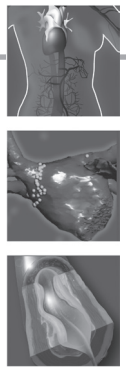

# Transcatheter mitral valve-in-valve procedures: an ongoing successful journey with unproven long-term benefit

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"*Currently, the common understanding is that it is of decisive importance to prevent the implantation of a valve that is too large into the rigid ring of a surgical bioprosthesis.*"

**KEYWORDS: hemodynamics ■ outcome ■ transcatheter mitral valve-in-valve implantation**



Mitral valvular heart disease increases sharply with age as a consequence of the predominance of degenerative valvular diseases, as well as being secondary to an increase in congestive heart failure. Nevertheless, owing to the rise in patients' life expectancy, redo valve surgery is increasingly necessary and owing to technical aspects [1] or poor clinical conditions [2], it is associated with increased operative mortalities. Extensive coverage by neoendocardium or calcification is frequently present, making reoperation sometimes extremely difficult. Sometimes irreparable damage, one of the greatest nightmares of a cardiac surgeon, may also occur [1]. Moreover, the remaining annulus, after decalcification and valvectomy, can be become very weak and paravalvular leaks do frequently ensue [3]. Thus, the avoidance of the removal of the malfunctioning bioprosthesis significantly decreases the surgical burden in these patients. Interestingly, excising only the leaflets of the damaged bioprosthesis and, thus, leaving the old ring *in situ* has already been proposed by surgeons approximately 20 years ago [1,4]. Given the frequency of comorbidities and the high risk of surgery in these elderly patients, a sharp rise in catheter-based techniques has emerged over the past 5 years.

"*Especially in the presence of comorbidities, the risk of morbidity and mortality during reoperation increases exponentially.*"

As mentioned above, the operative risk for reoperation of degenerated bioprosthetic valves or failing mitral-valve annuloplasty rings is much higher compared with the risk of the index isolated native valve repair or replacement. Especially in the presence of comorbidities, the risk of morbidity and mortality during reoperation increases exponentially. Thus, new catheter-based techniques are potentially attractive in many patients with a high risk or even a contraindication for surgery. Owing to the successful introduction of the concept to place a balloon-expandable valve into a degenerated aortic [5–9] or mitral xenograft [10–20], some investigators have even performed small series in aortic, as well as mitral, positions [Schäfer *et al.* Balloon-expandable valves for degenerated mitral xenografts or failing surgical rings (2013), Submitted] [21–23]. Besides the fact that the valve-in-valve approach is still considered as an off-label use intervention, transcatheter valve implantation has also been successfully performed into surgical rings after failing mitral valve annuloplasty [Schäfer *et al.* Balloon-expandable valves for degenerated mitral xenografts or failing surgical rings (2013), Submitted] [24,25]. With regards to failing xenografts in the mitral position, mainly transapical implantations of Edwards SAPIEN™ valves (Edwards Lifesciences Inc., CA, USA) have been reported in the literature [10–12,14,26].

Interestingly, the transcatheter mitral valve-in-valve implantation (TMViVI) concept was first demonstrated in a sheep model by Walther and colleagues, and the authors proposed a transatrial approach to the mitral valve [13]. The largest updated series of TMViVI comprises 11 patients (the initial series comprised seven patients [27]; n = 3 Edwards SAV 27 mm; n = 1 Edwards SAV 29 mm; n = 1 Medtronic Mosaic 27 mm; n = 1 Medtronic Intact 25 mm; and n = 1 Baxter Edwards 25 mm) was reported by Webb and colleagues [26]. In the first two patients, Webb and colleagues used a trans-septal approach, or a direct transatrial approach. Both attempts were unsuccessful because of the inability to align the valve coaxially within the prosthetic valve. The

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first patient died within 24 h of conversion to open heart surgery and the second patient, who was subsequently treated transapically, died on day 45. As a result, all subsequent implantations were performed transapically with excellent outcomes in this particular center. In their series, TMViVI was associated with a reduction in mean gradient from 12.9 to 8.0 mmHg and an increase in area from 0.7 to 1.7 $cm^2$. Recently, Cerillo and colleagues reported a series of three patients with failing mitral bioprosthesis (all CE PERIMOUNT 25 mm), treated only by transapical valve-in-valve implantation (Edwards SAPIEN valve 26 mm) [12]. Due to migration of the SAPIEN valve into the left ventricular outflow tract with subsequent severe subaortic obstruction, the first patient had to be converted to open-heart surgery; however, the patient died of multiorgan failure within 24 h. Currently, the common understanding is that it is of decisive importance to prevent the implantation of a valve that is too large into the rigid ring of a surgical bioprosthesis. An underexpanded SAPIEN valve within a small surgical prosthesis will definitely function suboptimally with an increased transvalvular gradient, impaired leaflet coaptation, reduced durability, or may even embolize during implantation (as described above). Despite these suboptimal initial results with TMViVI (in-hospital mortality 28.6% [27] and 33.3% [12]), transapical TMViVI has been repeatedly proposed to offer an alternative, safer approach for high-risk redo surgical patients. Indeed, within the updated largest published series of these 11 patients by Webb and coworkers, all patients had successfully been treated by transapical TMViVI with no 30-day mortality [26]. The improved results may have been related to the fact that less frail patients were treated in the subsequent series [12,26], and this assumption may be supported by the fact that the initial procedural-related fatalities occurred in patients with rather high logistic EUROscores (31.2 and 37.3% [27], as well as 81.5% [12]). This is in line with the observation that a logistic EUROscore >30% has been reported to be the single most important predictor of death after transapical transcatheter aortic valve implantation [28]. In our series comprising 11 patients (four trans-septal and seven transapical; logistic EUROscore: 11.1–93.7%), we did not observe a single fatality, irrespective of the fact that six out of ten patients had a logistic EUROscore >30% [Schäfer *et al.* Balloon-expandable valves for degenerated mitral xenografts or failing surgical rings (2013), Submitted]. In addition, as frequently hypothesized by surgeons, we did not see any significant pressure gradient across the aortic valve or along the left ventricular outflow tract after TMViVI, again demonstrating the feasibility of TMViVI without hemodynamic compromise to the left ventricular outflow tract.

Meanwhile, by contrast to the preferentially proposed transapical technique for TMViV, several investigators (including our group) have successfully performed an antegrade trans-septal approach [15–17,29–31]. This has been done despite the fact that Webb and colleagues had deemed the trans-septal approach or even the direct transatrial approach as unfavorable. The most frequent reasons for rejecting the transapical approach in ours and in others series were anatomical considerations, such as very large mammaries or excessive scars of the skin after sternotomy, and clinical considerations (i.e., to spare the patient from intubation and ventilation if the patient has severe pulmonary lung disease). Moreover, in a quick search of the literature, at least 12 cases with a false left ventricular apical aneurysm as a late complication after transapical aortic valve replacement were found [12,32,33]. Thus, due to these unfavorable facts associated with the transapical approach, and the clinical need for a less invasive procedure, we and others have been intrigued to use the trans-septal approach, despite the discouraging reports with this approach [27]. Despite the greater trauma of the transapical approach, its advantage over the transvenous and trans-septal method is the direct access to the failing mitral bioprothesis or annuloplasty ring with a very short distance and immediate steering possibilities. One of the disadvantages of the transapical approach might be the fact that the bioprosthesis needs to be crossed in a retrograde fashion, possibly leading to more extensive damage of the surgical bioprosthesis with a higher likelihood of a hemodynamic compromise. Conversely, with the trans-septal approach, valve crossing can be done in an antegrade fashion and, thus, has a lower risk of damaging the bioprosthesis. Nevertheless, crossing the septum during TMViVI might be a hurdle, especially if performed via the transjugular route [16], favoring the establishment of an arterial-venous wire-loop that allows for push and pull manipulations [15–17]. So far, valve-in-ring implantations have been mainly done with the transapical approach, but the trans-septal approach has also recently been successfully performed [25]. It might be worth noting that valve-in-ring implantations should only be done in full circular annuloplasty

rings, or in rings without any sign of a weakened suture. If a para-annular leak is present, valve-in-ring implantation should be avoided, since tearing out of the mitral annuloplasty-ring may ensue.

> *"...TMViVI might be considered in all patients for the future, if the risk for repeated heart surgery is deemed as high."*

In general, orientation with either the transapical or the trans-septal approach can mainly be derived from the radiopaque struts of the bioprosthesis/ring. With any approach, perfect results with almost complete abolishment of any regurgitation and very acceptable transvalvular gradients, can be achieved. In fact, hemodynamics does not reveal any significant increase in transmitral pressure gradients. The latter is largely explained by the very low profile of these catheter heart valves, if proper size matching of the inner diameter of the xenograft to the SAPIEN valve is performed, thereby, preventing central leakage or significant intravalvular obstruction with high residual gradients.

## Conclusion & future perspective

In general, most reports demonstrated the feasibility and safety of TMViVI for the treatment of a degenerated mitral bioprosthesis or recurrent mitral regurgitation after surgical ring implantation using a balloon-expandable valve. With TMViVI, complete resolution of mitral regurgitation can be achieved in the vast majority of patients, indicating complete expansion of the frame within the degenerated xenografts. Despite initial fatalities with TMViV that may be attributed to a learning-curve (as with any invention in medicine), it is important to note, that especially with the trans-septal approach, a more sophisticated planning and practical knowledge is needed. The initial complicated experience with the trans-septal approach has recently been turned back to similar success rates if compared for the transapical approach. Thus, any of these approaches can be used in a balanced manner to tailor the best approach to the patients' individual needs. Despite the fact that general anesthesia was used in most of these reports, it might be substituted for analgo-sedation if a transvenous and trans-septal approach is used and transesophageal echocardiography is omitted. Hence, TMViVI might be considered in all patients for the future, if the risk for repeated heart surgery is deemed as high. However, in light of these new perspectives for the treatment of patients at high surgical risk, these techniques need to definitely be investigated in terms of safety and long-term efficacy in the future. Nevertheless, with increasing knowledge of the best suitable approach, transcatheter valve-in-valve or valve-in-ring implantation might become a valuable therapy option, subsequently leading to a fundamental change in the choice of valves and rings for treatment of mitral valvular disease during index surgery.

### Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

*No writing assistance was utilized in the production of this manuscript.*



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