EuroIntervention
2024;20:e271-e273
published online e-edition March 2024
DOI: 10.4244/EIJ-E-24-00002

EDITORIAL

Catheter-based versus surgical mitral valve intervention: choosing between the red pill and the blue pill

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-E-24-00002

Transcatheter mitral valve (MV) implantation (TMVI) for the treatment of severe mitral regurgitation (MR) has attracted increased interest in recent years. Several dedicated devices are being developed and trialled despite facing technical challenges due to the anatomical complexity of the MV and its proximity to other cardiac structures. Screening failure has been reported to be close to 60% in a study assessing 11 different TMVI devices[1]. Furthermore, the appropriate use of TMVI is yet to be established, and many available devices have a paucity of data to support their use **(Supplementary Table 1)**.

The transapical, tether-based Tendyne Mitral Valve System (Abbott) has emerged as a forerunner in the TMVI field. The 30-day, 1- and 2-year outcomes of 100 high surgical risk patients have been reported in a single-arm global feasibility study, showing a technical success rate (<1+ MR at 30 days) of 96% with sustained results at 1 and 2 years, while also reducing hospitalisations for heart failure[2,3]. These results in a high-risk population prompted the approval of the Tendyne device for commercial use in Europe (European conformity [CE] mark, 2020) for individuals with clinically significant MR and who were deemed ineligible for surgical mitral valve replacement (SMVR). This approval led to the establishment of the TENDyne European expeRience registry (TENDER)[4], whose data for 30-day outcomes align with the initial global study[2,3].

In this edition of EuroIntervention, Ziegelmueller and colleagues[5] aim to compare the 30-day outcomes of elderly patients at intermediate surgical risk undergoing either TMVI with Tendyne or SMVR. Among 1,278 SMVR performed between 2000 and 2022, a total of 454 SMVR patients were eligible for a 2:1 propensity score-matched (PSM) study of 80 SMVR and 40 Tendyne individuals. The median age of the population was 78 years, and 60% were female, with median Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) scores of 4.05 and 5.20 for SMVR and Tendyne, respectively (p=0.08). Technical success, where MR was essentially eliminated, was achieved in 97.5% of patients and was similar in both groups. However, device success (82.5% vs 57.5%; p=0.04), and procedural success (75.0% vs 52.5%; p=0.07) "favoured" TMVI compared to SMVR. No differences in 30-day mortality, major bleeding, stroke, or requirement for dialysis were noted.

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The authors should be commended for attempting this complex and courageous comparison; however, further data are needed to truly assess the role of TMVI versus SMVR rather than Tendyne on its own. Several observations must be highlighted to help interpret the current study. First, STS-PROM score calculations were partially conducted after matching and for the matched cohorts only. Second, the populations under comparison were heterogeneous, even after matching. Among others, there were differences regarding the aetiology of MR (primary MR: 69.0% and 45.0%, secondary MR: 2.5% and 17.5%, mixed aetiology: 22.5% and 27.5%; p=0.01), the prevalence of coronary artery disease (32.5% and 67.5%; p<0.001) and previous PCI (25.0% and 47.5%; p=0.023) for SMVR and Tendyne, respectively. Furthermore, 30% of SMVR patients underwent concomitant tricuspid valve repair, and two Tendyne patients received concomitant transcatheter aortic valve implantation (TAVI). These differences may be expected and are indeed difficult to match given that the current paradigm would suggest TMVI use only in those individuals who are unsuitable for SMVR or even transcatheter edge-to-edge

repair (TEER). Moreover, while the TMVI patients represent a contemporary population, to obtain the actual PSM populations, the SMVR patients are from a 22-year period in the large German Heart Center Munich registry experience; this long period, during which surgical techniques and postoperative care certainly progressed, again potentially affected outcomes.

The main results of this study are not unexpected when comparing SMVR to minimally invasive catheter-based procedures, given the nature of the TMVI prosthesis. Greater device success in the TMVI arm was driven mainly because SMVR patients experienced a greater proportion of unplanned surgical re-intervention. One may wonder if this need for re-intervention was secondary to bleeding, which is often encountered in surgical patients and particularly on long pump runs versus the very unlikely scenario of SMVR "device-related" issues. In addition, higher residual transvalvular gradients were observed in the SMVR group; again, comparing valve haemodynamics between stented and stentless bioprotheses is like comparing apples to oranges, even more so considering the slender self-expanding engineering of the Tendyne TMVI compared with standard SMVR bioprostheses. Along these lines, greater procedural success in the TMVI group was also predominantly driven by a larger number of periprocedural events occurring in the SMVR group, such as postoperative hypotension requiring vasopressors, prolonged intubation, etc. It should be noted that the authors reported outcomes using the Mitral Valve Academic Research Consortium (MVARC) criteria[6], which may have been the only sensible option considering TMVI as a comparator. Nonetheless, as stated by the authors, MVARC is meant to standardise definitions for outcome reporting of TMVI/TEER studies rather than for SMVR; hence, its applicability remains grossly uncertain, and perhaps this paper has correctly exposed this important matter.

The results of this study are therefore relevant and interesting in many aspects; however, they are insufficient to challenge current clinical practice. Indeed, comparing TMVI and SMVR may perhaps be a little too premature, particularly in an intermediate surgical risk group. Many unanswered questions remain, particularly regarding valve durability with TMVI devices – a question that has not yet been answered by the current literature which only extends to 2 years of reporting on the trajectory of MR and gradients in 44 and 32 patients, respectively[3].

Furthermore, a sizeable rate of major adverse events was reported in the initial studies, including bleeding complications and device-specific events, such as valve thrombosis, endocarditis, migration or dislodgement, paravalvular leaks leading to haemolysis, and valve reintervention, most of which occurred within the first months after TMVI[2-4,7-10]. In fact, valve thrombosis was a major concern and has led to some of the TMVI devices being put on hold[9]. Paravalvular leaks during follow-up are also a major concern and relate to the mechanism of fixation and anchoring of the Tendyne. Therefore, one would expect that upon left ventricular remodelling or apical fatigue, leakage and valve dislodgement may become clinically meaningful during follow-up, thereby making it necessary to retension the tether or upsize the apical pad of the Tendyne device[10].

In summary, the trajectory of catheter-based MV technologies is promising; however, a head-to-head comparison with SMVR in a randomised controlled trial setting would be desirable. Nonetheless, based upon the difficulties mentioned above in the screening of these patients, mainly because of anatomical suitability and multiple devices with different intrinsic technical features, such a trial may be difficult to undertake. Paraphrasing Morpheus in The Matrix, "There is a difference between knowing the path and walking the path." The present study adds to the growing evidence on the use of TMVI with Tendyne but also puts the "blue pill" into context – we do not want the story to end, since there are a substantial proportion of individuals who are ineligible for TMVI, so SMVR should remain the preferred option in this instance. Rather, we face the reality of a complex subject matter exposed by the "red pill" and our willingness to change. A long walk on the path of catheter-based treatment of MV disease has started with the "red pill", and only time will tell if this is the right path, though this must be through critical thinking and science.

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Conflict of interest statement

R. Bagur is a consultant for Medtronic. A. McInerney has no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Studies reporting data on transcatheter mitral valves.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-E-24-00002

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Supplementary Table 1. Studies reporting data on transcatheter mitral valves.

Device	Description	Valve anchoring	Prevention of PVL	Vascular access site	Delivery system	Recapture / Reposition	Valve sizes	Current data
Tendyne Abbott Vascular	Inner frame: trileaflet bovine pericardial valve Outer frame: conforms to MV annulus. Frames connected with a PET cuff.	• Apical epicardial pad	Tensioning of the tether to the apex	Transapical	34-36 Fr	Yes	Low profile: EOA 2.2cm^2 Standard profile: EOA 3.0cm^2 Outer stent perimeter ranges from 119-156mm	**Global Feasibility**[2,3] n=100 Technical success 96% <1+ MR at 30-day PVL more than trace 30-day 10% 98.8% (n=84), at 1-year 98.4% (n=62) and 2-year 93.2% (n=44) 30-day mortality 6% 1-year mortality 26% 1-year heart failure hospitalisation 32.1% Valve reintervention 1-year, 4 patients 2-year mortality 39% 2-year heart failure hospitalisation 38.8% Valve reintervention 2-year, 5 patients **The TENDyne European expeRience registry (TENDER)**[4] n=108 Technical success 96% <1+ MR at 30-day 96% (n=74) PVL more than trace 30-day 10% 30-day mortality 12%

								30-day heart failure hospitalisation 13%
Intrepid[7] Medtronic	Inner stent housing the trileaflet bovine pericardial valve. Outer stent forms a fixation ring.	• Oversizing • Radial force • Three rows of frictional elements engage the native annulus	PET covering	Transapical Transeptal	35 Fr	Yes	Inner valve: 27mm Outer stent 42 and 48mm	n=33 Major vascular complications 24.2% <1+ MR at 30-day 90% and at 1-year 96% (n=23) 30-day mortality 0% 1-year mortality 6.7% 1-year cardiovascular hospitalisation 22.3%
HighLife[8] High-life Medical	Two components: Sub-annular implant (SAI) delivered transfemorally encircles the native mitral valve leaflets and subval-vular apparatus. 28 mm trileaflet bovine pericardial valve delivered transeptally and implanted into the SAI	• Radial force • Sub-annular ring	Native leaflets and SAI	Transeptal and Transfemoral	TS 30 Fr TF 18 Fr	No	28mm	n=30 Technical success 90% <1+ MR at 30-day 88% and at 1-year 78% (n=23) 1-year mortality 17% 1-year heart failure hospitalisation 23%
CardioValve[11] Cardiovalve	Atrial and ventricular frames containing a trileaflet bovine pericardium valve	• Grasping legs on ventricular frame and anchor to annulus • Radial force	Atrial flange	Transeptal	30 Fr	Partially	Three sizes from 40-50mm	n=5 Technical success 100% <1+ MR at 30-day 80%
Tiara[12] Neovasc	Self-expanding nitinol stent with a trileaflet bovine pericardial valve. Saddle-shape conforms to annulus.	• Radial force • Three ventricular tabs on native MV annulus	Atrial skirt	Transapical	32-36 Fr	Yes	35mm, 40mm	n=71 Procedural success 94% <1+ MR at 30-day 85% 30-day mortality 11.3%
SAPIEN M3[13] Edwards Lifesciences	Two components: Sub-valvular nitinol dock which encases the valve and sub-valvular apparatus	• Radial force • Sub-valvular dock	PET skirt	Transeptal	20 Fr	Partially: sub-valvular dock is retrievable	29mm	n=10 Technical success 90% <1+ MR at 30-day 89% 30-day mortality 0%

	Balloon expandable trileaflet SAPIEN valve implanted into sub-valvular dock							
EVOQUE[14] Edwards Lifesciences	Self-expanding nitinol frame with a trileaflet bovine pericardial valve	• Ventricular anchors capture MV leaflets and sub-valvular apparatus. • Radial force	Fabric skirt	Transeptal	28 Fr	No	44, 48 mm	n=14 Technical success 92.9% <1+ MR at 30-day 83% 30-day mortality 7.1%
Cephea[15] Abbott	Atrial and ventricular disks with a central column which houses a trileaflet bovine pericardium valve	• Mitral annulus • Radial force	Atrial disk	Transeptal	38 Fr	Yes	32, 36, 40mm	n=3 Technical success 100% <1+ MR at 30-day 100% 30-day mortality 0%
AltaValve[16] 4C Medical Technologies	Supra-annular device A 27mm trileaflet bovine pericardial valve is located above an annular ring and housed in a nitinol sphere.	• Oversizing • Atrial fixation • Radial force at annular ring	PET skirt	Transapical Transeptal	32 Fr	Yes	27mm valve Annular ring: 40, 46, 54mm Spherical nitinol frame 50-90mm	n=3 Technical success 100% 30-days “good valve function”

Fr: French, PVL: Paravalvular leak, PET: Polyethylene terephthalate, EOA: effective orifice area. MR: mitral regurgitation.