring, the anatomy of the implant area (the area in which the mitral prosthesis is released), the subvalvular mitral apparatus (position and number of papillary muscles), the size and shape of the ventricle and the left atrium, the mitro-aortic angle [to assess the risk of obstruction of the left ventricular outflow tract (LVOT)], relationships with neighbouring structures (circumflex artery and coronary sinus), and the type of access (transapical and transfemoral). Furthermore, a simulation of the procedure is usually carried out to predict the final result and the possible complications.

Valves with experiences in clinical area

In recent years, several implantable mitral valve devices have been developed. Some of them are still in the pre-clinical phase, while others are being studied in humans.

Regardless of the type of valve used, all procedures are performed under fluoroscopic guidance and transoesophageal echocardiography. Generally, the implant consists in a

Table 1 Thirty days results of the main endovascular mitral valve prostheses

	CardiaQ (transseptal)	Intrepid	Tendyne	Tiara
Patients number	12	50	100	58
Procedural success	75%	96%	97%	95%
Mortality	17%	14%	6%	10.3%

^aReformatted data (PCR London Valve Meeting, September 2018, London, UK).

stent expanding through the native valve, anchoring it to the native valve and releasing it. All available valves are self-expanding and recoverable up to certain steps in the procedure.

Among the most important valves that have already reported a clinical experience, we recall:

- Edwards CardiAQ (Figure 1A): the first percutaneous mitral valve implanted in humans. It presents a dual anchoring mechanism, to the leaflets and the subvalvular apparatus and is implantable both transapically and transfemoral.⁷ To date, 12 patients have already been treated with a transfemoral approach, with encouraging results (Table 1).
- Medtronic Intrepid (Figure 1B): this valve has two stents, one external that anchors the apparatus to the annulus and one inside where is allocated the valve.

This valve is implantable only by transapical route, but the version that can be positioned by means of a transseptal approach is under development. To date, ~50 cases have been performed, with a high procedural success rate (96%) and an acceptable 30-day survival (86%).⁸ The ongoing randomized APOLLO study (NCT03242642) will evaluate safety and the effectiveness of this valve in patients with severe mitral valve incompetence (both functional and degenerative) at high operative risk, compared to traditional mitral valve replacement surgery.

- Abbott Tendyne (*Figure 1C*): it is also implantable only by transapical route.⁹ It consists of a double frame in nitinol and a transventricular cable that still holds the valve at the apex of the ventricle. So far more than 100 cases have been performed, with excellent results in terms of safety (6% mortality at 30 days). A randomized trial comparing surgery (SUMMIT) is also underway for this valve.
- Neovasc Tiara (*Figure 1D*): the peculiarity of this valve is the characteristic 'D' shape that conforms to the physiological mitral anatomy.¹⁰ It is currently implantable only by transapical route.
- Caisson: consists of an anchor that has three atrial anchoring rings, four anchoring feet for subannular anchorage, and the actual valve that has a particular D shape. So far 17 patients have been successfully implanted.
- HighLife: based on the 'valve-in-ring' principle. The implant consists of two steps: the first consists in surrounding the mitral leaflets at the subvalvular level with a guide on which a ring is passed which is closed on itself; the second step is to install the valve inside it. It can be implanted either transapically or transseptally. To date, 15 patients have been treated.
- Cardiovalve: this valve has a design very similar to surgical valves. It is implantable by a transseptal route (introducer 28 F). To date, five patients have been treated with promising results (absence of regurgitation, low gradients, and low procedural times). The pilot feasibility study (AHEAD) is currently underway, which will recruit 30 patients.
- Edwards Sapien M3: represents an adaptation of the Sapien 3 valve, used for the percutaneous treatment of aortic valve stenosis. It is a transseptal implantable valve, consisting of a device that is anchored to the valve ring, inside of which the valve is released. So far 10 cases have been carried out, with encouraging results (no patient died within 30 days).

Valves in pre-clinical phase

- Accufit: once it expands inside the mitral ring, the Accufit shortens by plicating and trapping the mitral leaflets between special ventricular and atrial structures, maximizing anchoring and minimizing valve insufficiency and the risk of obstruction of the outflow tract of the left ventricle.
- Saturn: consists of two elements, an annular structure, in contact with the mitral annulus, and a central

valve. The transapical approach has already been validated in animal models, while the transseptal version is still under development.

- Cephoea: it has a self-expanding double disc structure, of modular type, which allows the adaptation of the valve to different mitral anatomies. The first plants on humans are expected by the end of 2018.

Preliminary results

Despite the innumerable advantages provided by a mitral valve, we cannot but consider some problems: (i) the atrial obstruction can favour the thrombosis of the valve, (ii) in patients with an unfavourable mitro-aortic angle or with marked hypertrophy of the interventricular septum, there is a significant risk for obstruction of the LVOT. Especially in the initial experiences, there were also problems with anchoring the valve with consequent instability.

However, it is to be hoped that these complications will diminish in the future thanks to technological development and better patient selection.

Also, in terms of mortality, there has been a marked improvement going from rates that reached 50% in the preliminary studies, to a mortality oscillating between 6% and 17% in the most recent experiences.

Peculiar aspects of the percutaneous mitral substitution

Percutaneous mitral valve replacement presents some intrinsic difficulties.

In the first instance, the mitral ring is not usually calcific and has a D-shape, characteristics that make the anchorage of the valve more problematic. Furthermore, unlike the transcatheter aortic valve implantation, which benefits from aortic valve calcifications, in percutaneous mitral replacement, the presence of an excessive amount of calcium not only makes ultrasound visualization more difficult but can also compromise adequate anchorage of the valve determining residual valve insufficiency. The solutions developed in order to offer adequate anchoring of percutaneous mitral prostheses are manifold, from the presence of ventricular anchors applied to the native valve leaflets, to the implantation of a ring or an anchoring system inside which the valve is released.

As far as access is concerned, to date the transapical approach, although it may be burdened with a greater risk of bleeding and damage to the heart muscle compared to the transseptal one, is still the most used access route. This is due in part to the possibility of establishing greater coaxiality with the mitral ring and the possibility of using introducers, which are large enough for the implantation of a valve much larger than the aortic valve. In the last year, the cases carried out by a transseptal approach have grown more and more with encouraging results, so it can be hypothesized that with the improvement of the technology (valves of smaller dimensions and with a better profile, more manoeuvrable catheters) this will be the preferred access route.

Repair vs. replacement

Percutaneous mitral valve replacement undoubtedly offers some advantages over repair techniques:

In theory it:

- it is more versatile, allowing treatment of even more complex anatomies;
- it is more efficient, allowing in most cases a complete abolition of mitral regurgitation;
- it is technically less complex, more reproducible and faster; and
- does not preclude a future procedure of valve-in-valve in case of degeneration of the prosthesis.

However:

- has a risk of recurrence of mitral regurgitation due to mechanical detachment and endocarditis;
- has a higher thrombo-embolic risk; and
- it could have a negative impact on the systolic function of the left ventricle, especially in patients with extreme ventricular dysfunction at baseline.

To date, however, no direct comparison data are available between transcatheter repair techniques and percutaneous mitral valve replacement, so the debate on which is the best strategy remains open.¹¹

Conclusions

In recent years, alongside transcatheter repair techniques, there has been a significant development in the field of percutaneous implantation of mitral valve prostheses. The results available so far are promising in terms of feasibility of the procedure and short-term efficacy (abolition of mitral regurgitation and low gradients), but the mortality of this type of operation with some valves implanted via the transseptal route remains high also because of the extreme-risk profile of treated patients.

In the near future, with the technological development and a more adequate selection of patients, an improvement of these results is foreseeable.

We must keep in mind that at this time the clinical applicability of these procedures remains limited and transcatheter repair systems prevail.

Conflict of interest: none declared.

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